BMJ Open

# The Diffusion of Indirect Comparison Meta-Analytic Methods to Study Drugs: Systematic Review and Co-Authorship Network Analysis



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-019110 |
| Article Type: | Research |
| Date Submitted by the Author: | 11-Aug-2017 |
| Complete List of Authors: | Ban, Joann; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Tadrous, Mina; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Lu, Amy; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Cicinelli, Erin; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Cadarette, Suzanne; University of Toronto, Leslie Dan Faculty of Pharmacy |
| Primary Subject Heading: | Research methods |
| Secondary Subject Heading: | Communication |
| Keywords: | Diffusion of innovations, Indirect comparisons, Methodological innovation, Network meta-analysis, Social networks |



Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.

Supplemental Material 1.avi
Supplemental Material 2.avi

# The Diffusion of Indirect Comparison Meta-Analytic Methods to Study Drugs: Systematic Review and Co-Authorship Network Analysis

Joann K. Ban,[1] Mina Tadrous,[1] Amy X. Lu, [1] Erin A. Cicinelli,[1] Suzanne M. Cadarette[1]

[1]Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

**Correspondence to:** Mina Tadrous, Leslie L. Dan Pharmacy Building, University of Toronto, 144 College Street, Toronto, Ontario, M5S 3M2 Canada. Tel: 416-864-6060, E-mail: mina.tadrous@mail.utoronto.ca

**Conflict of Interest:** None related to this work.

**Word Count:** 3387 (MAX 4,000 WORDS)

**Subject Heading:** Research methods (primary), Communication (secondary)

**Keywords:** Diffusion of Innovations, Indirect Comparisons, Methodological Innovation, Network Meta-Analysis, Social Networks

## ABSTRACT

**Objective:** To characterize the diffusion of indirect comparison meta-analytic methods in the study of drugs.

**Design:** Systematic literature review with co-authorship networks.

**Data sources:** Cochrane Database of Systematic Reviews, EMBASE, MEDLINE, Scopus, and Web of Science.

**Study selection:** English language papers that used indirect comparison meta-analytic methods to study the efficacy or safety of three or more interventions, where at least one was a drug.

**Data extraction:** The number of publications and authors were plotted by year and type: methodological contribution, review, or empirical application. Author and methodological details were summarized for empirical applications, and animated co-authorship networks were created to visualize contributors by country and affiliation type (academia, industry, government, or other) over time.

**Results:** We identified 477 papers (74 methodological contributions, 42 reviews, and 361 empirical applications) by 1,689 distinct authors from 1997 to 2013. Prior to 2002, only three applications were published, with contributions from the United States (n=2) and Canada (n=1). The number of applications gradually increased annually with rapid uptake between 2011 and 2013 (n=254, 71%). Early diffusion occurred primarily in Europe with the first application credited to the United Kingdom in 2003. Application spread to other European countries in 2005, supported by regulatory requirements for drug approval. By the end of 2013, contributions included 49% credited to Europe (22% United Kingdom, 27% other), 37% credited to North America (11% Canada, 26% United States), and 14% from other regions.

**Conclusion:** Indirect comparison meta-analytic methods are an important innovation for health-research. Although Canada and the United States were the first to apply these methods, Europe led the diffusion. The increase in uptake of indirect comparison meta-analytic methods has likely been facilitated by acceptance of these methods by regulatory agencies, which are calling for more comparative drug effect data to assist in drug accessibility and reimbursement decisions.

**Abstract word count:** 300 (MAX 300 WORDS)

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our study includes English language papers that used indirect comparison meta-analytic methods published in peer-reviewed journals indexed in the Cochrane Database of Systematic Reviews, EMBASE, MEDLINE, Scopus, and Web of Science through to December 2013. We did not consider methodological and reporting quality of eligible empirical applications.
- We summarize the history of indirect comparison meta-analytic methods and examine author contributions by country and affiliation type (academia, industry, government, and other) to visualize uptake over time.
- We characterize and examined the impact of social systems on the diffusion of indirect comparison meta-analytic methods over time.

## INTRODUCTION

Randomized controlled trials (RCT) are essential for bringing novel pharmaceutical products to market. RCTs for drug approval typically compare new treatment efficacy to placebo and provide safety data for only common adverse effects. However, RCTs are often not powered to identify all important drug efficacy and safety endpoints and thus meta-analytic methods were developed. Meta-analysis is a statistical method that combines the results of two or more studies to evaluate the same intervention in comparison to a control such as placebo, to obtain a more precise estimate of the intervention's effects relative to that control [1-3]. The term *meta-analysis* was first coined by G. V. Glass in 1976, yet use of statistical methods to combine the results of multiple studies dates back to the early part of the 20$^{th}$ century, with early methodological techniques proposed by R. Fisher and W. Cochran in the 1930s [1, 2].

When completed using high quality RCTs, meta-analyses are regarded as providing the highest level of evidence [4]. However, traditional pairwise meta-analysis is limited by only being able to combine and estimate the benefits or harms of two treatments if they have been compared directly. In addition, meta-analysis cannot compare more than two treatments at a time [3, 5]. This presents a challenge to policy-makers, clinicians, and patients who often need to select the most optimal treatment from several competing options [6]. Indirect comparisons have been made informally using point estimates and 95% confidence intervals of treatments [7]. However, this informal approach does not provide a precise estimate of the relative difference between two treatments because the relative effects are not measured.

In 1997, the *adjusted indirect comparison* method was proposed by H. C. Bucher, as an innovative meta-analytic approach that utilizes indirect evidence to estimate the relative benefits and risks between two treatments [8]. Unlike traditional pairwise meta-analysis, adjusted indirect

comparisons estimate the relative effects of two treatments that have not been compared directly by leveraging results from each treatment that has been compared to a common comparator, such as a placebo [6, 8, 9]. However, the adjusted indirect comparison method ignores direct evidence, even when available. In 2002, *network meta-analysis* was proposed as an extension of the adjusted indirect comparison method that combines direct and indirect comparative data across several sets of pairwise treatment comparisons [5, 10]. The combination of direct and indirect data yields more precise effect estimates [6]. A similar method, coined *mixed treatment comparison*, was proposed in 2004 [11], and the term *multiple treatment meta-analysis* was also introduced to describe concepts of combining both direct and indirect evidence in 2005 [5], **Table 1**.

Indirect comparison meta-analytic methods have become valuable tools in clinical and policy decision making, and have thus, been rapidly adopted since their introduction [7, 12-14]. However, application of these methodological innovations varies widely [6, 12, 15]. We set out to characterize the diffusion of indirect comparison meta-analytic methods used to study drugs with emphasis on how the social system may have influenced the diffusion of these methods over time.

## MATERIALS AND METHODS

We recently examined the diffusion of two confounder summary score methods and illustrate the importance of innovation attributes (**relative advantage, compatibility, simplicity, trialability,** and **observability**) and seminal author engagement on the uptake of methodological innovations using Rogers' Diffusion of Innovations Model [16]. In addition to innovation attributes, Rogers' Model identifies key aspects of the social system that may impact the rate of adoption [17]. In particular, a methodological innovation will have a quicker rate of adoption if members within the social system (e.g., researchers, clinicians, and policymakers) share similar system norms. For example, regulatory agencies make decisions for drug approval and formulary coverage. Regulatory agencies are therefore well-positioned to influence the uptake of methodological innovations that support the drug approval process. If these methodological innovations become a requirement for drug approval, pharmaceutical companies, which share a vested interest in the drug approval process, may also be willing to adopt the methodological innovation in question. We used Rogers' Diffusion of Innovations Model to summarize changes to the social system related to the diffusion of indirect comparison meta-analytic methods used in the study of drugs over time.

We completed a systematic literature search to identify all papers that utilized indirect comparison meta-analytic methods to study drug effects in humans. We searched the Cochrane Database of Systematic Reviews®, EMBASE®, and MEDLINE® from their dates of inception to 31 December 2013 using keywords based on a recent search, **Appendix A** (refer to the technical appendix in the online supplement] [18]. We then used SCOPUS® and Web of Science® to perform a citation search to identify papers that referenced key seminal papers [8,

10], major methodological contributions [19-21], and reviews [7, 13-15, 22, 23] on indirect comparison meta-analytic methods [18].

All English language papers that used indirect meta-analytic methods to compare the clinical efficacy or safety of three or more interventions among humans were eligible if at least one intervention was a drug. We excluded abstracts, letters, commentaries, cost-effectiveness studies, overviews of systematic reviews, protocols, and papers with no identifiable authors. Papers that used informal indirect comparisons (e.g., simply compared point estimates with 95% confidence intervals) or did not clearly describe the techniques used to perform indirect comparisons were also excluded. Two authors (JKB and MT) independently searched and screened all titles and abstracts for eligibility. Discrepancies following full text review were resolved by a third author (SMC).

The number of papers and cumulative authors were plotted by calendar year and type: methodological contribution, review paper, or empirical application, and important social system events (e.g., publication of seminal papers) were added to the graph. We then focused exclusively on empirical applications. A proportional Venn diagram was used to illustrate the yield of each database search strategy that contributed to the identification of eligible empirical applications. We abstracted: author(s), journal, year of publication, area of study, primary outcomes (efficacy, safety, or both), first and last author institutional affiliations, terminology used to describe methods, and presence and details of network diagrams. If no primary outcomes were explicitly stated, all outcomes were considered primary. When multiple diagrams were present, the total number of unique comparators across all network diagrams was taken. Two authors (JKB and EAC) abstracted all the data, and another (MT) verified the data.

An Excel macro™ was used to generate a co-authorship matrix from author names of empirical applications downloaded into Microsoft Excel 2010 from Endnote X5 (Thomson Reuters, 2011). Names of authors presented in multiple forms were collapsed into the most common presentation or, in the event of a tie, the one with more initials. Publication (authors and order) and paper characteristics (country and institutional type ascribed) were imported into R®, version 3.3.1 (R Foundation for Statistical Computing, 2016), leveraging RStudio®, version 0.99.887 (RStudio, Inc., 2009); to generate directed co-authorship networks, and identify components. Co-authorship networks depict authors as "nodes", with "ties" between authors or nodes denoting co-authorship. Directed co-authorship networks clarify network structure by sending "ties" depicted as arrows, from first authors to co-authors. A component is a group of authors connected directly as co-authors on the same paper, or indirectly through a mutual co-author on separate papers. Institutional affiliations and corresponding countries of the first and last authors of each empirical application were used to ascribe credit to each application and the network [16]. Institutions were categorized by country and type (academia, government, industry, or other). Node size was created proportional to the number of publications by that author. Node colour was created, first based on country affiliation attributed to each paper, and second based on institutional type. The network was animated by calendar year of publication to visualize growth in application and country contributions over time.

## RESULTS

We identified 477 eligible papers: 74 methodological contributions (**Appendix B**), 42 review papers (**Appendix C**), and 361 empirical applications (**Appendix D**), **Figure 1**, published by 1,691 distinct authors between 1997 and 2013. A steady increase in the number of eligible papers was seen over time, and proportionally more were published in recent years, **Figure 2**.

Focusing exclusively on the 361 empirical applications, the keyword search strategy identified most applications (n=314, 87%; 30% unique). EMBASE® identified the most (n=282, 78%; 6% unique), followed by MEDLINE® (n=239, 66%; 3% unique), and relatively few were identified by the Cochrane Database of Systematic Reviews® (n=20, 6%; <1% unique), **Figure 3A**. The citation search identified an additional 47 (13%) papers outside keyword searches, **Figure 3B**.

The indirect comparison meta-analytic applications were published in 188 different journals. The most common areas of study were cardiovascular disorders (22%), cancers (12%), musculoskeletal disorders (12%), infectious diseases (10%), and psychiatry (9%), **Table 2**. Sixty-nine percent of primary outcomes assessed therapeutic efficacy, 25% assessed efficacy and drug safety, and 6% assessed drug safety alone. Of the 361 empirical applications, only 161 (45%) published network diagrams illustrating the direct or indirect comparisons. The majority of these papers (n=119, 74%) compared fewer than ten interventions (median=7, interquartile range of 5, min=3, max=145). The most common terminology used was network meta-analysis (38%), followed by mixed treatment comparison (26%), Bucher's method (24%), and adjusted indirect comparison (21%).

The co-authorship network included 361 empirical applications, 1,513 unique authors, and 129 components, **Figure 4**. The largest component included 143 (40%) papers and 567

(37%) authors, including innovators Guyatt GH, Lu G, and Ades AE, **Appendix D1-143**. Of the remaining 128 components, ninety (70%) included only a single paper, demonstrating a highly disconnected co-authorship network. Early application of indirect comparison meta-analytic methods to study drugs started in 2000, with three papers published by 2002 [24-26]; and each referencing the innovator paper [8]. Authors were from Canada (red) and the United States (blue), and published in isolation of each other, **Appendix E** (animation available in the online supplement, **Supplemental Material 1**). In 2003, five papers were published in isolation of each other, with two credited to the United States (blue), and three credited to the United Kingdom (yellow). The majority referenced innovator Bucher [8], yet one paper referenced innovator Lumley [10].

By 2004, an increase in collaboration between authors from different countries was noted, with the first multi-paper component (France) noted in 2004, and the first single-paper component with institutional affiliations from multiple countries (United States and Belgium) noted in 2005. By 2006, another 13 papers were published: 11 papers referenced innovator Bucher with institutional affiliations credited to many countries worldwide (Belgium, Canada, France, Germany, India, United States), and two papers referenced innovators Lumley, Lu and Ades, with one paper credited to the United States, the United Kingdom, and Greece, and the other credited to the United Kingdom. From 2007 to 2013, we noted an increase in the number of indirect comparison meta-analytic papers published over time, with fastest uptake noted in 2011, and an increase in authors publishing from a broad range of countries depicted by the increase in colours observed in the network. In particular, a rapid increase in the number of industry-sponsored papers was noted in 2008 with double the number of industry-sponsored papers published (n=3). Furthermore, a rapid increase in collaboration between authors was noted in

2009, as demonstrated by the merging of smaller components into larger components. Europe led the diffusion of indirect comparison meta-analytic methods with node colours of yellow (United Kingdom), light yellow (all other Europe), and combinations of yellow with other primary colours comprising the majority of nodes in the co-authorship network. The online supplement maps the growth of the network by country affiliation and institution type over time, **Appendix E-F** (animations available in the online supplement, **Supplemental Material 1-2**).

Overall, institutional credit was given to 358 unique institutions around the world. Europe led the diffusion with 49% of credited papers (22% United Kingdom, 27% other); 37% were credited to North America (26% United States, 11% Canada), and 14% to other regions, **Table 3**. The majority of contributions (77%) were from academic institutions, yet 18% were credited to industry (**Table 2**).

## DISCUSSION

Indirect comparison meta-analytic methods are an important methodological innovation that has become valuable in providing comparative drug effect data in the absence of head-to-head trials. In this paper, we focused on the impact of the social system on uptake of these methods across institutions and countries over time; and found that the geographic distribution of applications was concentrated primarily in Europe (49%) and North America (37%), with the majority published from academic institutions (77%). Our results are not surprising given that refined methods were published by core innovators from the Universities of Bristol and Washington [10, 11]. However, early use of indirect comparison meta-analytic applications predominated from the United Kingdom, and was likely the result of an increase in demand by government for more comparative effectiveness research. In particular, demand for more evidence of safety and effectiveness of newly marketed drugs to assist clinicians and policy-makers with clinical practice guideline development and drug funding decisions. The need for clinical practice guideline development was one of the major reasons for the establishment of the National Institute for Health and Clinical Excellence (NICE) in 1999 [27], which has since become a world leader in providing guidance on the clinical- and cost-effectiveness of new and established health technologies (including drugs) using several health technology appraisal methods, with indirect comparison meta-analytic methods as an integral component. NICE decisions are made by independent committees of researchers, clinicians, industry and lay representatives, and have included innovator Ades, and early adopters from the NICE Guidelines Technical Support Unit, University of Bristol, who have worked closely with the innovator to develop methods [5, 20, 28-30].

The steady increase in the use of indirect comparison meta-analytic methods, and effective diffusion to Europe and North America, may be partially explained by consideration of the five key innovation attributes described in Rogers' Diffusion of Innovations Model (**relative advantage, compatibility, simplicity, trialability,** and **observability**); and recently evaluated in relation to methodological innovations in pharmacoepidemiology [16]. The Multi-Parameter Evidence Synthesis (MPES) Research Group (from which the NICE Guidelines Technical Support Unit is based) has offered introductory short-courses, workshops, sample datasets, and statistical code on pairwise, indirect, and mixed treatment comparisons to facilitate understanding and application of these methods to health economists, statisticians, and policy-makers worldwide in collaboration with other academic institutions in the United Kingdom (Universities of Sheffield and York) since 2002 (**observability, simplicity, trialability**) [30, 31]. In addition, the MPES Research Group published tutorials and case-studies highlighting the advantages of using pairwise, indirect comparison, and network meta-analyses for evidence synthesis (**advantage**), and highlighting the validity of using these methods to inform clinical and policy decision-making (**compatibility**) [28, 32-35]. We noted rapid uptake since 2011, coinciding with the publication of guidelines and reviews on these methods by health technology and reimbursement agencies (e.g., Canadian Agency for Drugs and Technologies in Health, Hauté Autorité de Santé, Institute for Quality and Efficiency in Health Care, Pharmaceutical Benefits Advisory Committee, and Scottish Medicines Consortium) from many countries around the world [19, 36-41].

Given the economic pressure on payers to allocate healthcare resources more efficiently, many regulatory agencies are calling for the use of comparative effectiveness research to assist in drug accessibility and reimbursement decisions [40, 41]. In addition, applications focused on

drug efficacy ties into payer demand for more cost-effectiveness analyses of newly marketed drugs in comparison with competing or existing therapies. Many pharmaceutical companies and contract research organizations have started to apply these methods, and we noted collaboration with core innovators from academia and an increase in the number of industry-sponsored applications published since 2009. For example, the International Society for Pharmaceutical Outcomes Research Indirect Comparisons Good Research Practice Task Force published models and statistical code adopted from the MPES Research Group to provide guidance to researchers, clinicians, and policy-makers on good research practices for indirect comparisons, and to address key issues [6, 15]. Co-authors on this two-part report mainly comprised of research experts from pharmaceutical companies and contract research organizations (including J. P. Jansen who collaborated with innovator A. E. Ades and co-authors from the MPES Research Group), spreading use of these methods into industry. In addition, publication of this report may partially explain rapid and large uptake from 2011 since co-authors from the two-part report were from multiple countries (Belgium, Canada, the Netherlands, the United Kingdom, the United States); and by highlighting key authors involved in the dissemination of these methods.

Our findings demonstrated rapid increase in the use of indirect comparison meta-analytic methods in recent years, with contributions increasing worldwide. With 70% (n=90) of the co-authorship network comprised of single paper components and 81% (n=1,121) of authors having published only a single paper, use of indirect comparison meta-analytic methods has indeed spread to many distinct research groups, yet uptake of methods has been diffuse as many authors are publishing in isolation of each (e.g., smaller, single paper components). Furthermore, we noted a lack of standardization in the terminology used to describe the indirect comparison meta-analytic methods used. Rapid and widespread use by academics, and more recently, industry,

suggests that indirect comparison meta-analytic methods have diffused and are no longer in the early stages of adoption, but are rather, mainstream and accepted methods. We encourage the use of one term, network meta-analysis, to describe refined methods by Lumley, Lu, and Ades, as it is clearer than mixed treatment or multiple treatments meta-analysis, which may be assumed to indicate the concomitant administration of two or more drug therapies (e.g., adjuvant therapy), and the separation of this term from Bucher's adjusted indirect comparison method, to improve standardization of terminology.

Our systematic review is subject to some limitations. First, our analysis focused on the co-authorship of journal articles that applied indirect comparison meta-analytic methods in the study of drugs through to 2013 and that were identifiable using electronic search engines. The influence of authors that used these methods to compare other clinical interventions (e.g., medical device and non-drug therapies) and the publication of these applications in grey literature (e.g., conference proceedings, technical reports), which likely influenced adoption of these methods, were not accounted for. In addition, recent applications were not considered. Indeed, the term matching-adjusted indirect comparison, an extension of the adjusted indirect comparison which was introduced in 2010 and uses individual patient data from single-comparator-RCTs to adjust for differences in patient characteristics across studies was not considered in our analysis [42]. However, 6 eligible papers were published using this term, and we expect to see an increase in the future. Furthermore, collaboration between authors through societal memberships, participation at conferences, and interviews of core innovators, which may have impacted the diffusion of these methods, were outside the scope of our analysis. Finally, this study did not consider the methodological and reporting quality of eligible empirical applications. Given the large number of authors who published in isolation of each other, it is

possible that the degree of interconnectedness between authors in the network may have influenced the quality of eligible empirical applications. Although inconsistencies in methodological and reporting quality of indirect comparison meta-analytic methods have been documented [18], a recent systematic review of network meta-analyses in clinical research demonstrated improvement in methodological and reporting quality over time, which may be due to increased accessibility and availability of statistical techniques [43].

In conclusion, prior research identified challenges with integrating new statistical methods into practice [44, 45]. We recently identified the importance of considering the five innovation attributes from Rogers' Diffusion of Innovations Model to facilitate knowledge translation of new methods for rapid integration [16]. In this paper, we used indirect comparison meta-analytic methods to examine the impact of social systems on the diffusion of novel methods. We demonstrated rapid adoption by effective consideration of innovation attributes by innovators, and rapid adoption due to collaboration between innovators from the United Kingdom and a large number of early adopters from many countries around the world. The social system plays a major role in facilitating the adoption of innovative methods, here through regulation, and by the increase in demand by government for more comparative effectiveness research. As many health technology assessment and regulatory agencies have started to call for more evidence synthesis methods to assist in drug accessibility and reimbursement decisions [41], use of indirect comparison meta-analytic methods has become more widely accepted. We encourage authors to consider the five innovation attributes when integrating new methods into practice (**relative advantage, compatibility, simplicity, trialability,** and **observability**), with emphasis on early collaboration with potential adopters.

## Acknowledgements

Authors thank Dave Dubins, PhD for initial work in creating Excel macros for co-authorship matrix generation; and Gina Matesic, MLIS for helping with search strategies.

Contributors: JB, MT, and SC were responsible for the conception and design of this study. JB, EC, and MT collected the data, and verified the results with SC. Data analysis was performed by JB and AL. JB led drafting of the manuscript in consultation with MT and SC. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

Funding: No specific funding was received to support this work. Joann K. Ban was supported in part by a Canadian Institute of Health Research (CIHR) Program in Drug Safety and Effectiveness Cross-Disciplinary Training. Mina Tadrous was supported in part by a CIHR Frederick Banting and Charles Best Canada Graduate Scholarship (GSD-11342). Erin A. Cicinelli was supported in part by a CIHR Health Professional Student Research Award. This research was presented at the Canadian Association for Health Services and Policy Research (CAHSPR) Annual Conference in Toronto, ON, Canada, May 2016, and at the International Conference on Pharmacoepidemiology and Therapeutic Risk Management (ICPE) in Dublin, Ireland, August 2016. Participation at CAHSPR was supported by a CAHSPR Student Travel Bursary, and participation at ICPE was supported by an ICPE Travel Scholarship, the Leslie Dan Faculty of Pharmacy Student Experience Fund, and a University of Toronto School of Graduate Studies Conference Grant.

Data sharing: technical appendix and supplemental material available at [/doi].

## References


[1] Friedman HP, Goldberg JD. Meta-analysis: an introduction and point of view. *Hepatology*. 1996;23:917-28.
[2] O'Rourke K. An historical perspective on meta-analysis: dealing quantitatively with varying study results. *J R Soc Med*. 2007;100:579-82.
[3] Jansen JP, Naci H. Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect modifiers. *BMC Med*. 2013;11:159.
[4] Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg*. 2011;128:305-10.
[5] Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ*. 2005;331:897-900.
[6] Jansen JP, Fleurence R, Devine B, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. *Value Health*. 2011;14:417-28.
[7] Edwards SJ, Clarke MJ, Wordsworth S, et al. Indirect comparisons of treatments based on systematic reviews of randomised controlled trials. *Int J Clin Pract*. 2009;63:841-54.
[8] Bucher HC, Guyatt GH, Griffith LE, et al. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol*. 1997;50:683-91.
[9] Song F, Altman DG, Glenny AM, et al. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ*. 2003;326:472.
[10] Lumley T. Network meta-analysis for indirect treatment comparisons. *Stat Med*. 2002;21:2313-24.
[11] Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med*. 2004;23:3105-24.
[12] Lee AW. Review of mixed treatment comparisons in published systematic reviews shows marked increase since 2009. *J Clin Epidemiol*. 2014;67:138-43.
[13] Song F, Loke YK, Walsh T, et al. Methodological problems in the use of indirect comparisons for evaluating healthcare interventions: survey of published systematic reviews. *BMJ*. 2009;338:b1147.
[14] Donegan S, Williamson P, Gamble C, et al. Indirect comparisons: a review of reporting and methodological quality. *PLoS One*. 2010;5:e11054.
[15] Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. *Value Health*. 2011;14:429-37.
[16] Cadarette SM, Ban JK, Consiglio GP, et al. Diffusion of Innovations model helps interpret the comparative uptake of two methodological innovations: co-authorship network analysis and recommendations for integration of novel methods in practice. *J Clin Epidemiol*. 2017;84:150-160.
[17] Rogers EM. Diffusion of Innovations. Fifth ed. Toronto: Free Press; 2003.
[18] Bafeta A, Trinquart L, Seror R, et al. Analysis of the systematic reviews process in reports of network meta-analyses: methodological systematic review. *BMJ*. 2013;347:f3675.
[19] Wells GA, Sultan SA, Chen L, et al. Indirect Evidence: Indirect Treatment Comparisons in Meta-Analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.

[20] Lu G, Ades AE, Sutton AJ, et al. Meta-analysis of mixed treatment comparisons at multiple follow-up times. *Stat Med*. 2007;26:3681-99.
[21] Salanti G, Higgins JP, Ades AE, et al. Evaluation of networks of randomized trials. *Stat Methods Med Res*. 2008;17:279-301.
[22] Glenny AM, Altman DG, Song F, et al. Indirect comparisons of competing interventions. *Health Technol Assess*. 2005;9:1-134, iii-iv.
[23] Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol*. 2011;64:163-71.
[24] Wilhelmus KR. The treatment of herpes simplex virus epithelial keratitis. *Trans Am Ophthalmol Soc*. 2000;98:505-32.
[25] Packer M, Antonopoulos GV, Berlin JA, et al. Comparative effects of carvedilol and metoprolol on left ventricular ejection fraction in heart failure: results of a meta-analysis. *Am Heart J*. 2001;141:899-907.
[26] Sauriol L, Laporta M, Edwardes MD, et al. Meta-analysis comparing newer antipsychotic drugs for the treatment of schizophrenia: evaluating the indirect approach. *Clin Ther*. 2001;23:942-56.
[27] Chalkidou K. Comparative effectiveness review within the U.K.'s National Institute for Health and Clinical Excellence. Issue Brief (Commonw Fund). 2009;59:1-11.
[28] Caldwell DM, Welton NJ, Ades AE. Mixed treatment comparison analysis provides internally coherent treatment effect estimates based on overviews of reviews and can reveal inconsistency. *J Clin Epidemiol*. 2010;63:875-82.
[29] Dias S, Welton NJ, Caldwell DM, et al. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med*. 2010;29:932-44.
[30] University of Bristol. Multi-parameter Evidence Synthesis Research. Multi-parameter Evidence Synthesis Research Group | School of Social and Community Medicine | University of Bristol. 2017. http://www.bristol.ac.uk/social-community-medicine/centres/cresyda/mpes/ (accessed 23 Jul 2017).
[31] University of Bristol. Multi-parameter Evidence Synthesis Research. Multi-parameter Evidence Synthesis Research Group | School of Social and Community Medicine | University of Bristol. 2017.http://www.bristol.ac.uk/social-community-medicine/centres/cresyda/mpes/ (accessed 23 Jul 2017).
[32] Dias S, Sutton AJ, Ades AE, et al. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making*. 2013;33:607-17.
[33] Sutton A, Ades AE, Cooper N, et al. Use of indirect and mixed treatment comparisons for technology assessment. *Pharmacoeconomics*. 2008;26:753-67.
[34] Dias S, Sutton AJ, Welton NJ, et al. Evidence synthesis for decision making 3: heterogeneity--subgroups, meta-regression, bias, and bias-adjustment. *Med Decis Making*. 2013;33:618-40.
[35] Dias S, Welton NJ, Sutton AJ, et al. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making*. 2013;33:641-56.
[36] Haute Autorité de Santé. Indirect Comparisons: Methods and Validity. Saint-Denis: Haute Autorité de Santé; 2009.

[37] Indirect Comparisons Working Group. Report of the Indirect Comparisons Working Group to the Pharmaceutical Benefits Advisory Committee: assessing indirect comparisons. Canberra: Australian Government Department of Health and Ageing; 2013.
[38] Pharmaceutical Benefits Advisory Committee. Guidelines for Preparing Submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Australian Government Department of Health and Ageing; 2008.
[39] National Institute for Health and Care Excellence. Guide to the Methods of Technology Appraisal 2013, Process and Method Guides. National Institute for Healh and Care Excellence; 2013.
[40] Lebioda A, Gasche D, Dippel FW, et al. Relevance of indirect comparisons in the German early benefit assessment and in comparison to HTA processes in England, France and Scotland. *Health Econ Rev*. 2014;4:31.
[41] Laws A, Kendall R, Hawkins N. A comparison of national guidelines for network meta-analysis. *Value Health*. 2014;17:642-54.
[42] Signorovitch JE, Wu EQ, Yu AP, et al. Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept. *Pharmacoeconomics*. 2010;28:935-45.
[43] Petropoulou M, Nikolakopoulou A, Veroniki AA, et al. Bibliographic study showed improving statistical methodology of network meta-analyses published between 1999 and 2015. *J Clin Epidemiol*. 2017;82:20-28.
[44] Altman DG, Goodman SN. Transfer of technology from statistical journals to the biomedical literature. Past trends and future predictions. *JAMA*. 1994;272:129-32.
[45] Pullenayegum EM, Platt RW, Barwick M, et al. Knowledge translation in biostatistics: a survey of current practices, preferences, and barriers to the dissemination and uptake of new statistical methods. *Stat Med*. 2016;35:805-18.
[46] Institute for Quality and Efficiency in Health Care. General Methods (Version 4.1). Cologne: Institute for Quality and Efficiency in Health Care; 2013.

# In-Text Figures and Tables

## Tables

**Table 1:** Timeline of Meta-analytic Methodological Innovations

| Innovation | Year | Innovators | Institution | Country | Description |
|---|---|---|---|---|---|
| Traditional Pairwise Meta-Analysis [1] | 1904 | Pearson K | University College London | UK | Combines direct evidence from multiple RCTs comparing the same intervention and comparator (e.g., placebo) to strengthen the intervention's effect estimate relative to that comparator. |
| | 1935 | Fisher R | Rothamsted Experimental Station | UK | |
| | 1937 | Cochran W | Rothamsted Experimental Station | UK | |
| | 1976 | Glass GV | University of Colorado | USA | |
| Adjusted Indirect Comparison [8] | 1997 | Bucher HC<br>Guyatt GH<br>Griffith LE<br>Walter SD | McMaster University | Canada | Combines odds ratios from multiple RCTs comparing one of two interventions of interest to a common comparator (e.g. placebo) to estimate the effects of two interventions that have not been compared directly. |
| Network Meta-Analysis* [10] | 2002 | Lumley T | University of Washington | USA | Combines direct and indirect data from multiple RCTs to compare several sets of pairwise treatment comparisons. |
| Mixed Treatment Comparison* [11] | 2004 | Lu G<br>Ades AE | University of Bristol | UK | |

RCT: randomized controlled trials, UK: United Kingdom, USA: United States of America

* To our knowledge, Caldwell et al. (2005) introduced the term *multiple treatments meta-analysis* to describe the concept of combining direct and indirect evidence to compare multiple treatments connected by a network of RCTs, as seen in both methods [5].

**Table 2:** Characteristics of empirical indirect comparison meta-analytic applications in the study of drugs, N=361

| Characteristics | N | % |
|---|---|---|
| **Area of Study** | | |
| Blood Disorders | 1 | 0.3 |
| Cancers | 45 | 12.5 |
| Cardiovascular Disorders | 79 | 21.9 |
| Dermatology/Skin Disorders | 11 | 3.0 |
| Endocrine/Metabolic Disorders | 18 | 5.0 |
| Gastrointestinal Disorders | 8 | 2.2 |
| Genitourinary Disorders | 4 | 1.1 |
| Infectious Diseases | 36 | 10.0 |
| Musculoskeletal Disorders | 45 | 12.5 |
| Neurologic Disorders | 21 | 5.8 |
| Ophthalmic Disorders | 6 | 1.7 |
| Pain | 20 | 5.5 |
| Pregnancy | 4 | 1.1 |
| Psychiatric Disorders | 31 | 8.6 |
| Renal Disorders | 2 | 0.6 |
| Respiratory Disorders | 16 | 4.4 |
| Sexual Health | 6 | 1.7 |
| Surgery | 8 | 2.2 |
| **Primary Outcome** | | |
| Efficacy Only | 249 | 69.0 |
| Safety Only | 23 | 6.4 |
| Both Efficacy and Safety | 89 | 24.6 |
| **Terminology** | | |
| Adjusted Indirect Comparison | 75 | 20.8 |
| Bucher's Method | 88 | 24.4 |
| Indirect Comparison | 45 | 12.5 |
| Matching-Adjusted Indirect Comparison | 6 | 1.7 |
| Mixed Treatment Comparison | 95 | 26.3 |
| Multiple Treatments Meta-Analysis | 29 | 8.0 |
| Network Meta-Analysis | 137 | 38.0 |
| **Network Diagram(s)** | 161 | 44.6 |
| Interventions* | | |
| 3 | 7 | 4.3 |
| 4 | 16 | 9.9 |
| 5 | 23 | 14.3 |
| 6 | 24 | 14.9 |

| | | |
|---|---|---|
| 7 | 18 | 11.2 |
| 8 | 17 | 10.6 |
| 9 | 14 | 8.7 |
| 10-19 | 30 | 18.6 |
| 20+ | 12 | 7.4 |

* Based on the total number of interventions studied, indicated in the network diagram(s) published, N=161.

**Table 3:** Institutional affiliations by country (N=35) and institution type (N=7) for the entire indirect comparison meta-analytic applications network

| Institution | First and Last Author Credit (%) |
|---|---|
| **Country** | |
| Australia | 2.0 |
| Belgium | 1.7 |
| Brazil | 2.4 |
| Canada | 11.3 |
| China | 3.0 |
| France | 3.0 |
| Germany | 3.6 |
| Greece | 1.9 |
| India | 1.0 |
| Italy | 4.7 |
| Netherlands | 3.8 |
| Spain | 1.8 |
| Switzerland | 2.5 |
| Taiwan | 1.7 |
| United Kingdom | 22.1 |
| United States of America | 26.0 |
| Other* | 7.4 |
| **Type** | |
| **Academic** | **77.4** |
| School | 56.4 |
| Hospital | 21.0 |
| **Government** | **1.5** |
| **Industry** | **17.5** |
| Contract Research Organization | 11.3 |
| Pharmaceutical Company | 6.2 |
| **Other** | **3.6** |
| Independent Research Groups | 1.1 |
| Non-profit Organizations | 2.4 |
| Trade Associations | 0.1 |

* Institutional affiliations from other countries with <1% first and last author credit each (Austria, Bahrain, Cameroon, Croatia, Denmark, Hong Kong, Ireland, Israel, Japan, New Zealand, Nigeria, Norway, Peru, Poland, Portugal, Saudi Arabia, South Africa, South Korea, and Thailand).

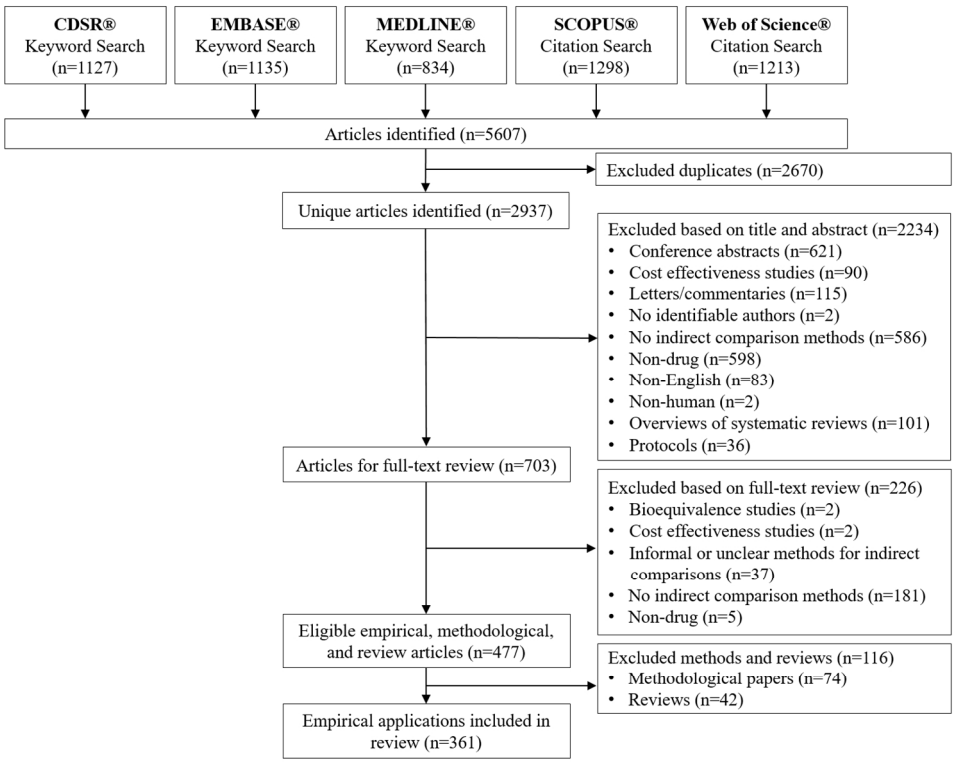



Figure 1: Flow diagram of systematic search results.

135x106mm (300 x 300 DPI)

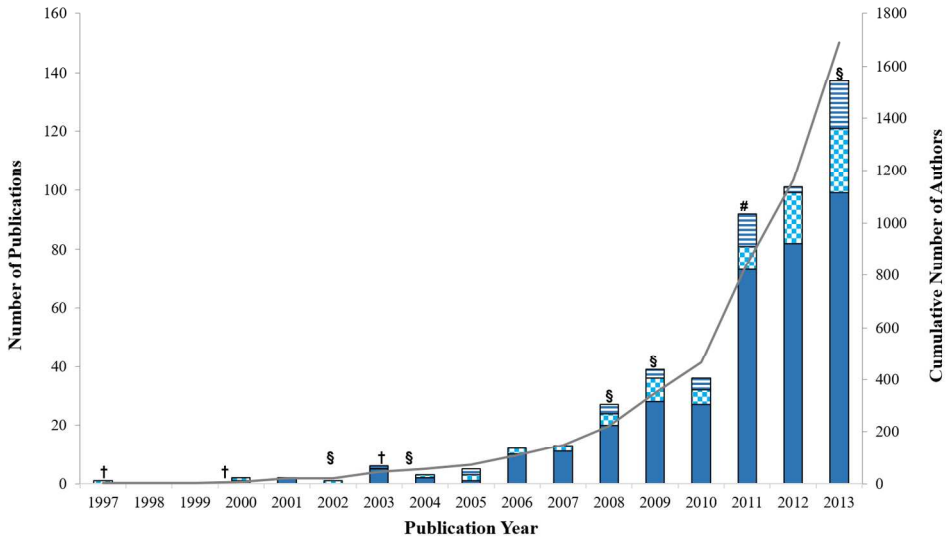



Figure 2: Number of publications on indirect comparison meta-analytic methods by year of publication, n=477. Methodological contributions (checkered bar), review papers (horizontal stripes), and empirical applications (solid). Cumulative number of unique authors represented by the solid grey line, n=1689. †Innovators by seminal publication: Bucher et al. 1997 (Canada) [8]; Lumley (USA) 2002 [10]; Lu and Ades 2004 (UK) [11]. Early adopters: §government-sponsored academic groups and health technology and reimbursement assessment agencies (National Institute for Health and Clinical Excellence Guidelines Technical Support Unit 2002 (UK) [30]; Pharmaceutical Benefits Advisory Committee 2005 (Australia) [37, 38]; Canadian Agency for Drugs and Technologies in Health 2009 (Canada) [19]; Haute Autorité de Santé 2009 (France) [35]; Institute for Quality and Efficiency in Health Care 2013 (Germany) [36]); #independent research organizations: Indirect Treatment Comparisons Good Research Practices Task Force 2011 (Canada, The Netherlands, USA, UK) [6, 15].

144x79mm (300 x 300 DPI)

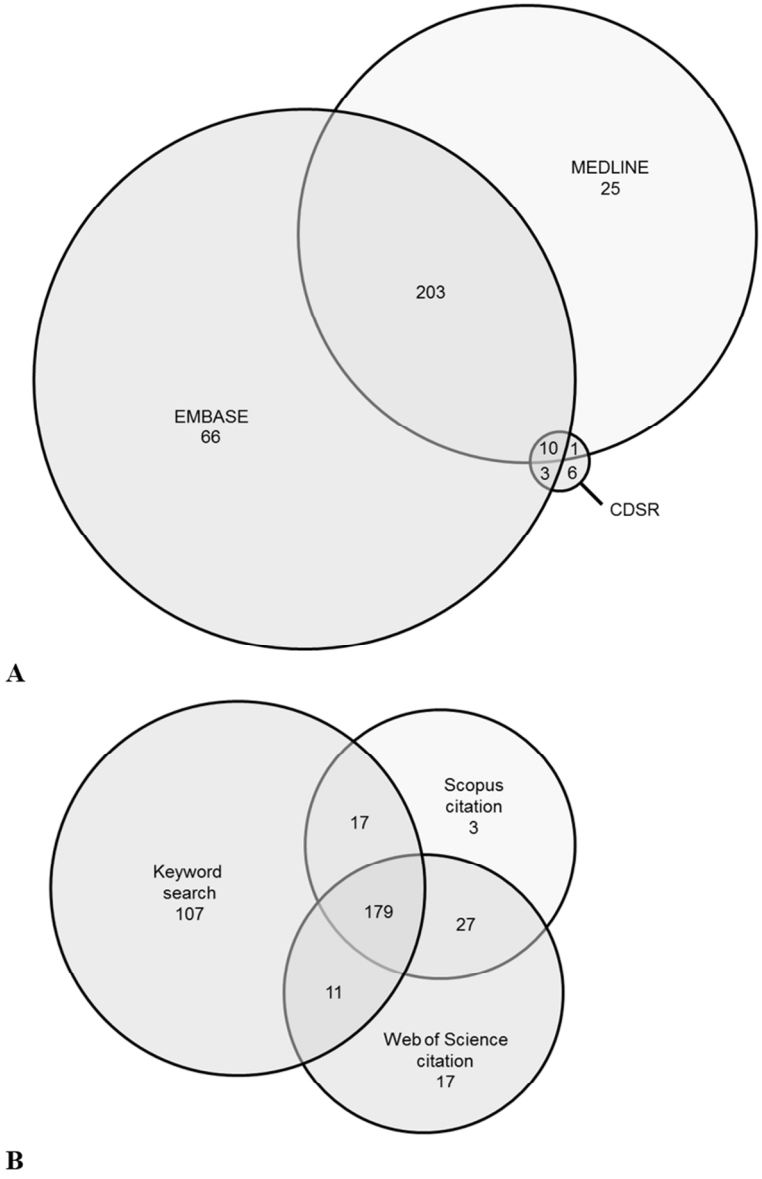



Figure 3: Proportional Venn diagrams of systematic search yields for indirect comparison meta-analytic empirical applications depicting unique and overlap applications identified by each search strategy, N=361. Circle size is proportional to the number of papers identified from each search strategy.
A. Empirical applications identified by each keyword search, N=314 (EMBASE keyword, n=282; MEDLINE keyword, n=239; and Cochrane Database of Systematic Reviews (CDSR) keyword, n=20).
B. Empirical applications identified by each keyword and citation search, N=361 (keyword (EMBASE, MEDLINE, CDSR), n=314; Web of Science citation, n=234; Scopus citation, n=226).

85x108mm (300 x 300 DPI)

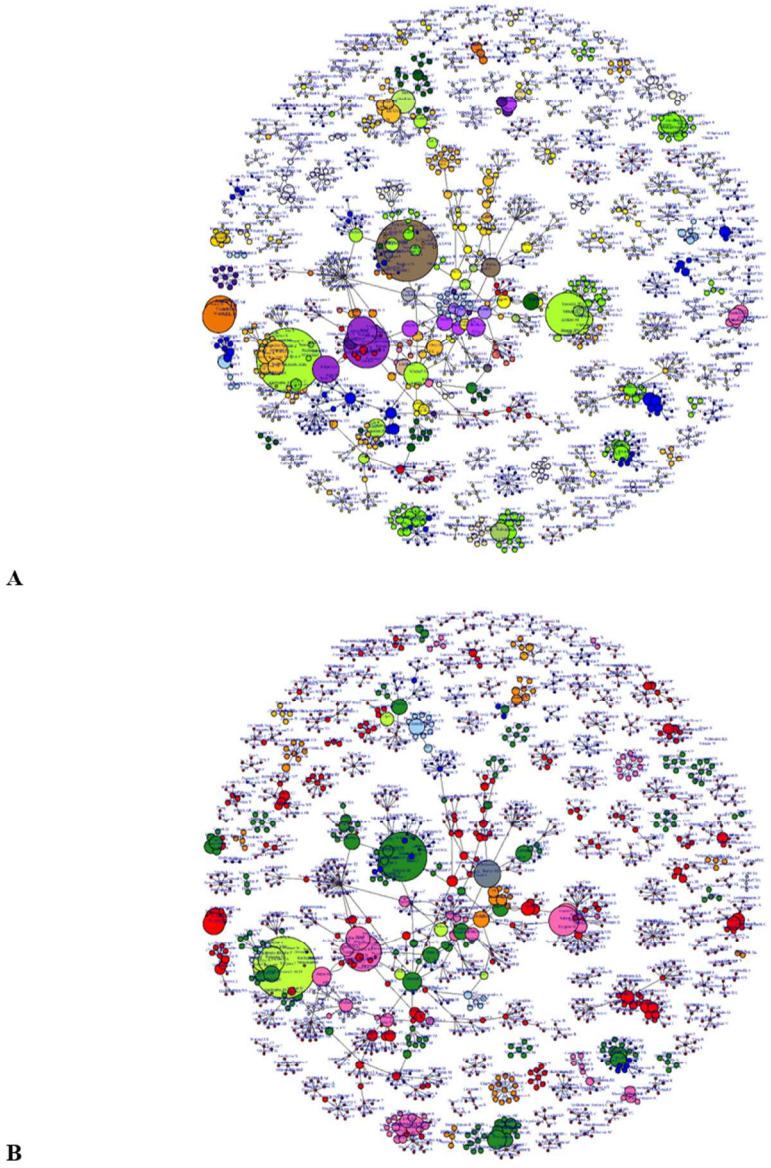



Figure 4: Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. The lines represent the relationships (co-authorship) between authors, with arrows directed from first author to co-authors of each paper. Node size is proportional to the number of published articles.

A. Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), while authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow).

B. Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliation

types from academia and government were coloured orange (a combination of red and yellow), while authors on papers affiliated with academic, industry, and other were coloured light purple (a combination of red, blue, and white).

82x110mm (300 x 300 DPI)

# Appendix A: Systematic Literature Search

| **Appendix Table A:** Systematic Literature Keyword Search | | | |
|---|---|---|---|
| **Databases:** | Cochrane Database of Systematic Reviews® | MEDLINE® | EMBASE® |
| **Limits:** | - Date of inception to 31 December 2013 | - Date of inception to 31 December 2013<br>- English language<br>- Humans<br>- Publication types: meta-analysis, systematic reviews | |
| **Keywords:** | "network meta-analysis" OR "network meta-regression" OR "multiple treatment meta-analysis" OR "multiple treatments meta-analysis" OR "mixed treatment comparison" OR "mixed treatment comparisons" OR "mixed treatment" OR "mixed treatments" OR "multiple treatment" OR "multiple treatments" OR "treatment network" OR "treatment networks" OR "multiple comparison" OR "multiple comparisons" OR "indirect comparison" OR "indirect comparisons" OR "overview of reviews" OR "umbrella review" OR "overview of systematic reviews" OR "overview of meta-analyses" OR "multiple systematic reviews" OR "multiple meta-analyses" OR "overview of Cochrane reviews" OR "multiple Cochrane reviews" OR "overview of Cochrane" | | |

# Appendix B: List of references of identified methodological contributions of indirect comparison meta-analytic methods

[B1] Achana FA, Cooper NJ, Dias S, Lu G, Rice SJ, Kendrick D, et al. Extending methods for investigating the relationship between treatment effect and baseline risk from pairwise meta-analysis to network meta-analysis. *Stat Med* 2013; 32(5):752-71.

[B2] Ades AE, Mavranezouli I, Dias S, Welton NJ, Whittington C, Kendall T. Network meta-analysis with competing risk outcomes. *Value Health* 2010;13(8):976-83.

[B3] Ballesteros, J. Orphan comparisons and indirect meta-analysis: a case study on antidepressant efficacy in dysthymia comparing tricyclic antidepressants, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors by using general linear models. *J Clin Psychpharmacol* 2005;25(2):127-31.

[B4] Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol* 1997;50(6):683-91.

[B5] Caldwell DM, Welton NJ, Ades AE. Mixed treatment comparison analysis provides internally coherent treatment effect estimates based on overviews of reviews and can reveal inconsistency. *J Clin Epidemiol* 2010;63(8):875-82.

[B6] Chaimani A, Vasiliadis HS, Pandis N, Schmid CH, Welton NJ, Salanti G. Effects of study precision and risk of bias in networks of interventions: a network meta-epidemiological study. *Int J Epidemiol* 2013;42(4):1120-131.

[B7] Chaimani A, Higgins JP, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One* 2013;8(10):e76654.

[B8] Chootrakool H, Shi JQ, Yue R. Meta-analysis and sensitivity analysis for multi-arm trials with selection bias. *Stat Med* 2011;30(11):1183-98.

[B9] Chung H, Lumley T. Graphical exploration of network meta-analysis data: the use of multidimensional scaling. *Clin Trials* 2008;5(4):301-7.

[B10] Cooper NJ, Sutton AJ, Morris D, Ades AE, Welton NJ. Addressing between-study heterogeneity and inconsistency in mixed treatment comparisons: application to stroke prevention treatments in individuals with non-rheumatic atrial fibrillation. *Stat Med* 2009;28(14):1861-81.

[B11] Cooper NJ, Peters J, Lai MC, Juni P, Wandel S, Palmer S, et al. How valuable are multiple treatment comparison methods in evidence-based health-care evaluation? *Value Health* 2011;14(2):371-80.

[B12] Cope S, Jansen JP. Quantitative summaries of treatment effect estimates obtained with network meta-analysis of survival curves to inform decision-making. *BMC Med Res Methodol* 2013;13:147.

[B13] Del Giovane C, Vacchi L, Mavridis D, Filippini G, Salanti G. Network meta-analysis models to account for variability in treatment definitions: application to dose effects. *Stat Med* 2013;32(1):25-39.

[B14] Dias S, Welton NJ, Caldwell DM, Ades AE. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med* 2010;29:932-44.

[B15] Dias S, Welton NJ, Marinho VCC, Salanti G, Higgins JPT, Ades AE. Estimation and adjustment of bias in randomized evidence by using mixed treatment comparison meta-analysis. *J R Statist Soc A* 2010;173(3):613-29.

[B16] Ding Y, Fu H. Bayesian indirect and mixed treatment comparisons across longitudinal time points. *Stat Med* 2013;32(15):2613-28.

[B17] Donegan S, Williamson P, D'Alessandro U, Tudur Smith C. Assessing the consistency assumption by exploring treatment by covariate interactions in mixed treatment comparison meta-analysis: individual patient-level covariates versus aggregate trial-level covariates. *Stat Med* 2012;31(29):3840-57.

[B18] Donegan S, Williamson P, D'Alessandro U, Garner P, Smith CT. Combining individual patient data and aggregate data in mixed treatment comparison meta-analysis: individual patient data may be beneficial if only for a subset of trials. *Stat Med* 2013;32(6):914-30.

[B19] Druyts E, Thorlund K, Humphreys S, Lion M, Cooper CL, Mills EJ. Interpreting discordant indirect and multiple treatment comparison meta-analyses: an evaluation of direct acting antivirals for chronic hepatitis C infection. *Clin Epidemiol* 2013;5(1):173-183.

[B20] Eckermann S, Coory M, Willan AR. Indirect comparison: relative risk fallacies and odds solution. *J Clin Epidemiol* 2009;62:1031-6.

[B21] Fu H, Price KL, Nilsson ME, Ruberg SJ. Identifying potential adverse events dose-response relationships via Bayesian indirect and mixed treatment comparison models. *J Biopharm Stat* 2013;23(1):26-42.

[B22] Griffin S, Bojke L, Main C, Palmer S. Incorporating direct and indirect evidence using bayesian methods: an applied case study in ovarian cancer. *Value Health* 2006;9(2):123-31.

[B23] Gross JL, Rogers J, Polhamus D, Gillespie W, Friedrich C, Gong Y, et al. A novel model-based meta-analysis to indirectly estimate the comparative efficacy of two medications: an example using DPP-4 inhibitors, sitagliptin and linagliptin, in treatment of type 2 diabetes mellitus. *BMJ Open* 2013;3(3):e001844.

[B24] Gwaza L, Gordon J, Welink J, Potthast H, Hansson H, Stahl M, et al. Statistical approaches to indirectly compare bioequivalence between generics: a comparison of

methodologies employing artemether/lumefantrine 20/120 mg tablets as prequalified by WHO. *Eur J Clin Pharmacol* 2012;68(12):1611-8.

[B25] Hawkins N, Scott DA, Woods B. How far do you go? Efficient searching for indirect evidence. *Med Decis Making* 2009;29(3):273-81.

[B26] Hawkins N, Scott DA, Woods BS, Thatcher N. No study left behind: a network meta-analysis in non-small-cell lung cancer demonstrating the importance of considering all relevant data. *Value Health* 2009;12(6):996-1003.

[B27] Hong H, Carlin BP, Shamliyan TA, Wyman JF, Ramakrishnan R, Sainfort F, et al. Comparing Bayesian and frequentist approaches for multiple outcome mixed treatment comparisons. *Med Decis Making* 2013;33(5):702-14.

[B28] Jansen JP, Cope S. Meta-regression models to address heterogeneity and inconsistency in network meta-analysis of survival outcomes. *BMC Med Res Method* 2012;12:152.

[B29] Jansen JP, Schmid CH, Salanti G. Directed acyclic graphs can help understand bias in indirect and mixed treatment comparisons. *J Clin Epidemiol* 2012;65(7):798-807.

[B30] Jansen JP. Network meta-analysis of survival data with fractional polynomials. *BMC Med Res Methodol* 2011;11:61.

[B31] König J, Krahn U, Binder H. Visualizing the flow of evidence in network meta-analysis and characterizing mixed treatment comparisons. *Stat Med* 2013;32(30): 5414-29.

[B32] Krahn U, Binder H, König J. A graphical tool for locating inconsistency in network meta-analyses. *BMC Med Res Methodol* 2013;13(1):35.

[B33] Lee C, Hunsche E, Balshaw R, Kong SX, Scnitzer TJ. Need for common internal controls when assessing the relative efficacy of pharmacologic agents using a meta-analytic approach: Case study of cyclooxygenase 2-selective inhibitors for the treatment of osteoarthritis. *Arthritis Rheum* 2005;53(4):510-8.

[B34] Lu G, Ades A. Modeling between-trial variance structure in mixed treatment comparisons. *Biostatistics* 2009;10(4):792-805.

[B35] Lu G, Ades AE. Assessing evidence inconsistency in mixed treatment comparisons. *JASA* 2006;101(474):447-459.

[B36] Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med* 2004;23(20):3105-24.

[B37] Lu G, Ades AE, Sutton AJ, Cooper NJ, Briggs AH, Caldwell DM. Meta-analysis of mixed treatment comparisons at multiple follow-up times. *Stat Med* 2007;26(20):3681-99.

[B38] Lumley T. Network meta-analysis for indirect treatment comparisons. *Stat Med* 2002;21(16):2313-24.

[B39] Lunn D, Barrett J, Sweeting M, Thompson S. Fully Bayesian hierarchical modelling in two stages, with application to meta-analysis. *J R Stat Soc C Appl Stat* 2013;62(4):551-72.

[B40] Madan J, Stevenson MD, Cooper KL, Ades AE, Whyte S, Akehurst R. Consistency between direct and indirect trial evidence: is direct evidence always more reliable? *Value Health* 2011;14(6):953-60.

[B41] Mavridis D, Sutton A, Cipriani A, Salanti G. A fully Bayesian application of the Copas selection model for publication bias extended to network meta-analysis. *Stat Med* 2013;32(1):51-66.

[B42] Mills EJ, Ghement I, O'Regan C, Thorlund K. Estimating the power of indirect comparisons: a simulation study. *PLoS One* 2011;6(1):e16237.

[B43] Mills EJ, Kanters S, Thorlund K, Chaimani A, Veroniki AA, Ioannidis JP. The effects of excluding treatments from network meta-analyses: survey. *BMJ* 2013;347:f5195.

[B44] Mills, E.J., K. Thorlund, and J.P.A. Ioannidis, Calculating additive treatment effects from multiple randomized trials provides useful estimates of combination therapies. *J Clin Epidemiol* 2012;65(12):1282-8.

[B45] Norton EC, Miller MM, Wang JJ, Coyne K, Kleinman LC. Rank reversal in indirect comparisons. *Value Health* 2012;15(8):1137-40.

[B46] O'Regan C, Ghement I, Eyawo O, Guyatt GH, Mills EJ. Incorporating multiple interventions in meta-analysis: an evaluation of the mixed treatment comparison with the adjusted indirect comparison. *Trials* 2009;10:86.

[B47] Piepho HP, Williams ER, Madden LV. The use of two-way linear mixed models in multitreatment meta-analysis. *Biometrics* 2012;68(4):1269-77.

[B48] Price MJ, Welton NJ, Ades AE. Parameterization of treatment effects for meta-analysis in multi-state Markov models. *Stat Med* 2011;30(2):140-51.

[B49] Salanti G, Dias S, Welton NJ, Ades AE, Golfinopoulos V, Kyrgiou M, et al. Evaluating novel agent effects in multiple-treatments meta-regression. *Stat Med* 2010;29(23):2369-83.

[B50] Salanti G, Higgins JP, Ades AE, Ioannidis JP. Evaluation of networks of randomized trials. *Stat Methods Med Res* 2008;17(3):279-301.

[B51] Salanti G, Kavvoura FK, Ioannidis JP. Exploring the geometry of treatment networks. *Ann Intern Med* 2008;148(7):544-53.

[B52] Salanti G, Marinho V, Higgins JP. A case study of multiple-treatments meta-analysis demonstrates that covariates should be considered. *J Clin Epidemiol* 2009;62(8):857-64.

[B53] Saramago P, Sutton AJ, Cooper NJ, Manca A. Mixed treatment comparisons using aggregate and individual participant level data. *Stat Med* 2012;31(28):3516-36.

[B54] Schmidli H, Wandel S, Neuenschwander B. The network meta-analytic-predictive approach to non-inferiority trials. *Stat Methods Med Res* 2013;22(2):219-40.

[B55] Schmitz S, Adams R, Walsh C. The use of continuous data versus binary data in MTC models: a case study in rheumatoid arthritis. *BMC Med Res Methodol* 2012;12:167.

[B56] Signorovitch JE, Sikirica V, Erder MH, Xie J, Lu M, Hodgkins PS, et al. Matching-adjusted indirect comparisons: a new tool for timely comparative effectiveness research. *Value Health* 2012;15(6):940-7.

[B57] Song F, Glenny AM, Altman DG, Indirect comparison in evaluating relative efficacy illustrated by antimicrobial prophylaxis in colorectal surgery. *Control Clin Trials* 2000;21(5):488-97.

[B58] Song F, Xiong T, Parekh-Bhurke S, Loke YK, Sutton AJ, Eastwood AJ, et al. Inconsistency between direct and indirect comparisons of competing interventions: meta-epidemiological study. *BMJ* 2011;343:d4909.

[B59] Song F, Clark A, Bachmann MO, Maas J. Simulation evaluation of statistical properties of methods for indirect and mixed treatment comparisons. *BMC Med Res Methodol* 2012;12:138.

[B60] Song F, Harvey I, Lilford R. Adjusted indirect comparison may be less biased than direct comparison for evaluating new pharmaceutical interventions. *J Clin Epidemiol* 2008;61(5):455-63.

[B61] Spineli LM, Higgins JP, Cipriani A, Leucht S, Salanti G. Evaluating the impact of imputations for missing participant outcome data in a network meta-analysis. *Clin Trials* 2013;10(3):378-88.

[B62] Thorlund K, Mills E. Stability of additive treatment effects in multiple treatment comparison meta-analysis: a simulation study. *Clin Epidemiol* 2012;4(1):75-85.

[B63] Thorlund K, Mills EJ. Sample size and power considerations in network meta-analysis. *Syst Rev* 2012;1(1):41.

[B64] Thorlund K, Thabane L, Mills EJ. Modelling heterogeneity variances in multiple treatment comparison meta-analysis - are informative priors the better solution? *BMC Med Res Methodol* 2013;13:2.

[B65] Trinquart L, Abbé A, Ravaud P. Impact of reporting bias in network meta-analysis of antidepressant placebo-controlled trials. *PLoS One* 2012;7(4):e35219.

[B66] Trinquart L, Chatellier G, Ravaud P. Adjustment for reporting bias in network meta-analysis of antidepressant trials. *BMC Med Res Methodol* 2012;12:150.

[B67] van Valkenhoef G, Tervonen T, de Brock B, Hillege H. Algorithmic parameterization of mixed treatment comparisons. *Stat Comput* 2012;22(5):1099-111.

[B68] van Valkenhoef G, Tervonen T, Zhao J, de Brock B, Hillege HL, Postmus D. Multicriteria benefit-risk assessment using network meta-analysis. *J Clin Epidemiol* 2012;65(4):394-403.

[B69] Vandermeer BW, Buscemi N, Liang Y, Witmans M. Comparison of meta-analytic results of indirect, direct, and combined comparisons of drugs for chronic insomnia in adults: a case study. *Med Care* 2007;45(10):S166-72.

[B70] Veroniki AA, Vasiliadis HS, Higgins JP, Salanti G. Evaluation of inconsistency in networks of interventions. *Int J Epidemiol* 2013;42(1):332-45.

[B71] Wei YH, Higgins JP. Bayesian multivariate meta-analysis with multiple outcomes. *Stat Med* 2013;32(17):2911-34.

[B72] Wells GA, Sultan SA, Chen L, Khan M, Coyle D. Indirect Evidence: Indirect Treatment Comparisons in Meta-analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2009.

[B73] White IR. Multivariate random-effects meta-regression: updates to mvmeta. *Stata J* 2011;11(2):255-70.

[B74] Xiong T, Parekh-Bhurke S, Loke YK, Abdelhamid A, Sutton AJ, Eastwood AJ, et al. Overall similarity and consistency assessment scores are not sufficiently accurate for predicting discrepancy between direct and indirect comparison estimates. *J Clin Epidemiol* 2013;66(2):184-91.

# Appendix C: List of references of identified reviews of indirect comparison meta-analytic methods

[C1] Ades AE, Madan J, Welton NJ. Indirect and mixed treatment comparisons in arthritis research. *Rheumatology* 2011;50 Suppl 4:iv5-9.

[C2] Bafeta A, Trinquart L, Seror R, Ravaud P. Analysis of the systematic reviews process in reports of network meta-analyses: methodological systematic review. *BMJ* 2013;347:f3675.

[C3] Buti J, Glenny AM, Worthington HV, Nieri M, Baccini M. Network meta-analysis of randomised controlled trials: direct and indirect treatment comparisons. *Eur J Oral Implantol* 2011;4(1):55-62.

[C4] Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005;331:897-900.

[C5] Caro JJ, Ishak KJ. No head-to-head trial? Simulate the missing arms. *Pharmacoeconomics* 2010;28(10):957-67.

[C6] Carpiuc KT, Rosti G, Castagnetti F, Treur M, Stephens J. Indirect comparisons of second-generation tyrosine kinase inhibitors in CML: case study using baseline population characteristics. *Onco Targets Ther* 2010;3:205-10.

[C7] Cepeda MS, Fife D, Lobanov V, Sutton A. Can soccer predictions boost the use of indirect comparison to assess the safety of drugs? *Open Drug Saf J* 2011;2(1):25-8.

[C8] Chu J, Sloan CE, Freedberg KA, Yazdanpanah Y, Losina E. Drug efficacy by direct and adjusted indirect comparison to placebo: an illustration by Mycobacterium avium complex prophylaxis in HIV. *AIDS Res Ther* 2011;8:14.

[C9] Cipriani A, Higgins JP, Geddes JR, Salanti G. Conceptual and technical challenges in network meta-analysis. *Ann Intern Med* 2013;159(2):130-7.

[C10] Cipriani A, Barbui C, Rizzo C, Salanti G. What is a multiple treatments meta-analysis? *Epidemiol Psychiatr Sci* 2012;21(2):151-3.

[C11] Cooper NJ, Spiegelhalter D, Bujkiewicz S, Dequen P, Sutton AJ. Use of implicit and explicit bayesian methods in health technology assessment. *Int J Technol Assess Health Care* 2013;29(3):336-42.

[C12] Dias S, Sutton AJ, Ades AE, Welton NJ. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making* 2013;33(5):607-17.

[C13] Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making* 2013;33(5):641-56.

[C14] Dias S, Welton NJ, Sutton AJ, Ades AE. Evidence synthesis for decision making 5: the baseline natural history model. *Med Decis Making* 2013;33(5):657-70.

[C15] Donegan S, Williamson P, Gamble C, Tudur-Smith C. Indirect comparisons: a review of reporting and methodological quality. *PLoS One* 2010;5(11):e11054.

[C16] Edwards SJ, Clarke MJ, Wordsworth S, Borrill J. Indirect comparisons of treatments based on systematic reviews of randomised controlled trials. *Int J Clin Pract* 2009;63:841-54.

[C17] Gartlehner G, Moore CG. Direct versus indirect comparisons: a summary of the evidence. *Int J Technol Assess Health Care* 2008;24:170-7.

[C18] Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R, et al. Indirect comparisons of competing interventions. *Health Technol Assess* 2005;9(26):1-134, iii-iv.

[C19] Harenberg J, Weiss C. Clinical trials with new oral anticoagulants. Additive value of indirect comparisons also named network meta-analyses. *Hamostaseologie* 2013;33(1):62-70.

[C20] Hoaglin DC, Hawkins N, Jansen JP, Scott DA, Itzler R, Cappelleri JC, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. *Value Health* 2011;14(4):429-37.

[C21] Ioannidis JP. Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. *CMAJ* 2009;181(8):488-93.

[C22] Jansen JP, Naci H. Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect modifiers. *BMC Med* 2013;11(1):159.

[C23] Jansen JP, Crawford B, Bergman G, Stam W. Bayesian meta-analysis of multiple treatment comparisons: an introduction to mixed treatment comparisons. *Value Health* 2008;11(5):956-64.

[C24] Jansen JP, Fleurence R, Devine B, Itzler R, Barrett A, Hawkins N, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. *Value Health* 2011;14(4):417-28.

[C25] Jones B, Roger J, Lane PW, Lawton A, Fletcher C, Cappelleri JC, et al. Statistical approaches for conducting network meta-analysis in drug development. *Pharm Stat* 2011;10(6): 523-31.

[C26] Mavridis D, Salanti G. A practical introduction to multivariate meta-analysis. *Stat Methods Med Res* 2013;22(2):133-58.

[C27] Mills EJ, Ioannidis JP, Thorlund K, Schünemann HJ, Puhan MA, Guyatt GH. How to use an article reporting a multiple treatment comparison meta-analysis. *JAMA* 2012;308(12):1246-53.

[C28] Mills EJ, Bansback N, Ghement I, Thorlund K, Kelly S, Puhan MA, et al. Multiple treatment comparison meta-analyses: a step forward into complexity. *Clin Epidemiol* 2011;3(1):193-202.

[C29] Mills EJ, Thorlund K, Ioannidis JP. Demystifying trial networks and network meta-analysis. *BMJ* 2013;346:f2914.

[C30] Naci H, O'Connor AB. Assessing comparative effectiveness of new drugs before approval using prospective network meta-analyses. *J Clin Epidemiol* 2013;66(8):812-6.

[C31] Naci H, Fleurence R. Using indirect evidence to determine the comparative effectiveness of prescription drugs: do benefits outweigh risks? *Health Outcomes Res Med* 2011;2(4):e241-9.

[C32] Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol* 64(2):163-71.

[C33] Schacht A, Dyachkova Y, Walton RJ. Critical evaluation of mixed treatment comparison meta-analyses using examples assessing antidepressants and opioid detoxification treatments. Int *J Methods Psychiatr Res* 2013;22(2):166-74.

[C34] Senn S, Gavini F, Magrez D, Scheen A. Issues in performing a network meta-analysis. *Stat Methods Med Res* 2013;22(2):169-89.

[C35] Snapinn S, Jiang Q. Indirect comparisons in the comparative efficacy and non-inferiority settings. *Pharm Stat* 2011;10(5):420-6.

[C36] Sobieraj DM, Cappelleri JC, Baker WL, Phung OJ, White CM, Coleman CI. Methods used to conduct and report Bayesian mixed treatment comparisons published in the medical literature: a systematic review. *BMJ Open* 2013;3(7):e003111.

[C37] Song F, Loke YK, Walsh T, Glenny AM, Eastwood AJ, Altman DG. Methodological problems in the use of indirect comparisons for evaluating healthcare interventions: survey of published systematic reviews. *BMJ* 2009;338:b1147.

[C38] Song F, Altman DG, Glenny AM, Deeks JJ. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ* 2003;326(7387):472-5.

[C39] Sutton A, Ades AE, Cooper N, Abrams K. Use of indirect and mixed treatment comparisons for technology assessment. *Pharmacoeconomics* 2008;26(9):753-67.

[C40] Tan SH, Bujkiewicz S, Sutton A, Dequen P, Cooper N. Presentational approaches used in the UK for reporting evidence synthesis using indirect and mixed treatment comparisons. *J Health Serv Res Policy* 2013;18(4):224-32.

[C41] Thorlund K, Druyts E, Aviña-Zubieta JA, Wu P, Milles EJ. Why the findings of published multiple treatment comparison meta-analyses of biologic treatments for rheumatoid

arthritis are different: an overview of recurrent methodological shortcomings. *Ann Rheum Dis* 2013;72(9): 1524-35.

[C42] Woods BS, Hawkins N, Scott DA. Network meta-analysis on the log-hazard scale, combining count and hazard ratio statistics accounting for multi-arm trials: a tutorial. *BMC Med Res Methodol* 2010;10:54.

# Appendix D: List of references of identified empirical applications of indirect comparison meta-analytic methods

Component 1: D1-143
Component 2: D144-152
Component 3: D153-160
Component 4: D161-166
Component 5: D167-171
Component 6: D172-176
Component 7: D177-181
Component 8: D182-186
Component 9: D187-191
Component 10: D192-196
Component 11: D197-200
Component 12: D201-204
Component 13: D205-208
Component 14: D209-212
Component 15: D213-216
Component 16: D217-220
Component 17: D221-224
Component 18: D225-227
Component 19: D228-230
Component 20: D231-233
Component 21: D234-235
Component 22: D236-237
Component 23: D238-239
Component 24: D240-241
Component 25: D242-243
Component 26: D244-245
Component 27: D246-247
Component 28: D248-249
Component 29: D250-251
Component 30: D252-253
Component 31: D254-255
Component 32: D256-257
Component 33: D258-259
Component 34: D260-261
Component 35: D262-263
Component 36: D264-265
Component 37: D266-267
Component 38: D268-269
Component 39: D270-271
Component 40: D272
Component 41: D273
Component 42: D274

Component 43: D275
Component 44: D276
Component 45: D277
Component 46: D278
Component 47: D279
Component 48: D280
Component 49: D281
Component 50: D282
Component 51: D283
Component 52: D284
Component 53: D285
Component 54: D286
Component 55: D287
Component 56: D288
Component 57: D289
Component 58: D290
Component 59: D291
Component 60: D292
Component 61: D293
Component 62: D294
Component 63: D295
Component 64: D296
Component 65: D297
Component 66: D298
Component 67: D299
Component 68: D300
Component 69: D301
Component 70: D302
Component 71: D303
Component 72: D304
Component 73: D305
Component 74: D306
Component 75: D307
Component 76: D308
Component 77: D309
Component 78: D310
Component 79: D311
Component 80: D312
Component 81: D313
Component 82: D314
Component 83: D315
Component 84: D316
Component 85: D317
Component 86: D318
Component 87: D319
Component 88: D320

Component 89: D321
Component 90: D322
Component 91: D323
Component 92: D324
Component 93: D325
Component 94: D326
Component 95: D327
Component 96: D328
Component 97: D329
Component 98: D330
Component 99: D331
Component 100: D332
Component 101: D333
Component 102: D334
Component 103: D335
Component 104: D336
Component 105: D337
Component 106: D338
Component 107: D339
Component 108: D340
Component 109: D341
Component 110: D342
Component 111: D343
Component 112: D344
Component 113: D345
Component 114: D346
Component 115: D347
Component 116: D348
Component 117: D349
Component 118: D350
Component 119: D351
Component 120: D352
Component 121: D353
Component 122: D354
Component 123: D355
Component 124: D356
Component 125: D357
Component 126: D358
Component 127: D359
Component 128: D360
Component 129: D361

[D1] Akbar A, Abu Dayyeh BK, Baron TH, Wang Z, Altayar O, Murad MH. Rectal nonsteroidal anti-inflammatory drugs are superior to pancreatic duct stents in preventing pancreatitis after endoscopic retrograde cholangiopancreatography: a network meta-analysis. *Clin Gastroenterol Hepatol* 2013;11(7):778-83.

[D2] Akshintala VS, Hutfless SM, Colantuoni E, Kim KJ, Khashab MA, Li T, et al. Systematic review with network meta-analysis: pharmacological prophylaxis against post-ERCP pancreatitis. *Aliment Pharmacol Ther* 2013;38(11-12):1325-37.

[D3] Alberton M, Wu P, Druyts E, Briel M, Mills EJ. Adverse events associated with individual statin treatments for cardiovascular disease: an indirect comparison meta-analysis. *QJM* 2012;105(2):145-57.

[D4] Alonso-Coello P, Zhou Q, Guyatt G. Home-monitoring of oral anticoagulation vs. dabigatran. An indirect comparison. *Thromb Haemost* 2012;108(4):647-53.

[D5] Baker WL, Baker EL, Coleman CI. Pharmacologic treatments for chronic obstructive pulmonary disease: a mixed-treatment comparison meta-analysis. *Pharmacotherapy* 2009;29(8): 891-905.

[D6] Baker WL, Phung OJ. Systematic review and adjusted indirect comparison meta-analysis of oral anticoagulants in atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2012;5(5):711-9.

[D7] Bekkering GE, Abou-Setta AM, Kleijnen J. The application of quantitative methods for identifying and exploring the presence of bias in systematic reviews: PDE-5 inhibitors for erectile dysfunction. *Int J Impot Res* 2008;20(3):264-77.

[D8] Bekkering GE, Soares-Weiser K, Reid K, Kessels AG, Dahan A, Treede RD, et al. Can morphine still be considered to be the standard for treating chronic pain? A systematic review including pair-wise and network meta-analyses. *Curr Med Res Opin* 2011;27(7):1477-91.

[D9] Bergman GJ, Hochberg MC, Boers M, Wintfeld N, Kielhorn A, Jansen JP. Indirect comparison of tocilizumab and other biologic agents in patients with rheumatoid arthritis and inadequate response to disease-modifying antirheumatic drugs. *Semin Arthritis Rheum* 2010;39(6):425-41.

[D10] Berry SM, Broglio KR, Berry DA. Addressing the incremental benefit of histamine dihydrochloride when added to interleukin-2 in treating acute myeloid leukemia: a Bayesian meta-analysis. *Cancer Invest* 2011;29(4):293-9.

[D11] Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet* 2013;382(9894):769-79.

[D12] Bottomley JM, Taylor RS, Ryttov J. The effectiveness of two-compound formulation calcipotriol and betamethasone dipropionate gel in the treatment of moderately severe scalp psoriasis: a systematic review of direct and indirect evidence. *Curr Med Res Opin* 2011;27(1):251-68.

[D13] Buscemi N, Vandermeer B, Friesen C, Bialy L, Tubman M, Ospina M, et al. The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs. *J Gen Intern Med* 2007;22(9):1335-50.

[D14] Buser N, Ivic S, Kessler TM, Kessels AG, Bachmann LM. Efficacy and adverse events of antimuscarinics for treating overactive bladder: network meta-analyses. *Eur Urol* 2012;62(6):1040-60.

[D15] Castellucci LA, Cameron C, Le Gal G, Rodger MA, Coyle D, Wells PS, et al. Efficacy and safety outcomes of oral anticoagulants and antiplatelet drugs in the secondary prevention of venous thromboembolism: systematic review and network meta-analysis. *BMJ* 2013;347:f5133.

[D16] Choy E, Marshall D, Gabriel ZL, Mitchell SA, Gylee E, Dakin HA. A systematic review and mixed treatment comparison of the efficacy of pharmacological treatments for fibromyalgia. *Semin Arthritis Rheum* 2011;41(3):335-45.e6.

[D17] Cipriani A, Furukawa TA, Salanti G, Geddes JR, Higgins JP, Churchill R, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* 2009;373(9665):746-58.

[D18] Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, et al. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. *Lancet* 2011;378(9799):1306-15.

[D19] Cohen A, Drost P, Marchant N, Mitchell S, Orme M, Rublee D, et al. The efficacy and safety of pharmacological prophylaxis of venous thromboembolism following elective knee or hip replacement: systematic review and network meta-analysis. *Clin Appl Thromb Hemost* 2012;18(6):611-27.

[D20] Coleman CI, Baker WL, Kluger J, White CM. Antihypertensive medication and their impact on cancer incidence: a mixed treatment comparison meta-analysis of randomized controlled trials. *J Hypertens* 2008;26(4):622-9.

[D21] Cooper CL, Druyts E, Thorlund K, Nachega JB, El Khoury AC, O'Regan C, et al. Boceprevir and telaprevir for the treatment of chronic hepatitis C genotype 1 infection: an indirect comparison meta-analysis. *Ther Clin Risk Manag* 2012;8:105-30.

[D22] Cooper C, Lester R, Thorlund K, Druyts E, El Khoury AC, Yaya S, et al. Direct-acting antiviral therapies for hepatitis c genotype 1 infection: a multiple treatment comparison meta-analysis. *QJM* 2013;106(2):153-63.

[D23] Cooper NJ, Sutton AJ, Lu G, Khunti K. Mixed comparison of stroke prevention treatments in individuals with nonrheumatic atrial fibrillation. Arch Intern Med 2006;166(12):1269-75.

[D24] Cope S, Cupkun-Niggli G, Gale R, Jardim JR, Jansen JP. Comparative efficacy of indacaterol 150 mug and 300 mug versus fixed-dose combinations of formoterol + budesonide or

salmeterol + fluticasone for the treatment of chronic obstructive pulmonary disease - a network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2011;6(1):329-44.

[D25] Cope S, Zhang J, Williams J, Jansen JP. Efficacy of once-daily indacaterol 75 µg relative to alternative bronchodilators in COPD: a study level and a patient level network meta-analysis. BMC Pulm Med 2012;12:29.

[D26] Cope S, Kraemer M, Zhang J, Capkun-Niggli G, Jansen JP. Efficacy of indacaterol 75 mug versus fixed-dose combinations of formoterol-budesonide or salmeterol-fluticasone for COPD: a network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2012;7:415-20.

[D27] Cope S, Capkun-Ziggli G, Gale R, Lassen C, Owen R, Ouwens MJ, et al. Efficacy of once-daily indacaterol relative to alternative bronchodilators in COPD: a patient-level mixed treatment comparison. *Value Health* 2012;15(3):524-33.

[D28] Cope S, Donohue JF, Jansen JP, Kraemer M, Capkun-Niggli G, Baldwin M, et al. Comparative efficacy of long-acting bronchodilators for COPD: a network meta-analysis. *Respir Res* 2013;14:100.

[D29] Cope S, Ouwens MJ, Jansen JP, Schmid P. Progression-free survival with fulvestrant 500 mg and alternative endocrine therapies as second-line treatment for advanced breast cancer: a network meta-analysis with parametric survival models. *Value Health* 2013;16(2):403-17.

[D30] Dakin H, Fidler C, Harper H. Mixed treatment comparison meta-analysis evaluating the relative efficacy of nucleos(t)ides for treatment of nucleos(t)ide-naive patients with chronic hepatitis B. *Value Health* 2010;13(8):934-45.

[D31] Dakin HA, Welton NJ, Ades AE, Collins S, Orme M, Kelly S. Mixed treatment comparison of repeated measurements of a continuous endpoint: an example using topical treatments for primary open-angle glaucoma and ocular hypertension. *Stat Med* 2011;30(20):2511-35.

[D32] Dequen P, Lorigan P, Jansen JP, van Baardewijk M, Ouwens MJ, Kotapati S. Systematic review and network meta-analysis of overall survival comparing 3 mg/kg ipilimumab with alternative therapies in the management of pretreated patients with unresectable stage III or IV melanoma. *Oncologist* 2012;17(11):1376-85.

[D33] Dunkley AJ, Charles K, Gray LJ, Camosso-Stefinovic J, Davies MJ, Khunti K. Effectiveness of interventions for reducing diabetes and cardiovascular disease risk in people with metabolic syndrome: systematic review and mixed treatment comparison meta-analysis. *Diabetes Obes Metab* 2012;14(7):616-25.

[D34] Eckert L, Falissard B. Using meta-regression in performing indirect-comparisons: Comparing escitalopram with venlafaxine XR. *Curr Med Res Opin* 2006;22(11):2313-21.

[D35] Eckert L, Lançon C. Duloxetine compared with fluoxetine and venlafaxine: use of meta-regression analysis for indirect comparisons. *BMC Psychiatry* 2006;6:30.

[D36] Edwards SJ, Lind T, Lundell L, Das R. Systematic review: standard- and double-dose proton pump inhibitors for the healing of severe erosive oesophagitis - a mixed treatment comparison of randomized controlled trials. *Aliment Pharmacol Ther* 2009;30(6):547-56.

[D37] Edwards SJ, Smith CJ. Tolerability of atypical antipsychotics in the treatment of adults with schizophrenia or bipolar disorder: a mixed treatment comparison of randomized controlled trials. *Clin Ther* 2009;31:1345-59.

[D38] Edwards SJ, Clarke MJ, Wordsworth S, Welton NJ. Carbapenems versus other beta-lactams in the treatment of hospitalised patients with infection: a mixed treatment comparison. *Curr Med Res Opin* 2009;25(1):251-61.

[D39] Eisenberg MJ, Fillion KB, Yavin D, Bélisle P, Mottillo S, Joseph L, et al. Pharmacotherapies for smoking cessation: a meta-analysis of randomized controlled trials. *CMAJ* 2008;179(2):135-44.

[D40] Fakhoury W, Lockhart I, Kotchie RW, Aagren M, LeReun C. Indirect comparison of once daily insulin detemir and glargine in reducing weight gain and hypoglycaemic episodes when administered in addition to conventional oral anti-diabetic therapy in patients with type-2 diabetes. *Pharmacology* 2008;82(2):156-63.

[D41] Filippini G, Del Giovane C, Vacchi L, D'Amico R, Di Pietrantonj C, Beecher D, et al. Immunomodulators and immunosuppressants for multiple sclerosis: a network meta-analysis. *Cochrane Database of Syst Rev* 2013;6;CD008933.

[D42] Fox BD, Kahn SR, Langleben D, Eisenberg MJ, Shimony A. Efficacy and safety of novel oral anticoagulants for treatment of acute venous thromboembolism: direct and adjusted indirect meta-analysis of randomised controlled trials. *BMJ* 2012;345:e7498.

[D43] Freemantle N, Lafuente-Lafuente C, Mitchell S, Eckert L, Reynolds M. Mixed treatment comparison of dronedarone, amiodarone, sotalol, flecainide, and propafenone, for the management of atrial fibrillation. *Europace* 2011;13(3):329-45.

[D44] Freemantle N, Tharmanathan P, Herbrecht R. Systematic review and mixed treatment comparison of randomized evidence for empirical, pre-emptive and directed treatment strategies for invasive mould disease. *J Antimicrob Chemother* 2011;66 Suppl 1:i25-35.

[D45] Freemantle N, Cooper C, Diez-Perez A, Gitlin M, Radcliffe H, Shepherd S, et al. Results of indirect and mixed treatment comparison of fracture efficacy for osteoporosis treatments: a meta-analysis. *Osteoporos Int* 2013;24(1):209-17.

[D46] Golfinopoulos V, Salanti G, Pavlidis N, Ioannidis JP. Survival and disease-progression benefits with treatment regimens for advanced colorectal cancer: a meta-analysis. *Lancet Oncol* 2007;8(10):898-911.

[D47] Golfinopoulos V, Pentheroudakis G, Salanti G, Nearchou AD, Ioannidis JP, Pavlidis N. Comparative survival with diverse chemotherapy regimens for cancer of unknown primary site: multiple-treatments meta-analysis. *Cancer Treat Rev* 2009;35(7):570-3.

[D48] Gray LJ, Cooper N, Dunkley A, Warren FC, Ara R, Abrams K, et al. A systematic review and mixed treatment comparison of pharmacological interventions for the treatment of obesity. *Obes Rev* 2012;13(6):483-98.

[D49] Guyot P, Taylor P, Christensen R, Pericleous L, Poncet C, Lebmeier M, et al. Abatacept with methotrexate versus other biologic agents in treatment of patients with active rheumatoid arthritis despite methotrexate: a network meta-analysis. *Arthritis Res Ther* 2011;13(6):R204.

[D50] Haas DM, Caldwell DM, Kirkpatrick P McIntosh JJ, Welton NJ. Tocolytic therapy for preterm delivery: systematic review and network meta-analysis. *BMJ* 2012;345:e6226.

[D51] Halpin DM, Gray J, Edwards SJ, Morais J, Singh D. Budesonide/formoterol vs. salmeterol/fluticasone in COPD: a systematic review and adjusted indirect comparison of pneumonia in randomised controlled trials. *Int J Clin Pract* 2011;65(7):764-74.

[D52] Harenberg J, Marx S, Diener HC, Lip GY, Marder VJ, Wehling M, et al. Comparison of efficacy and safety of dabigatran, rivaroxaban and apixaban in patients with atrial fibrillation using network meta-analysis. *Int Angiol* 2012;31(4):330-9.

[D53] Harenberg J, Marx S, Dahl OE, Marder VJ, Schulze A, Wehling M, et al. Interpretation of endpoints in a network meta-analysis of new oral anticoagulants following total hip or total knee replacement surgery. *Thromb Haemost* 2012;108(5):903-12.

[D54] Hartling L, Fernandes RM, Bialy L, Milne A, Johnson D, Plint A, et al. Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis. *BMJ* 2011;342:d1714.

[D55] Häuser W, Petzke F, Sommer C. Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. *J Pain* 2010;11(6):505-21.

[D56] Häuser W, Petzke F, Üçeyler N, Sommer C. Comparative efficacy and acceptability of amitriptyline, duloxetine and milnacipran in fibromyalgia syndrome: a systematic review with meta-analysis. *Rheumatology* 2011;50(3):532-43.

[D57] Henry D, Carless P, Fergusson D, Laupacis A. The safety of aprotinin and lysine-derived antifibrinolytic drugs in cardiac surgery: a meta-analysis. *CMAJ* 2009;180(2):183-93.

[D58] Hochberg MC, Tracy JK, Hawkins-Holt M, Flores RH. Comparison of the efficacy of the tumour necrosis factor α blocking agents adalimumab, etanercept, and infliximab when added to methotrexate in patients with active rheumatoid arthritis. *Ann Rheum Dis* 2003;62 Supply 2:13-6.

[D59] Hochberg MC, Berry S, Broglio K, Rosenblatt L, Nadkarni A, Trivedi D, et al. Mixed treatment comparison of efficacy and tolerability of biologic agents in patients with rheumatoid arthritis. *Curr Med Res Opin* 2013;29(10):1213-22.

[D60] Hopkins RB, Goeree R, Pullenayegum E, Adachi JD, Papaioannou A, Xie F, et al. The relative efficacy of nine osteoporosis medications for reducing the rate of fractures in post-menopausal women. *BMC Musculoskelet Disord* 2011;12:209.

[D61] Howell N, Senanayake E, Freemantle N, Pagano D. Putting the record straight on aprotinin as safe and effective: results from a mixed treatment meta-analysis of trials of aprotinin. *J Thorac Cardiovasc Surg* 2013;145(1):234-40.

[D62] Hutton B, Joseph L, Fergusson D, Mazer CD, Shapiro S, Tinmouth A. Risks of harms using antifibrinolytics in cardiac surgery: systematic review and network meta-analysis of randomised and observational studies. BMJ 2012;345:e5798.

[D63] Jansen JP, Bergman GJ, Huels J, Olson M. Prevention of vertebral fractures in osteoporosis: mixed treatment comparison of bisphosphonate therapies. *Curr Med Res Opin* 2009;25(8):1861-8.

[D64] Jansen JP, Bergman GJ, Huels J, Olson M. The efficacy of bisphosphonates in the prevention of vertebral, hip, and nonvertebral-nonhip fractures in osteoporosis: a network meta-analysis. *Semin Arthritis Rheum* 2011;40(4):275-84.e1-2.

[D65] Kinnaird T, Medic G, Casella G, Schiele F, Kaul U, Radke PW, et al. Relative efficacy of bivalirudin versus heparin monotherapy in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: a network meta-analysis. *J Blood Med* 2013;4:129-40.

[D66] Knottnerus BJ, Grigoryan L, Geerlings SE, Moll van Charante EP, Verheij TJ, Kessels AG, et al. Comparative effectiveness of antibiotics for uncomplicated urinary tract infections: network meta-analysis of randomized trials. *Fam Pract* 2012;29(6):659-70.

[D67] Krogh TP, Bartels EM, Ellingsen T, Stengaard-Pedersen K, Buchbinder R, Fredberg U, et al. Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network meta-analysis of randomized controlled trials. *Am J Sports Med* 2013;41(6):1435-46.

[D68] Kwok CS, Yeong JK, Loke YK. Meta-analysis: risk of fractures with acid-suppressing medication. *Bone* 2011;48(4):768-76.

[D69] Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, Loke YK. Risk of Clostridium difficile infection with acid suppressing drugs and antibiotics: meta-analysis. *Am J Gastroenterol* 2012;107(7):1011-9.

[D70] Kwok CS, Pradhan S, Yeong JK, Loke YK. Relative effects of two different enoxaparin regimens as comparators against newer oral anticoagulants: meta-analysis and adjusted indirect comparison. *Chest* 2013;144(2):593-600.

[D71] Kyrgiou M, Salanti G, Pavlidis N, Paraskevaidis E, Ioannidis JP. Survival benefits with diverse chemotherapy regimens for ovarian cancer: meta-analysis of multiple treatments. *J Natl Cancer Inst* 2006;98(22):1655-63.

[D72] Lanas A, Wu P, Medin J, Mills EJ. Low doses of acetylsalicylic acid increase risk of gastrointestinal bleeding in a meta-Analysis. *Clin Gastroenterol Hepatol* 2011;9(9):762-82.e6.

[D73] Lang SH, Manning N, Armstrong N, Misso K, Allen A, Di Nisio M, et al. Treatment with tirofiban for acute coronary syndrome (ACS): a systematic review and network analysis. *Curr Med Res Opin* 2012;28(3):351-70.

[D74] Larkin J, Paine A, Tumur I, Cappelleri JC, Healey PJ Sr, Foley G, et al. Second-line treatments for the management of advanced renal cell carcinoma: systematic review and meta-analysis. *Expert Opin Pharmacother* 2013;14(1):27-39.

[D75] Lereun C, Wells P, Diamantopoulos A, Rasul F, Lees M, Sengupta N. An indirect comparison, via enoxaparin, of rivaroxaban with dabigatran in the prevention of venous thromboembolism after hip or knee replacement. J Med Econ 2011;14(2):238-44.

[D76] Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, Richter F, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet* 2013;382(9896):951-62.

[D77] Lip GYH, Larsen TB, Skjøth F, Rasmussen LH. Indirect comparisons of new oral anticoagulant drugs for efficacy and safety when used for stroke prevention in atrial fibrillation. *J Am Coll Cardiol* 2012;60(8):738-46.

[D78] Littlewood KJ, Higashi K, Jansen JPO, Capkun-Niggli G, Balp MM, Doering G, et al. A network meta-analysis of the efficacy of inhaled antibiotics for chronic Pseudomonas infections in cystic fibrosis. *J Cyst Fibros* 2012;11(5):419-26.

[D79] Loke YK, Kwok CS. Dabigatran and rivaroxaban for prevention of venous thromboembolism - systematic review and adjusted indirect comparison. *J Clin Pharm Ther* 2011;36(1):111-24.

[D80] Manzoli L, Salanti G, De Vito C, Boccia A, Ioannidis JP, Villari P. Immunogenicity and adverse events of avian influenza A H5N1 vaccine in healthy adults: multiple-treatments meta-analysis. *Lancet Infect Dis* 2009;9(8):482-92.

[D81] Manzoli L, De Vito C, Salanti G, D'Addario M, Villari P, Ioannidis JP. Meta-analysis of the immunogenicity and tolerability of pandemic influenza A 2009 (H1N1) vaccines. PLoS One 2011;6(9):e24384.

[D82] Mauri D, Polyzos NP, Salanti G, Pavlidis N, Ioannidis JP. Multiple-treatments meta-analysis of chemotherapy and targeted therapies in advanced breast cancer. *J Natl Cancer Inst* 2008;100(24):1780-91.

[D83] McIntosh B, Cameron C, Singh SR, Yu C, Ahuja T, Welton NJ, et al. Second-line therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed-treatment comparison meta-analysis. *Open Med* 2011;5(1):35-48.

[D84] McIntosh B, Cameron C, Singh SR, Yu C, Dolovich L, Houlden R. Choice of therapy in patients with type 2 diabetes inadequately controlled with metformin and a sulphonylurea: a systematic review and mixed-treatment comparison meta-analysis. *Open Med* 2012;6(2):e62-74.

[D85] Meissner K, Fässler M, Rücker G, Kleijnen J, Hróbjartsson A, Schneider A, et al. Differential effectiveness of placebo treatments: a systematic review of migraine prophylaxis. *JAMA Intern Med* 2013;173(21):1941-51.

[D86] Mills EJ, Rachlis B, Wu P, Devereaux PJ, Arora P, Perri D. Primary prevention of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients. *J Am Coll Cardiol* 2008;52(22):1769-81.

[D87] Mills EJ, Perri D, Cooper C, Nachega JB, Wu P, Tleyjeh I, et al. Antifungal treatment for invasive Candida infections: a mixed treatment comparison meta-analysis. *Ann Clin Microbiol Antimicrob* 2009;8:23.

[D88] Mills EJ, Rachlis B, O'Regan C, Thabane L, Perri D. Metastatic renal cell cancer treatments: an indirect comparison meta-analysis. *BMC Cancer* 2009;9:34.

[D89] Mills EJ, Wu P, Spurden D, Ebbert JO, Wilson K. Efficacy of pharmacotherapies for short-term smoking abstinance: a systematic review and meta-analysis. Harm Reduct J 2009;6:25.

[D90] Mills EJ, Druyts E, Ghement I, Puhan MA. Pharmacotherapies for chronic obstructive pulmonary disease: a multiple treatment comparison meta-analysis. *Clin Epidemiol* 2011;3(1):107-29.

[D91] Mills EJ, Wu P, Chong G, Ghement I, Singh S, Akl EA, et al. Efficacy and safety of statin treatment for cardiovascular disease: a network meta-analysis of 170,255 patients from 76 randomized trials. *QJM* 2011;104(2):109-24.

[D92] Mills EJ, Wu P, Lockhart I, Thorlund K, Phuan M, Ebbert JO. Comparisons of high-dose and combination nicotine replacement therapy, varenicline, and bupropion for smoking cessation: a systematic review and multiple treatment meta-analysis. *Ann Med* 2012;44(6):588-97.

[D93] Mitchell SA, Simon TA, Raza S, Jakouloff D, Orme ME, Lockhart I, et al. The efficacy and safety of oral anticoagulants in warfarin-suitable patients with nonvalvular atrial fibrillation: systematic review and meta-analysis. *Clin Appl Thromb Hemost* 2013;19(6):619-31.

[D94] Murad MH, Drake MT, Mullan RJ, Mauck KF, Stuart LM, Lane MA, et al. Clinical review. Comparative effectiveness of drug treatments to prevent fragility fractures: a systematic review and network meta-analysis. *J Clin Endocrinol Metab* 2012;97(6):1871-80.

[D95] Naci H, Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ* 2013;347:f5577.

[D96] Naci H, Brugts JJ, Ades T. Comparative tolerability and harms of individual statins: a study-level network meta-analysis of 246 955 participants from 135 randomized, controlled trials. *Circ Cardiovasc Qual Outcomes* 2013;6(4):390-9.

[D97] Naci H, Brugts JJ, Fleurence R, Tsoi B, Toor H, Ades AE. Comparative benefits of statins in the primary and secondary prevention of major coronary events and all-cause mortality: a network meta-analysis of placebo-controlled and active-comparator trials. *Eur J Prev Cardiol* 2013;20(4):641-57.

[D98] Naci H, Brugts JJ, Fleurence R, Ades AE. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. *Eur J Prev Cardiol* 2013;20(4):658-70.

[D99] Naci H, Brugts JJ, Fleurence R, Ades AE. Comparative effects of statins on major cerebrovascular events: a multiple-treatments meta-analysis of placebo-controlled and active-comparator trials. *QJM* 2013;106(4):299-306.

[D100] Naudet F, Millet B, Charlier P, Reymann JM, Maria AS, Falissard B. Which placebo to cure depression? A thought-provoking network meta-analysis. *BMC Med* 2013;11(1):230.

[D101] Navarese EP, Buffon A, Andreotti F, Kozinski M, Welton N, Fabiszak T, et al. Meta-analysis of impact of different types and doses of statins on new-onset diabetes mellitus. *Am J Cardiol* 2013;111(8):1123-30.

[D102] Nüesch E, Häuser W, Bernardy K, Barth J, Jüni P. Comparative efficacy of pharmacological and non-pharmacological interventions in fibromyalgia syndrome: network meta-analysis. *Ann Rheum Dis* 2013;72(6):955-62.

[D103] Orme M, Collins S, Dakin H, Kelly S, Loftus J. Mixed treatment comparison and meta-regression of the efficacy and safety of prostaglandin analogues and comparators for primary open-angle glaucoma and ocular hypertension. *Curr Med Res Opin* 2010;26(3):511-28.

[D104] Orme ME, Macgilchrist KS, Mitchell S, Spurden D, Bird A. Systematic review and network meta-analysis of combination and monotherapy treatments in disease-modifying antirheumatic drug-experienced patients with rheumatoid arthritis: analysis of American college of Rheumatology criteria scores 20, 50, and 70. *Biologics* 2012;6:429-64.

[D105] Phung OJ, Scholle JM, Talwar M, Coleman CI. Effect of noninsulin antidiabetic drugs added to metformin therapy on glycemic control, weight gain, and hypoglycemia in type 2 diabetes. *JAMA* 2010;303(14):1410-8.

[D106] Phung OJ, Kahn SR, Cook DJ, Murad MH. Dosing frequency of unfractionated heparin thromboprophylaxis: a meta-analysis. *Chest* 2011;140(2):374-81.

[D107] Phung OJ, Sood NA, Sill BE, Coleman CI. Oral anti-diabetic drugs for the prevention of Type 2 diabetes. *Diabet Med* 2011;28(8):948-64.

[D108] Puhan MA, Bachmann LM, Kleijnen J, Ter Riet G, Kessels AG. Inhaled drugs to reduce exacerbations in patients with chronic obstructive pulmonary disease: a network meta-analysis. *BMC Med* 2009;7:2.

[D109] Quilici S, Abrams KR, Nicolas A, Martin M, Petit C, Lleu PL, et al. Meta-analysis of the efficacy and tolerability of pramipexole versus ropinirole in the treatment of restless legs syndrome. *Sleep Med* 2008;9(7):715-26.

[D110] Quilici S, Chancellor J, Löthgren M, Simon D, Said G, Le TK, et al. Meta-analysis of duloxetine vs. pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain. *BMC Neurol* 2009;9:6.

[D111] Rashiq S, Vandermeer B, Abou-Setta AM, Beaupre LA, Jones CA, Dryden DM. Efficacy of supplemental peripheral nerve blockade for hip fracture surgery: multiple treatment comparison. *Can J Anesth* 2013;60(3):230-43.

[D112] Rasmussen LH, Larsen TB, Graungaard T, Skjøth F, Lip GY. Primary and secondary prevention with new oral anticoagulant drugs for stroke prevention in atrial fibrillation: indirect comparison analysis. *BMJ* 2012;345:e7097.

[D113] Riemsma R, Simons JP, Bashir Z, Gooch CL, Kleijnen J. Systematic Review of topotecan (Hycamtin) in relapsed small cell lung cancer. *BMC Cancer* 2010;10:436.

[D114] Riemsma R, Forbes CA, Kessels A, Lykopoulos K, Amonkar MM, Rea DW, et al. Systematic review of aromatase inhibitors in the first-line treatment for hormone sensitive advanced or metastatic breast cancer. *Breast Cancer Res Treat* 2010;123(1):9-24.

[D115] Riemsma R, Forbes C, Harker J, Worthy G, Misso K, Schäfer M, et al. Systematic review of tapentadol in chronic severe pain. *Curr Med Res Opin* 2011;27(10):1907-30.

[D116] Riemsma R, Forbes CA, Amonkar MM, Lykopoulos K, Diaz JR, Kleijnen J, et al. Systematic review of lapatinib in combination with letrozole compared with other first-line treatments for hormone receptor positive(HR+) and HER2+ advanced or metastatic breast cancer(MBC). *Curr Med Res Opin* 2012;28(8):1263-79.

[D117] Roskell NS, Lip GY, Noack H, Clemens A, Plumb JM. Treatments for stroke prevention in atrial fibrillation: a network meta-analysis and indirect comparisons versus dabigatran etexilate. *Thromb Haemost* 2010;104(6):1106-15.

[D118] Roskell NS, Beard SM, Zhao Y, Le TK. A meta-analysis of pain response in the treatment of fibromyalgia. *Pain Pract* 2011;11(6):516-27.

[D119] Roskell NS, Zimovetz EA, Rycroft CE, Eckert BJ, Tyas DA. Annualized relapse rate of first-line treatments for multiple sclerosis: a meta-analysis, including indirect comparisons versus fingolimod. *Curr Med Res Opin* 2012;28(5):767-80.

[D120] Salliot C, Finckh A, Katchamart W, Lu Y, Sun Y, Bombardier C, et al. Indirect comparisons of the efficacy of biological antirheumatic agents in rheumatoid arthritis in patients with an inadequate response to conventional disease-modifying antirheumatic drugs or to an anti-tumour necrosis factor agent: a meta-analysis. *Ann Rheum Dis* 2011;70(2):266-71.

[D121] Singh JA, Christensen R, Wells GA, Suarez-Almazor ME, Buchbinder R, Lopez-Olivo MA, et al. A network meta-analysis of randomized controlled trials of biologics for rheumatoid arthritis: a Cochrane overview. *CMAJ* 2009;181(11):787-96.

[D122] Singh JA, Wells GA, Christensen R, Tanjong Ghogomu E, Maxwell L, Macdonald JK, et al. Adverse effects of biologics: a network meta-analysis and Cochrane overview. *Cochrane Database Syst Rev* 2011;(2):CD008794.

[D123] Skoetz N, Trelle S, Rancea M, Haverkamp H, Diehl V, Engert A, et al. Effect of initial treatment strategy on survival of patients with advanced-stage Hodgkin's lymphoma: a systematic review and network meta-analysis. *Lancet Oncol* 2013;14(10):943-52.

[D124] Snedecor SJ, Sudharshan L, Cappelleri JC, Sadosky A, Desai R, Jalundhwala YJ, et al. Systematic review and comparison of pharmacologic therapies for neuropathic pain associated with spinal cord injury. *J Pain Res* 2013;6:539-47.

[D125] Stam WB, Jansen J, Taylor S. Efficacy of etoricoxib, celecoxib, lumiracoxib, non-selective NSAIDs, and acetaminophen in osteoarthritis: a mixed treatment comparison. *Open Rheumatol J* 2012;6(1):6-20.

[D126] Steiner S, Moertl D, Chen L, Coyle D, Wells GA. Network meta-analysis of prasugrel, ticagrelor, high- and standard-dose clopidogrel in patients scheduled for percutaneous coronary interventions. *Thromb Haemost* 2012;108(2):318-27.

[D127] Strassmann R, Bausch B, Spaar A, Kleijnen J, Braendli O, Puhan MA. Smoking cessation interventions in COPD: a network meta-analysis of randomised trials. *Eur Respir J* 2009;34(3):634-40.

[D128] Sundaresh V, Brito JP, Wang Z, Prokop LJ, Stan MN, Murad MH, et al. Comparative effectiveness of therapies for graves' hyperthyroidism: a systematic review and network meta-Analysis. *J Clin Endocrinol Metab* 2013;98(9):3671-7.

[D129] Thorlund K, Druyts E, Aviña-Zubieta JA, Mills EJ. Anti-tumor necrosis factor (TNF) drugs for the treatment of psoriatic arthritis: an indirect comparison meta-analysis. *Biologics* 2012;6:417-27.

[D130] Trelle S, Reichenbach S, Wandel S, Hildebrand P, Tschannen B, Villiger PM, et al. Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. *BMJ* 2011;342:c7086.

[D131] van de Kerkhof P, de Peuter R, Ryttov J, Jansen JP. Mixed treatment comparison of a two-compound formulation (TCF) product containing calcipotriol and betamethasone dipropionate with other topical treatments in psoriasis vulgaris. *Curr Med Res Opin* 2011;27(1): 225-38.

[D132] van der Mark LB, Lyklema PH, Geskus RB, Mohrs J, Bindels PJ, van Aalderen WM, et al. A systematic review with attempted network meta-analysis of asthma therapy recommended for five to eighteen year olds in GINA steps three and four. *BMC Pulm Med* 2012;12:63.

[D133] Vieira MC, Kumar RN, Jansen JP. Comparative effectiveness of efavirenz, protease inhibitors, and raltegravir-based regimens as first-line treatment for HIV-infected adults: a mixed treatment comparison. *HIV Clin Trials* 2011;12(4):175-89.

[D134] Vissers D, Stam W, Nolte T, Lenre M, Jansen J. Efficacy of intranasal fentanyl spray versus other opioids for breakthrough pain in cancer. *Curr Med Res Opin* 2010;26(5):1037-45.

[D135] Wandel S, Jüni P, Tendal B, Nüesch E, Villiger PM, Welton NJ, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ* 2010;341:c4675.

[D136] Wehren LE, Hosking D, Hochberg MC. Putting evidence-based medicine into clinical practice: comparing anti-resorptive agents for the treatment of osteoporosis. *Curr Med Res Opin* 2004;20(4):525-31.

[D137] Welton NJ, Cooper NJ, Ades AE, Lu G, Sutton AJ. Mixed treatment comparison with multiple outcomes reported inconsistently across trials: evaluation of antivirals for treatment of influenza A and B. *Stat Med* 2008;27(27):5620-39.

[D138] Wolff RF, Bala MM, Westwood M, Kessels AG, Kleijnen J. 5% lidocaine medicated plaster in painful diabetic peripheral neuropathy (DPN): a systematic review. *Swiss Med Wkly* 2010;140(21-22):297-306.

[D139] Wolff RF, Bala MM, Westwood M, Kessels AG, Kleijnen J. 5% lidocaine-medicated plaster vs other relevant interventions and placebo for post-herpetic neuralgia (PHN): a systematic review. *Acta Neurol Scand* 2011;123(5):295-309.

[D140] Wolff RF, Aune D, Truyers C, Hernandez AV, Misso K, Riemsma R, et al. Systematic review of efficacy and safety of buprenorphine versus fentanyl or morphine in patients with chronic moderate to severe pain. *Curr Med Res Opin* 2012;28(5):833-45.

[D141] Wu P, Wilson K, Dimoulas P, Mills EJ. Effectiveness of smoking cessation therapies: a systematic review and meta-analysis. *BMC Public Health* 2006;6:300.

[D142] Yazdanpanah Y, Sissoko D, Egger M, Mouton Y, Zwahlen M, Chêne G. Clinical efficacy of antiretroviral combination therapy based on protease inhibitors or non-nucleoside analogue reverse transcriptase inhibitors: indirect comparison of controlled trials. *BMJ* 2004;328(7434):249.

[D143] Zhou Z, Rahme E, Pilote L. Are statins created equal? Evidence from randomized trials of pravastatin, simvastatin, and atorvastatin for cardiovascular disease prevention. *Am Heart J* 2006;151(2):273-81.

[D144] Biondi-Zoccai G, Lotrionte M, Agostoni P, Abbate A, Romagnoli E, Sangiorgi G, et al. Adjusted indirect comparison meta-analysis of prasugrel versus ticagrelor for patients with acute coronary syndromes. *Int J Cardiol* 2011;150(3):325-31.

[D145] Biondi-Zoccai G, Malavasi V, D'Ascenzo F, Abbate A, Agostoni P, Lotrionte M, et al. Comparative effectiveness of novel oral anticoagulants for atrial fibrillation: evidence from pair-wise and warfarin-controlled network meta-analyses. *HSR Proc Intensive Care Cardiovasc Anesth* 2013;5(1):40-54.

[D146] Chatterjee S, Biondi-Zoccai G, Abbate A, D'Ascenzo F, Castagno D, Van Tassell B, et al. Benefits of beta blockers in patients with heart failure and reduced ejection fraction: network meta-analysis. *BMJ* 2013;346:f55.

[D147] Chatterjee S, Sardar P, Biondi-Zoccai G, Kumbhani DJ. New oral anticoagulants and the risk of intracranial hemorrhage: traditional and Bayesian meta-analysis and mixed treatment comparison of randomized trials of new oral anticoagulants in atrial fibrillation. *JAMA Neurol* 2013;70(12):1486-90.

[D148] Chatterjee S, Ghose A, Sharma A, Guha G, Mukherjee D, Frankel R. Comparing newer oral anti-platelets prasugrel and ticagrelor in reduction of ischemic events-evidence from a network meta-analysis. *J Thromb Thrombolysis* 2013;36(3):223-32.

[D149] Chatterjee S, Sardar P, Mukherjee D, Lichstein E, Aikat S. Timing and route of amiodarone for prevention of postoperative atrial fibrillation after cardiac surgery: a network regression meta-analysis. *Pacing Clin Electrophysiol* 2013;36(8):1017-23.

[D150] Landoni G, Greco T, Biondi-Zoccai G, Nigro Neto C, Febres D, Pintaudi M, et al. Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery. *Br J Anaesth* 2013;111(6):886-96.

[D151] Sardar P, Chatterjee S, Wu WC, Lichstein E, Ghosh J, Aikat S, Muhkerjee D. New oral anticoagulants are not superior to warfarin in secondary prevention of stroke or transient ischemic attacks, but lower the risk of intracranial bleeding: insights from a meta-analysis and indirect treatment comparisons. *PLoS One* 2013;8(10):e77694.

[D152] Testa L, Agnifili M, Latini RA, Mattioli R, Lanotte S, De Marco F, et al. Adjusted indirect comparison of new oral anticoagulants for stroke prevention in atrial fibrillation. *QJM* 2012;105(10):949-57.

[D153] Chen JM, Heran BS, Wright JM. Blood pressure lowering efficacy of diuretics as second-line therapy for primary hypertension. *Cochrane Database Syst Rev* 2009;(4):CD007187.

[D154] Chen JM, Heran BS, Perez MI, Wright JM. Blood pressure lowering efficacy of beta-blockers as second-line therapy for primary hypertension. *Cochrane Database Syst Rev* 2010;(1):CD007185.

[D155] Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin converting enzyme (ACE) inhibitors for primary hypertension. *Cochrane Database Syst Rev* 2008;(4):CD003823.

[D156] Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin receptor blockers for primary hypertension. *Cochrane Database Syst Rev* 2008;(4):CD003822.

[D157] Heran BS, Galm BP, Wright JM. Blood pressure lowering efficacy of alpha blockers for primary hypertension. *Cochrane Database Syst Rev* 2009;(4):CD004643.

[D158] Heran BS, Chen JM, Wang JJ, Wright JM. Blood pressure lowering efficacy of potassium-sparing diuretics (that block the epithelial sodium channel) for primary hypertension. *Cochrane Database Syst Rev* 2010;(1):CD008167.

[D159] Heran BS, Galm BP, Wright JM. Blood pressure lowering efficacy of alpha blockers for primary hypertension. *Cochrane Database Syst Rev* 2012;(8):CD004643.

[D160] Heran BS, Chen JM, Wang JJ, Wright JM. Blood pressure lowering efficacy of potassium-sparing diuretics (that block the epithelial sodium channel) for primary hypertension. Cochrane Database Syst Rev 2012;(11):CD008167.

[D161] Dewilde S, Hawkins N. Investigating incoherence gives insight: clopidogrel is equivalent to extended-release dipyridamole plus aspirin in secondary stroke prevention. *J Clin Epidemiol* 2012;65(8):835-45.

[D162] Gross JL, Kramer CK, Leitão CB, Hawkins N, Viana LV, Schaan BD, et al. Effect of antihyperglycemic agents added to metformin and a sulfonylurea on glycemic control and weight gain in type 2 diabetes: a network meta-analysis. *Ann Intern Med* 2011;154(10):672-9.

[D163] Khan N, Shah D, Tongbram V, Verdian L, Hawkins N. The efficacy and tolerability of perampanel and other recently approved anti-epileptic drugs for the treatment of refractory partial onset seizure: a systematic review and Bayesian network meta-analysis. *Curr Med Res Opin* 2013;29(8):1001-13.

[D164] Mealing S, Barcena L, Hawkins N, Clark J, Eaton V, Hirji I, Davis C. The relative efficacy of imatinib, dasatinib and nilotinib for newly diagnosed chronic myeloid leukemia: a systematic review and network meta-analysis. *Exp Hematol Oncol* 2013;2(1):5.

[D165] Reich K, Burden AD, Eaton JN, Hawkins NS. Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials. *Br J Dermatol* 2012;166(1):179-88.

[D166] Scott DA, Boye KS, Timlin L, Clark JF, Best JH. A network meta-analysis to compare glycaemic control in patients with type 2 diabetes treated with exenatide once weekly or liraglutide once daily in comparison with insulin glargine, exenatide twice daily or placebo. *Diabetes Obes Metab* 2013;15(3):213-23.

[D167] Desai RJ, Hansen RA, Rao JK, Wilkins TM, Harden EA, Yuen A, et al. Mixed treatment comparison of the treatment discontinuations of biologic disease-modifying antirheumatic drugs in adults with rheumatoid arthritis. *Ann Pharmacother* 2012;46(11):1491-505.

[D168] Gartlehner G, Hansen RA, Jonas BL, Thieda P, Lohr KN. The comparative efficacy and safety of biologics for the treatment of rheumatoid arthritis: a systematic review and metaanalysis. *J Rheumatol* 2006;33(12):2398-408.

[D169] Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, et al. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. *Ann Intern Med* 2011;155(11):772-85.

[D170] Hansen RA, Gartlehner G, Webb AP, Morgan LC, Moore CG, Jonas DE. Efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease: a systematic review and meta-analysis. *Clin Interv Aging* 2008;3(2):211-25.

[D171] Hansen RA, Gaynes BN, Gartlehner G, Moore CG, Tiwari R, Lohr KN. Efficacy and tolerability of second-generation antidepressants in social anxiety disorder. *Int Clin Psychopharmacol* 2008;23(3):170-9.

[D172] Signorovitch JE, Wu EQ, Yu AP, Gerrits CM, Kantor E, Bao Y, et al. Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept. *Pharmacoeconomics* 2010;28(10):935-45.

[D173] Signorovitch JE, Wu EQ, Swallow E, Kantor E, Fan L, Gruenberger JB. Comparative efficacy of vildagliptin and sitagliptin in Japanese patients with type 2 diabetes mellitus: a matching-adjusted indirect comparison of randomized trials. *Clin Drug Investig* 2011;31(9):665-74.

[D174] Signorovitch JE, Wu EQ, Betts KA, Parikh K, Kantor E, Guo A, et al. Comparative efficacy of nilotinib and dasatinib in newly diagnosed chronic myeloid leukemia: a matching-adjusted indirect comparison of randomized trials. *Curr Med Res Opin* 2011;27(6):1263-71.

[D175] Signorovitch J, Erder MH, Xie J, Sikirica V, Lu M, Hodgkins PS, Wu EQ. Comparative effectiveness research using matching-adjusted indirect comparison: an application to treatment with guanfacine extended release or atomoxetine in children with attention-deficit/hyperactivity disorder and comorbid oppositional defiant disorder. *Pharmacoepidemiol Drug Saf* 2012;21 Suppl 2:130-7.

[D176] Sikirica V, Findling RL, Signorovitch J, Erder MH, Dammerman R, Hodgkins P, et al. Comparative efficacy of guanfacine extended release versus atomoxetine for the treatment of attention-deficit/hyperactivity disorder in children and adolescents: applying matching-adjusted indirect comparison methodology. *CNS Drugs* 2013;27(11):943-53.

[D177] Ribeiro RA, Ziegelmann PK, Duncan BB, Stella SF, da Costa Vieira JL, Restelatto LM, et al. Impact of statin dose on major cardiovascular events: a mixed treatment comparison meta-analysis involving more than 175,000 patients. *Int J Cardiol* 2013;166(2):431-9.

[D178] Rotta I, Ziegelmann PK, Otuki MF, Riveros BS, Bernardo NL, Correr CJ. Efficacy of topical antifungals in the treatment of dermatophytosis: a mixed-treatment comparison meta-analysis involving 14 treatments. *JAMA Dermatol* 2013;149(3):341-9.

[D179] Sanches AC, Correr CJ, Venson R, Pontarolo R. Revisiting the efficacy of long-acting insulin analogues on adults with type 1 diabetes using mixed-treatment comparisons. *Diabetes Res Clin Pract* 2011;94(3):333-9.

[D180] Sanches ACC, Correr CJ, Venson R, Gonçalves PR, Garcia MM, Piantavini S, et al. Insulin analogues versus human insulin in type 1 diabetes: direct and indirect meta-analyses of efficacy and safety. *Braz J Pharm Sci* 2013;49(3):501-9.

[D181] Wiens A, Lenzi L, Venson R, Correr CJ, Rotta I, Pedroso ML, et al. Comparative efficacy of oral nucleoside or nucleotide analog monotherapy used in chronic hepatitis B: a mixed-treatment comparison meta-analysis. *Pharmacotherapy* 2013;33(2):144-51.

[D182] Anothaisintawee T, Attia J, Nickel JC, Thammakraisorn S, Numthavaj P, McEvoy M, et al. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. *JAMA* 2011;305(1):78-86.

[D183] Jones LJ, Craven PD, Attia J, Thakkinstian A, Wright I. Network meta-analysis of indomethacin versus ibuprofen versus placebo for PDA in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2011;96(1):F45-52.

[D184] Numthavaj P, Thakkinstian A, Dejthevaporn C, Attia J. Corticosteroid and antiviral therapy for Bell's palsy: a network meta-analysis. *BMC Neurol* 2011;11:1.

[D185] Thakkinstian A, Attia J, Anothaisintawee T, Nickel JC. α-blockers, antibiotics and anti-inflammatories have a role in the management of chronic prostatitis/chronic pelvic pain syndrome. *BJU Int* 2012;110(7):1014-22.

[D186] Vejakama P, Thakkinstian A, Lertrattananon D, Ingsathit A, Ngarmukos C, Attia J. Reno-protective effects of renin-angiotensin system blockade in type 2 diabetic patients: a systematic review and network meta-analysis. *Diabetologia* 2012;55(3):566-78.

[D187] Dranitsaris G, Jelincic V, Choe Y. Meta regression analysis to indirectly compare dalteparin to enoxaparin for the prevention of venous thromboembolic events following total hip replacement. *Thromb J* 2011;9(1):3.

[D188] Dranitsaris G, Jelincic V, Choe Y. Meta-regression analysis to indirectly compare prophylaxis with dalteparin or enoxaparin in patients at high risk for venous thromboembolic events. *Clin Appl Thromb Hemost* 2012;18(3):233-42.

[D189] Dranitsaris G, Schmitz S, Broom RJ. Small molecule targeted therapies for the second-line treatment for metastatic renal cell carcinoma: a systematic review and indirect comparison of safety and efficacy. *J Cancer Res Clin Oncol* 2013;139(11):1917-26.

[D190] Kieran J, Schmitz S, O'Leary A, Walsh C, Bergin C, Norris S, et al. The relative efficacy of boceprevir and telaprevir in the treatment of hepatitis C virus genotype 1. *Clin Infect Dis* 2013;56(2):228-35.

[D191] Schmitz S, Adams R, Walsh CD, Barry M, FitzGerald O. A mixed treatment comparison of the efficacy of anti-TNF agents in rheumatoid arthritis for methotrexate non-responders demonstrates differences between treatments: a Bayesian approach. *Ann Rheum Dis* 2012;71(2): 225-30.

[D192] Chou R, Fu R, Huffman LH, Korthuis PT. Initial highly-active antiretroviral therapy with a protease inhibitor versus a non-nucleoside reverse transcriptase inhibitor: discrepancies between direct and indirect meta-analyses. *Lancet* 2006;368(9546):1503-15.

[D193] Chou R, Carson S, Chan BK. Pegylated interferons for chronic hepatitis C virus infection: an indirect analysis of randomized trials. *J Viral Hepat* 2008;15(8):551-70.

[D194] Chou R, Carson S, Chan BK. Gabapentin versus tricyclic antidepressants for diabetic neuropathy and post-herpetic neuralgia: discrepancies between direct and indirect meta-analyses of randomized controlled trials. *J Gen Intern Med* 2009;24(2):178-88.

[D195] Norris SL, Carson S, Roberts C. Comparative effectiveness of pioglitazone and rosiglitazone in type 2 diabetes, prediabetes, and the metabolic syndrome: a meta-analysis. *Curr Diabetes Rev* 2007;3(2):127-40.

[D196] Peterson K, McDonagh MS, Fu R. Comparative benefits and harms of competing medications for adults with attention-deficit hyperactivity disorder: a systematic review and indirect comparison meta-analysis. *Psychopharmacology* 2008;197(1):1-11.

[D197] Chang JWC, Thongprasert S, Wright E, Tsang K, Kim HT, Ahn MJ, et al. An indirect comparison of bevacizumab plus cisplatin-gemcitabine and cisplatin plus pemetrexed treatment for patients with advanced first-line non-squamous non-small cell lung cancer in East Asia. *Asia Pac J Clin Oncol* 2011;7 Suppl 2:13-21.

[D198] Mickisch GHJ, Schwander B, Escudier B, Bellmunt J, Maroto Jp, Porta C, et al. Indirect treatment comparison of bevacizumab + interferon-α-2a vs tyrosine kinase inhibitors in first-line metastatic renal cell carcinoma therapy. *Clinicoecon Outcomes Res* 2011;3(1):19-27.

[D199] Nuijten M, Heigener DF, Bischoff HG, Chouaid C, Vergnenègre A, de Castro Carpeño J, et al. Effectiveness of bevacizumab- and pemetrexed-cisplatin treatment for patients with advanced non-squamous non-small cell lung cancer. *Lung Cancer* 2010;69 Suppl 1):S4-10.

[D200] Nuijten MJ, Aultman R, Carpeño Jde C, Vergnenègre A, Chouaid C, Walzer S, et al. An indirect comparison of the efficacy of bevacizumab plus carboplatin and paclitaxel versus pemetrexed with cisplatin in patients with advanced or recurrent non-squamous adenocarcinoma non-small cell lung cancer. *Curr Med Res Opin* 2011;27(11):2193-201.

[D201] Liao WC, Chien KL, Lin YL, Wu MS, Lin JT, Wang HP, et al. Adjuvant treatments for resected pancreatic adenocarcinoma: a systematic review and network meta-analysis. *Lancet Oncol* 2013;14(11):1095-103.

[D202] Liu SC, Tu YK, Chien MN, Chien KL. Effect of antidiabetic agents added to metformin on glycaemic control, hypoglycaemia and weight change in patients with type 2 diabetes: a network meta-analysis. *Diabetes Obes Metab* 2012;14(9):810-20.

[D203] Wu HY, Huang JW, Lin JH, Liao WC, Peng YS, Hung KY, et al. Comparative effectiveness of renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes: systematic review and bayesian network meta-analysis. *BMJ* 2013;347:f6008.

[D204] Wu MS, Tan SC, Xiong T. Indirect comparison of randomised controlled trials: comparative efficacy of dexlansoprazole vs. esomeprazole in the treatment of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2013;38(2):190-201.

[D205] Bakalos G, Miligkos M, Doxani C, Mpoulimari I, Rodopoulou P, Zintzaras E. Assessing the relative effectiveness and tolerability of treatments in small cell lung cancer: a network meta-analysis. *Cancer Epidemiol* 2013;37(5):675-82.

[D206] Hadjigeorgiou GM, Doxani C, Miligkos M, Ziakas P, Bakalos G, Papadimitriou D, et al. A network meta-analysis of randomized controlled trials for comparing the effectiveness and safety profile of treatments with marketing authorization for relapsing multiple sclerosis. *J Clin Pharm Ther* 2013;38(6):433-9.

[D207] Zintzaras E, Doxani Mprotsis T, Schmid CH, Hadjigeorgiou GM. Network analysis of randomized controlled trials in multiple sclerosis. *Clin Ther* 2012;34(4):857-69.e9.

[D208] Ziogas DC, Voulgarelis M, Zintzaras E. A network meta-analysis of randomized controlled trials of induction treatments in acute myeloid leukemia in the elderly. *Clin Ther* 2011;33(3):254-79.

[D209] Kumar A, Hozo I, Wheatley K, Djulbegovic B. Thalidomide versus bortezomib based regimens as first-line therapy for patients with multiple myeloma: a systematic review. *Am J Hematol* 2011;86(1):18-24.

[D210] Mhaskar R, Redzepovic J, Wheatley K, Clark OA, Miladinovic B, Glasmacher A, et al. Bisphosphonates in multiple myeloma. *Cochrane Database Syst Rev* 2010;(3):CD003188.

[D211] Mhaskar R, Redzepovic J, Wheatley K, Clark OA, Miladinovic B, Glasmacher A, et al., Bisphosphonates in multiple myeloma: a network meta-analysis. *Cochrane Database Syst Rev* 2012;(5):CD003188.

[D212] Terasawa T, Trikalinos NA, Djulbegovic B, Trikalinos TA. Comparative efficacy of first-line therapies for advanced-stage chronic lymphocytic leukemia: a multiple-treatment meta-analysis. *Cancer Treat Rev* 2013;39(4):340-9.

[D213] Cheng MM, Goulart B, Veenstra Dl, Blough DK, Devine EB. A network meta-analysis of therapies for previously untreated chronic lymphocytic leukemia. *Cancer Treat Rev* 2012;38(8):1004-11.

[D214] Devine EB, Alfonso-Cristancho R, Sullivan SD. Effectiveness of biologic therapies for rheumatoid arthritis: an indirect comparisons approach. *Pharmacotherapy* 2011;31(1):39-51.

[D215] Lin VW, Ringold S, Devine EB. Comparison of ustekinumab with other biological agents for the treatment of moderate to severe plaque psoriasis: a Bayesian network meta-analysis. *Arch Dermatol* 2012;148(12):1403-10.

[D216] Ney JP, Devine EB, Watanabe JH, Sullivan SD. Comparative efficacy of oral pharmaceuticals for the treatment of chronic peripheral neuropathic pain: meta-analysis and indirect treatment comparisons. *Pain Med* 2013;14(5):706-19.

[D217] Migliore A, Bizzi E, Broccoli S, Laganà B. Indirect comparison of etanercept, infliximab, and adalimumab for psoriatic arthritis: mixed treatment comparison using placebo as common comparator. *Clin Rheumatol* 2012;31(1):133-7.

[D218] Migliore A, Broccoli S, Massafra U, Bizzi E, Frediani B. Mixed-treatment comparison of anabolic (teriparatide and PTH 1-84) therapies in women with severe osteoporosis. *Curr Med Res Opin* 2012;28(3):467-73.

[D219] Migliore A, Broccoli S, Bizzi E, Laganà B. Indirect comparison of the effects of anti-TNF biological agents in patients with ankylosing spondylitis by means of a mixed treatment comparison performed on efficacy data from published randomised, controlled trials. *J Med Econ* 2012;15(3):473-80.

[D220] Migliore A, Broccoli S, Massafra U, Cassol M, Frediani B. Ranking antireabsorptive agents to prevent vertebral fractures in postmenopausal osteoporosis by mixed treatment comparison meta-analysis. *Eur Rev Med Pharmacol Sci* 2013;17(5):658-67.

[D221] Wilhelmus KR. The treatment of herpes simplex virus epithelial keratitis. *Trans Am Ophthalmol Soc* 2000;98:505-32.

[D222] Wilhelmus KR. Therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Reviews* 2007;(1):CD002898.

[D223] Wilhelmus KR. Therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev* 2008;(1):CD002898.

[D224] Wilhelmus KR. Antiviral treatment and other therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev* 2010;(12):CD002898.

[D225] Coomarasamy A, Knox EM, Gee H, Song F, Khan KS. Effectiveness of nifedipine versus atosiban for tocolysis in preterm labour: a meta-analysis with an indirect comparison of randomised trials. *BJOG* 2003;110(12):1045-9.

[D226] Lim E, Ali Z, Ali A, Routledge T, Edmonds L, Altman DG, et al. Indirect comparison meta-analysis of aspirin therapy after coronary surgery. *BMJ* 2003;327(7427):1309-11.

[D227] Lim E, Harris G, Patel A, Adachi I, Edmonds L, Song F. Preoperative versus postoperative chemotherapy in patients with resectable non-small cell lung cancer systematic review and indirect comparison meta-analysis of randomized trials. *J Thorac Oncol* 2009;4(11): 1380-8.

[D228] Bansback N, Sizto S, Sun H, Feldman S, Willian MK, Anis A. Efficacy of systemic treatments for moderate to severe plaque psoriasis: systematic review and meta-analysis. *Dermatology* 2009;219(3):209-18.

[D229] Nixon R, Bansback N, Brennan A. The efficacy of inhibiting tumour necrosis factor alpha and interleukin 1 in patients with rheumatoid arthritis: a meta-analysis and adjusted indirect comparisons. *Rheumatology* 2007;46(7):1140-7.

[D230] Nixon RM, Bansback N, Brennan A. Using mixed treatment comparisons and meta-regression to perform indirect comparisons to estimate the efficacy of biologic treatments in rheumatoid arthritis. *Stat Med* 2007;26(6):1237-54.

[D231] Jandhyala R. Relative potency of incobotulinumtoxinA vs onabotulinumtoxinA a meta-analysis of key evidence. *J Drugs Dermatol* 2012;11(6):731-6.

[D232] Jandhyala R, Fullarton JR, Bennett MI. Efficacy of rapid-onset oral fentanyl formulations vs. oral morphine for cancer-related breakthrough pain: a meta-analysis of comparative trials. *J Pain Symptom Manage* 2013;46(4):573-80.

[D233] Palmieri C, Fullarton JR, Brown J. Comparative efficacy of bisphosphonates in metastatic breast and prostate cancer and multiple myeloma: a mixed-treatment meta-analysis. *Clin Cancer Res* 2013;19(24):6863-72.

[D234] Di Lorenzo G, Casciano R, Malangone E, Buonerba C, Sherman S, Willet J, et al. An adjusted indirect comparison of everolimus and sorafenib therapy in sunitinib-refractory metastatic renal cell carcinoma patients using repeated matched samples. *Expert Opin Pharmacother* 2011;12(10):1491-7.

[D235] Thompson Coon JS, Liu Z, Hoyle M, Rogers G, Green C, Moxham T, et al. Sunitinib and bevacizumab for first-line treatment of metastatic renal cell carcinoma: a systematic review and indirect comparison of clinical effectiveness. *Br J Cancer* 2009;101(2):238-43.

[D236] Bodalia PN, Grosso AM, Sofat R, Macallister RJ, Smeeth L, Dhillon S, et al. Comparative efficacy and tolerability of anti-epileptic drugs for refractory focal epilepsy: systematic review and network meta-analysis reveals the need for long term comparator trials. *Br J Clin Pharmacol* 2013;76(5):649-67.

[D237] Samarasekera EJ, Sawyer L, Wonderling D, Tucker R, Smith CH. Topical therapies for the treatment of plaque psoriasis: systematic review and network meta-analyses. *Br J Dermatol* 2013;168(5):954-67.

[D238] Yuan J, Liu Y, Yang Z, Qin X, Yang K, Mao C. The efficacy and safety of alpha-1 blockers for benign prostatic hyperplasia: an overview of 15 systematic reviews. *Curr Med Res Opin* 2013;29(3):279-87.

[D239] Yuan JQ, Zhang R, Yang Z, Lee J, Liu Y, Tian J, et al. Comparative effectiveness and safety of oral phosphodiesterase type 5 inhibitors for erectile dysfunction: a systematic review and network meta-analysis. *Eur Urol* 2013;63(5):902-12.

[D240] Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, et al. Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. *JAMA* 2003;289(19):2534-44.

[D241] van der Valk R, Webers CA, Lumley T, Hendrikse F, Prins MH, Schouten JS. A network meta-analysis combined direct and indirect comparisons between glaucoma drugs to rank effectiveness in lowering intraocular pressure. *J Clin Epidemiol* 2009;62(12):1279-83.

[D242] Ford JA, Elders A, Shyangdan D, Royle P, Waugh N. The relative clinical effectiveness of ranibizumab and bevacizumab in diabetic macular oedema: an indirect comparison in a systematic review. *BMJ* 2012;345:e5182.

[D243] Ford JA, Jones R, Elders A, Mulatero C, Royle P, Sharma P, et al. Denosumab for treatment of bone metastases secondary to solid tumours: systematic review and network meta-analysis. *Eur J Cancer* 2013;49(2):416-30.

[D244] Dretzke J, Meadows A, Novielli N, Huissoon A, Fry-Smith A, Meads C. Subcutaneous and sublingual immunotherapy for seasonal allergic rhinitis: a systematic review and indirect comparison. *J Allergy Clin Immunol* 2013;131(5):1361-6.

[D245] Virgili G, Novielli N, Menchini F, Murro V, Giacomelli G. Pharmacological treatments for neovascular age-related macular degeneration: can mixed treatment comparison meta-analysis be useful? *Curr Drug Targets* 2011;12(2):212-20.

[D246] Fénix-Caballero S, Alegre-del Rey EJ, Castaño-Lara R, Puigventós-Latorre F, Borrero-Rubio JM, López-Vakkehi JF. Direct and indirect comparison of the efficacy and safety of adalimumab, etanercept, infliximab and golimumab in psoriatic arthritis. *J Clin Pharm Ther* 2013;38(4):286-93.

[D247] Gallego-Galisteo M, Villa-Rubio A, Alegre-del Rey E, Márquez-Fernáandez E, Ramos-Báez JJ. Indirect comparison of biological treatments in refractory rheumatoid arthritis. *J Clin Pharm Ther* 2012;37(3):301-7.

[D248] Germani G, Pleguezuelo M, Gurusamy K, Meyer T, Isgrò G, Burroughs AK. Clinical outcomes of radiofrequency ablation, percutaneous alcohol and acetic acid injection for hepatocelullar carcinoma: a meta-analysis. *J Hepatol* 2010;52(3):380-8.

[D249] Gurusamy KS, Pissanou T, Pikhart H, Vaughan J, Burroughs AK, Davidson BR. Methods to decrease blood loss and transfusion requirements for liver transplantation. *Cochrane Database Syst Rev* 2011;(12):CD009052.

[D250] Sultana A, Ghaneh P, Cunningham D, Starling N, Neoptolemos JP, Smith CT. Gemcitabine based combination chemotherapy in advanced pancreatic cancer-indirect comparison. *BMC Cancer* 2008;8:192.

[D251] Tudur Smith C, Marson AG, Chadwick DW, Williamson PR. Multiple treatment comparisons in epilepsy monotherapy trials. Trials 2007;8:34.

[D252] Caldeira D, Alarcão J, Vaz-Carneiro A, Costa J. Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. *BMJ* 2012;345:e4260.

[D253] Costa J, Fareleira F, Ascenção R, Borges M, Sampaio C, Vaz-Carneiro A. Clinical comparability of the new antiepileptic drugs in refractory partial epilepsy: a systematic review and meta-analysis. *Epilepsia* 2011;52(7):1280-91.

[D254] Del Santo F, Maratea D, Fadda V, Trippoli S, Messori A. Treatments for relapsing-remitting multiple sclerosis: summarising current information by network meta-analysis. *Eur J Clin Pharmacol* 2012;68(4):441-8.

[D255] Zaccara G, Giovannelli F, Maratea D, Fadda V, Verrotti A. Neurological adverse events of new generation sodium blocker antiepileptic drugs. Meta-analysis of randomized, double-blinded studies with eslicarbazepine acetate, lacosamide and oxcarbazepine. *Seizure* 2013;22(7):528-36.

[D256] Dumville JC, Soares MO, O'Meara S, Cullum N. Systematic review and mixed treatment comparison: dressings to heal diabetic foot ulcers. *Diabetologia* 2012;55(7):1902-10.

[D257] Dumville JC, McFarlane E, Edwards P, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev 2013;(3):CD003949.

[D258] Gagne JJ, Bykov K, Choudhry NK, Toomey TJ, Connolly JG, Avorn J. Effect of smoking on comparative efficacy of antiplatelet agents: Systematic review, meta-analysis, and indirect comparison. *BMJ* 2013;347(7927):f5307.

[D259] Schneeweiss S, Gagne JJ, Patrick AR, Choudhry NK, Avorn J. Comparative efficacy and safety of new oral anticoagulants in patients with atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2012;5(4):480-6.

[D260] Sun F, Yu K, Wu S, Zhang Y, Yang Z, Shi L, et al. Cardiovascular safety and glycemic control of glucagon-like peptide-1 receptor agonists for type 2 diabetes mellitus: a pairwise and network meta-analysis. *Diabetes Res Clin Pract* 2012;98(3):386-95.

[D261] Sun F, Yu K, Yang Z, Wu S, Zhang Y, Shi L, et al. Impact of GLP-1 receptor agonists on major gastrointestinal disorders for type 2 diabetes mellitus: a mixed treatment comparison meta-analysis. *Exp Diabetes Res* 2012;2012:230624.

[D262] Levi Marpillat N, Macquin-Mavier I, Tropeano AI, Bachoud-Levi AC, Maison P. Antihypertensive classes, cognitive decline and incidence of dementia: a network meta-analysis. *J Hypertens* 2013;31(6):1073-82.

[D263] Tropeano AI, Saleh N, Hawajri N, Macquin-Mavier I, Maison P. Do all antihypertensive drugs improve carotid intima-media thickness? A network meta-analysis of randomized controlled trials. *Fundam Clin Pharmacol* 2011;25(3):395-404.

[D264] Assiri A, Al-Majzoub O, Kanaan AO, Donovan JL, Silva M. Mixed treatment comparison meta-analysis of aspirin, warfarin, and new anticoagulants for stroke prevention in patients with nonvalvular atrial fibrillation. *Clin Ther* 2013;35(7):967-84.

[D265] Malloy RJ, Kanaan AO, Silva MA, Donovan JL. Evaluation of antiplatelet agents for secondary prevention of stroke using mixed treatment comparison meta-analysis. *Clin Ther* 2013;35(10):1490-500.

[D266] Lee YH, Ji JD, Song GG. Adjusted indirect comparison of celecoxib versus rofecoxib on cardiovascular risk. *Rheumatol Int* 2007;27(5):477-82.

[D267] Lee YH, Woo JH, Rho YH, Choi SJ, Ji JD, Song GG. Meta-analysis of the combination of TNF inhibitors plus MTX compared to MTX monotherapy, and the adjusted indirect comparison of TNF inhibitors in patients suffering from active rheumatoid arthritis. *Rheumatol Int* 2008;28(6):553-9.

[D268] Bolaños R, Francia J. Isoflavones versus hormone therapy for reduction of vertebral fracture risk: indirect comparison. Menopause 2010;17(6):1201-5.

[D269] Bolaños-Diaz R, Zavala-Gonzales JC, Mezones-Holguín E, Francia-Romero J. Soy extracts versus hormone therapy for reduction of menopausal hot flushes: indirect comparison. *Menopause* 2011;18(7):825-9.

[D270] Kabra SK, Lodha R, Pandey RM. Antibiotics for community acquired pneumonia in children. *Cochrane Database Syst Rev* 2006;(3):CD004874.

[D271] Kabra SK, Lodha R, Pandey RM. Antibiotics for community-acquired pneumonia in children. *Cochrane Database Syst Rev* 2010;(3):CD004874.

[D272] Abdullah AK, Khan S. Relative oral corticosteroid-sparing effect of 7 inhaled corticosteroids in chronic asthma: a meta-analysis. *Ann Allergy Asthma Immunol* 2008;101(1):74-81.

[D273] Baldwin D, Woods R, Lawson R, Taylor D. Efficacy of drug treatments for generalised anxiety disorder: systematic review and meta-analysis. *BMJ* 2011;342:d1199.

[D274] Bally M, Dendukuri N, Sinclair A, Ahern SP, Poisson M, Brophy J. A network meta-analysis of antibiotics for treatment of hospitalised patients with suspected or proven meticillin-resistant Staphylococcus aureus infection. *Int J Antimicrob Agents* 2012;40(6):479-95.

[D275] Bangalore S, Kumar S, Kjeldsen SE, Makani H, Grossman E, Wettersley J, et al. Antihypertensive drugs and risk of cancer: network meta-analyses and trial sequential analyses of 324,168 participants from randomised trials. *Lancet Oncol* 2011;12(1):65-82.

[D276] Bansal M, Farrugia A, Balboni S, Martin G. Relative survival benefit and morbidity with fluids in severe sepsis - a network meta-analysis of alternative therapies. *Curr Drug Saf* 2013;8(4):236-45.

[D277] Bash LD, Buono JL, Davies GM, Martin A, Fahrbach K, Phatak H, et al. Systematic review and meta-analysis of the efficacy of cardioversion by vernakalant and comparators in patients with atrial fibrillation. *Cardiovasc Drugs Ther* 2012;26(2):167-79.

[D278] Berner MM, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2006;18(3):229-35.

[D279] Bicket MC, Gupta A, Brown CH 4th, Cohen SP. Epidural injections for spinal pain: a systematic review and meta-analysis evaluating the "control" injections in randomized controlled trials. *Anesthesiology* 2013;119(4):907-31.

[D280] Blanchard P, Hill C, Guihenneuc-Jouyaux C, Baey C, Bourhis J, Pignon JP, et al. Mixed treatment comparison meta-analysis of altered fractionated radiotherapy and chemotherapy in head and neck cancer. *J Clin Epidemiol* 2011;64(9):985-92.

[D281] Boonen S, Lips P, Bouillon R, Bischoff-Ferrari HA, Vanderschueren D, Haentjens P. Need for additional calcium to reduce the risk of hip fracture with vitamin d supplementation: evidence from a comparative metaanalysis of randomized controlled trials. *J Clin Endocrinol Metab* 2007;92(4):1415-23.

[D282] Brigo F, Igwe SC, Nardone R, Tezzon F, Bongiovanni LG, Trinka E. A common reference-based indirect comparison meta-analysis of intravenous valproate versus intravenous phenobarbitone for convulsive status epilepticus. *Epileptic Disord* 2013;15(3):314-23.

[D283] Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev* 2013;(5):CD009329.

[D284] Carter B, Fedorowicz Z. Antiemetic treatment for acute gastroenteritis in children: an updated Cochrane systematic review with meta-analysis and mixed treatment comparison in a Bayesian framework. *BMJ Open* 2012;2(4):e000622.

[D285] Cates CJ, Oleszczuk M, Stovold E, Wieland LS. Safety of regular formoterol or salmeterol in children with asthma: an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2012;10:CD010005.

[D286] Cawston H, Davie A, Paget MA, Sklijarevski V, Happich M. Efficacy of duloxetine versus alternative oral therapies: an indirect comparison of randomised clinical trials in chronic low back pain. *Eur Spine J* 2013;22(9):1996-2009.

[D287] Chapell R, Gould AL, Alexander CM. Baseline differences in A1C explain apparent differences in efficacy of sitagliptin, rosiglitazone and pioglitazone. Diabetes Obes Metab 2009;11(11):1009-16.

[D288] Coleman KA, Xavier VY, Palmer TL, Meaney JV, Randalj LM, Canny LM. An indirect comparison of the efficacy and safety of desvenlafaxine and venlafaxine using placebo as the common comparator. *CNS Spectr* 2012;17(3):131-41.

[D289] Conde-Agudelo A, Romero R, Nicolaides K, Chaiworapongsa T, O'Brien JM, Cetingoz E, et al. Vaginal progesterone vs. cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. *Am J Obstet Gynecol* 2013;208(1):42.e1-42.e18.

[D290] Cooper KL, Fitzgerald P, Dillingham K, Helme K, Akehurst R. Romiplostim and eltrombopag for immune thrombocytopenia: methods for indirect comparison. *Int J Technol Assess Health Care* 2012;28(3):249-58.

[D291] Cota GF, de Sousa MR, Fereguetti TO, Rabello A. Efficacy of anti-leishmania therapy in visceral leishmaniasis among HIV infected patients: a systematic review with indirect comparison. *PLoS Negl Trop Dis* 2013;7(5):e2195.

[D292] Cure S, Diels J, Gavart S, Bianic F, Jones E. Efficacy of telaprevir and boceprevir in treatment-naive and treatment-experienced genotype 1 chronic hepatitis C patients: an indirect comparison using Bayesian network meta-analysis. *Curr Med Res Opin* 2012;28(11):1841-56.

[D293] Danchin N, Marzilli M, Parkhomenko A, Ribeiro JP. Efficacy comparison of trimetazidine with therapeutic alternatives in stable angina pectoris: a network meta-analysis. *Cardiology* 2011;120(2):59-72.

[D294] Datto C, Hellmund R, Siddiqui MK. Efficacy and tolerability of naproxen/esomeprazole magnesium tablets compared with non-specific NSAIDs and COX-2 inhibitors: a systematic review and network analyses. *Open Access Rheumatol* 2013;5:1-19.

[D295] de Menezes GB, Coutinho ES, Fontenelle LF, Vigne P, Figueira I, Versiani M. Second-generation antidepressants in social anxiety disorder: meta-analysis of controlled clinical trials. *Psychopharmacology* 2011;215(1):1-11.

[D296] Delahoy P, Thompson S, Marschner IC. Pregabalin versus gabapentin in partial epilepsy: a meta-analysis of dose-response relationships. *BMC Neurol* 2010;10:104.

[D297] Dong YH, Lin HH, Shau WY, Wu YC, Chang CH, Lai MS. Comparative safety of inhaled medications in patients with chronic obstructive pulmonary disease: systematic review and mixed treatment comparison meta-analysis of randomised controlled trials. *Thorax* 2013;68(1):48-56.

[D298] Elliott WJ, Meyer PM. Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis. Lancet 2007;369(9557):201-7.

[D299] Engelman E, Salengros JC, Barvais L. How much does pharmacologic prophylaxis reduce postoperative vomiting in children? Calculation of prophylaxis effectiveness and expected incidence of vomiting under treatment using Bayesian meta-analysis. *Anesthesiol* 2008;109(6):1023-35.

[D300] Fang Y, Ding Y, Guo Q, Xing J, Long Y, Zong Z. Radioiodine therapy for patients with differentiated thyroid cancer after thyroidectomy: direct comparison and network meta-analyses. *J Endocrinol Invest* 2013;36(10):896-902.

[D301] Fountoulakis KN, Veroniki AA, Siamouli M, Möller HJ. No role for initial severity on the efficacy of antidepressants: results of a multi-meta-analysis. *Ann Gen Psychiatry* 2013;12(1):26.

[D302] Fretheim A, Odgaard-Jensen J, Brørs O, Madsen S, Njølstad I, Norheim OF, et al. Comparative effectiveness of antihypertensive medication for primary prevention of cardiovascular disease: systematic review and multiple treatments meta-analysis. *BMC Med* 2012;10:33.

[D303] Galvan-Banqueri M, Marin Gil R, Santos Ramos B, Bautista Paloma FJ. Biological treatments for moderate-to-severe psoriasis: indirect comparison. *J Clin Pharm Ther* 2013;38(2):121-30.

[D304] Gao L, Xia L, Zhao FL, Li SC. Clinical efficacy and safety of the newer antiepileptic drugs as adjunctive treatment in adults with refractory partial-onset epilepsy: a meta-analysis of randomized placebo-controlled trials. *Epilepsy Res* 2013;103(1):31-44.

[D305] Ginés J, Sabater E, Martorell C, Grau M, Monroy M, Casado MA. Efficacy of taxanes as adjuvant treatment of breast cancer: a review and meta-analysis of randomised clinical trials. Clin Transl Oncol 2011;13(7):485-98.

[D306] Gómez-Outes A, Terleira-Fernández AI, Suárez-Gea ML, Vargas-Castrillón E. Dabigatran, rivaroxaban, or apixaban versus enoxaparin for thromboprophylaxis after total hip or knee replacement: systematic review, meta-analysis, and indirect treatment comparisons. *BMJ* 2012;344(7863):e3675.

[D307] Goralczyk AD, Cameron S, Amanzada A. Treatment of chronic HCV genotype 1 infection with telaprevir: a Bayesian mixed treatment comparison of fixed-length and response-guided treatment regimens in treatment-naive and -experienced patients. *BMC Gastroenterol* 2013;13(1):148.

[D308] Gupta AK, Paquet M. Network meta-analysis of the outcome 'participant complete clearance' in nonimmunosuppressed participants of eight interventions for actinic keratosis: a follow-up on a Cochrane review. *Br J Dermatol* 2013;169(2):250-9.

[D309] Hoaglin DC, Filonenko A, Glickman ME, Wasiak R, Gidwani R. Use of mixed-treatment-comparison methods in estimating efficacy of treatments for heavy menstrual bleeding. *Eur J Med Res* 2013;18(1):17.

[D310] Hofmeyr GJ, Gülmezoglu AM, Novikova N, Linder V, Ferreira S, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. *Bull World Health Organ* 2009;87(9):666-77.

[D311] Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, et al. Prevention of pain on injection of propofol: systematic review and meta-analysis. *BMJ* 2011;342:d1110.

[D312] Kalil AC, Mindru C, Florescu DF. Effectiveness of valganciclovir 900 mg versus 450 mg for cytomegalovirus prophylaxis in transplantation: direct and indirect treatment comparison meta-analysis. *Clin Infect Dis* 2011;52(3):313-21.

[D313] Karabis A, Lindner L, Mocarski M, Huisman E, Greening A. Comparative efficacy of aclidinium versus glycopyrronium and tiotropium, as maintenance treatment of moderate to severe COPD patients: a systematic review and network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2013;8:405-23.

[D314] Klemp M, Tvete IF, Skomedal T, Gaasemyr J, Natvig B, Aursnes I. A review and Bayesian meta-analysis of clinical efficacy and adverse effects of 4 atypical neuroleptic drugs compared with haloperidol and placebo. *J Clin Psychopharmacol* 2011;31(6):698-704.

[D315] Kotzé A, Scally A, Howell S. Efficacy and safety of different techniques of paravertebral block for analgesia after thoracotomy: a systematic review and metaregression. Br J Anaesth 2009;103(5):626-36.

[D316] Launois R, Avouac B, Berenbaum F, Blin O, Bru I, Fautrel B, et al. Comparison of certolizumab pegol with other anticytokine agents for treatment of rheumatoid arthritis: a multiple-treatment Bayesian metaanalysis. *J Rheumatol* 2011;38(5):835-45.

[D317] Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *BMJ* 2003;326(7404):1427-31.

[D318] Leung HW, Chan AL. Multikinase inhibitors in metastatic renal cell carcinoma: indirect comparison meta-analysis. *Clin Ther* 2011;33(6):708-16.

[D319] Levy AR, Johnston KM, Sambrook J, Donato B, Penrod JR, Corral M, et al. Indirect comparison of the efficacy of cetuximab and cisplatin in squamous cell carcinoma of the head and neck. *Curr Med Res Opin* 2011;27(12):2253-9.

[D320] Liu JL, Dong J, Wang L, Su Y, Yan P, Sun S. Comparative efficacy and acceptability of antidepressants in Parkinson's disease: a network meta-analysis. *Plos One* 2013;8(10):e76651.

[D321] Mantha S, Ansell J. An indirect comparison of dabigatran, rivaroxaban and apixaban for atrial fibrillation. *Thromb Haemost* 2012;108(3):476-84.

[D322] Martyn-St James M, Glanville J, McCool R, Duffy S, Cooper J, Hugel P, et al. The efficacy and safety of retigabine and other adjunctive treatments for refractory partial epilepsy: a systematic review and indirect comparison. *Seizure* 2012;21(9):665-78.

[D323] Maund E, McDaid C, Rice S, Wright K, Jenkins B, Woolacott N. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review. *Br J Anaesth* 2011;106(3):292-7.

[D324] Meader N. A comparison of methadone, buprenorphine and alpha2 adrenergic agonists for opioid detoxification: a mixed treatment comparison meta-analysis. Drug Alcohol Depend 2010;108(1-2):110-4.

[D325] Menzies D, Benedetti A, Paydar A, Martin I, Royce S, Pai M, et al. Effect of duration and intermittency of rifampin on tuberculosis treatment outcomes: a systematic review and meta-analysis. *PLoS Med* 2009;6(9):e1000146.

[D326] Mösges R, Nematian-Samani M, Hellmich M, Shah-Hosseini K. A meta-analysis of the efficacy of quinolone containing otics in comparison to antibiotic-steroid combination drugs in the local treatment of otitis externa. *Curr Med Res Opin* 2011;27(10):2053-60.

[D327] Ollendorf DA, Colby JA, Pearson SD. Comparative effectiveness of anti-vegf agents for diabetic macular edema. *Int J Technol Assess Health Care* 2013;29(4):392-401.

[D328] Otoul C, Arrigo C, van Rijckevorsel K, French JA. Meta-analysis and indirect comparisons of levetiracetam with other second-generation antiepileptic drugs in partial epilepsy. *Clin Neuropharmacol* 2005;28(2):72-8.

[D329] Otten MH, Anink J, Spronk S, van Suijlekom-Smit LW. Efficacy of biological agents in juvenile idiopathic arthritis: a systematic review using indirect comparisons. Ann Rheum Dis 2013;72(11):1806-12.

[D330] Owen A. Antithrombotic treatment for the primary prevention of stroke in patients with non valvular atrial fibrillation: a reappraisal of the evidence and network meta analysis. *Int J Cardiol* 2010;142(3):218-23.

[D331] Packer M, Antonopoulos GV, Berlin JA, Chittams J, Konstam MA, Udelson JE. Comparative effects of carvedilol and metoprolol on left ventricular election fraction in heart failure: results of a meta-analysis. *Am Heart J* 2001;141(6):899-907.

[D332] Piccini JP, Hasselblad V, Peterson ED, Washam JB, Califf RM, Kong DF. Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation. *J Am Coll Cardiol* 2009;54(12):1089-95.

[D333] Pink J, Pirmohamed M, Hughes DA. Comparative effectiveness of dabigatran, rivaroxaban, apixaban, and warfarin in the management of patients with nonvalvular atrial fibrillation. Clin Pharmacol Ther 2013;94(2):269-76.

[D334] Qi WX, Tang LN, He AN, Shen Z, Lin F, Yao Y. Erlotinib and pemetrexed as maintenance therapy for advanced non-small-cell lung cancer: a systematic review and indirect comparison. *Curr Med Res Opin* 2012;28(4):643-50.

[D335] Robenshtok E, Gafter-Gvili A, Goldberg E, Weinberger M, Yeshurun M, Leibovici L, et al. Antifungal prophylaxis in cancer patients after chemotherapy or hematopoietic stem-cell transplantation: systematic review and meta-analysis. *J Clin Oncol* 2007;25(34):5471-89.

[D336] Ronellenfitsch U, Schwarzbach M, Hofheinz R, Kienle P, Kieser M, Slanger TE, et al. Preoperative chemo(radio)therapy versus primary surgery for gastroesophageal adenocarcinoma: systematic review with meta-analysis combining individual patient and aggregate data. *Eur J Cancer* 2013;49(15):3149-58.

[D337] Roush GC, Holford TR, Guddati AK. Chlorthalidone compared with hydrochlorothiazide in reducing cardiovascular events: systematic review and network meta-analyses. *Hypertension* 2012;59(6):1110-7.

[D338] Rudroju N, Bansal D, Talakokkula ST, Gudala K, Hota D, Bhansali A, et al. Comparative efficacy and safety of six antidepressants and anticonvulsants in painful diabetic neuropathy: a network meta-analysis. *Pain Physician* 2013;16(6):E705-14.

[D339] Sauriol L, Laporta M, Edwardes MD, Deslandes M, Ricard N, Suissa S. Meta-analysis comparing newer antipsychotic drugs for the treatment of schizophrenia: evaluating the indirect approach. *Clin Ther* 2001;23(6):942-56.

[D340] Schoels M, Aletaha D, Smolen JS, Wong JB. Comparative effectiveness and safety of biological treatment options after tumour necrosis factor alpha inhibitor failure in rheumatoid arthritis: systematic review and indirect pairwise meta-analysis. *Ann Rheum Dis* 2012;71(8):1303-8.

[D341] Sciarretta S, Palano F, Tocci G, Baldini R, Volpe M. Antihypertensive treatment and development of heart failure in hypertension: a Bayesian network meta-analysis of studies in patients with hypertension and high cardiovascular risk. *Arch Intern Med* 2011;171(5):384-94.

[D342] Shamliyan TA, Choi JY, Ramakrishnan R, Miller JB, Wang SY, Taylor FR, et al. Preventive pharmacologic treatments for episodic migraine in adults. *J Gen Intern Med* 2013;28(9):1225-37.

[D343] Shi KQ, Liu WY, Pan ZZ, Ling XF, Chen SL, Chen YP, et al. Secondary prophylaxis of variceal bleeding for cirrhotic patients: a multiple-treatments meta-analysis. *Eur J Clin Invest* 2013;43(8):844-54.

[D344] Shu T, Chen GH, Rong L, Feng F, Yang B, Chen R, et al. Indirect comparison of anti-TNF-alpha agents for active ankylosing spondylitis: mixed treatment comparison of randomised controlled trials. Clin Exp Rheumatol 2013;31(5):717-22.

[D345] Stegeman BH, de Bastos M, Rosendaal FR, van Hylckama Vlieg A, Helmerhorst FM, Stijnen T, et al. Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis. *BMJ* 2013;347(7925):f5298.

[D346] Stevens JW, Simpson E, Harnan S, Squires H, Meng Y, Thomas S, et al. Systematic review of the efficacy of cilostazol, naftidrofuryl oxalate and pentoxifylline for the treatment of intermittent claudication. *Br J Surg* 2012;99(12):1630-8.

[D347] Szegedi A, Verweij P, van Duijnhoven W, Mackle M, Cazorla P, Fennema H. Meta-analyses of the efficacy of asenapine for acute schizophrenia: comparisons with placebo and other antipsychotics. J Clin Psychiatry 2012;73(12):1533-40.

[D348] Tang DH, Malone DC. A network meta-analysis on the efficacy of serotonin type 3 receptor antagonists used in adults during the first 24 hours for postoperative nausea and vomiting prophylaxis. *Clin Ther* 2012;34(2):282-94.

[D349] Thijs V, Lemmens R, Fieuws S. Network meta-analysis: simultaneous meta-analysis of common antiplatelet regimens after transient ischaemic attack or stroke. *Eur Heart J* 2008;29(9):1086-92.

[D350] Tonelli M, Lloyd A, Clement F, Conly J, Husereau D, Hemmelgarn B, et al. Efficacy of statins for primary prevention in people at low cardiovascular risk: a meta-analysis. *CMAJ* 2011;183(16):E1189-202.

[D351] Trkulja V, Kolundzic R. Rivaroxaban vs dabigatran for thromboprophylaxis after joint-replacement surgery: exploratory indirect comparison based on metaanalysis of pivotal clinical trials. *Croat Med J* 2010;51(2):113-23.

[D352] Turkstra E, Ng SK, Scuffham PA. A mixed treatment comparison of the short-term efficacy of biologic disease modifying anti-rheumatic drugs in established rheumatoid arthritis. *Curr Med Res Opin* 2011;27(10):1885-97.

[D353] Tzellos TG, Toulis KA, Goulis DG, Papazisis G, Zampeli VA, Vakfari A, et al. Gabapentin and pregabalin in the treatment of fibromyalgia: a systematic review and a meta-analysis. *J Clin Pharm Ther* 2010;35(6):639-56.

[D354] Uthman OA, Abdulmalik J. Comparative efficacy and acceptability of pharmacotherapeutic agents for anxiety disorders in children and adolescents: a mixed treatment comparison meta-analysis. Curr Med Res Opin 2010;26(1):53-9.

[D355] Verduyn SC, Biesma B, Schramel FM, van der Scheer FW, Langenfeld MK, de Peuter MA, et al. Estimating quality adjusted progression free survival of first-line treatments for EGFR mutation positive non small cell lung cancer patients in The Netherlands. *Health Qual Life Outcomes* 2012;10:108.

[D356] Whegang Youdom S, Samson A, Basco LK, Thalabard JC. Multiple treatment comparisons in a series of anti-malarial trials with an ordinal primary outcome and repeated treatment evaluations. *Malar J* 2012;11:147.

[D357] Woo G, Tomlinson G, Nishikawa Y, Kowgier M, Sherman M, Wong DK, et al. Tenofovir and entecavir are the most effective antiviral agents for chronic hepatitis B: a systematic review and Bayesian meta-analyses. *Gastroenterology* 2010;139(4):1218-29.

[D358] Yang Q, Wei Y, Chen YX, Zhou SW, Jiang ZM, Xie DR. Indirect comparison showed survival benefit from adjuvant chemoradiotherapy in completely resected gastric cancer with d2 lymphadenectomy. *Gastroenterol Res Pract* 2013;2013:634929.

[D359] Zagmutt FJ, Tarrants ML. Indirect comparisons of adverse events and dropout rates in early Parkinson's disease trials of pramipexole, ropinirole, and rasagiline. Int J Neurosci 2012;122(7):345-53.

[D360] Zeng L, Luo R, Zhang L. Efficacy of high-dose ACTH versus low-dose ACTH in infantile spasms: a meta-analysis with direct and indirect comparison of randomized trials. *J Pediatr Neurol* 2011;9(2):141-9.

[D361] Zou YD, Sheng Z, Niu S, Wang H, Yu J, Xu J. Lenalidomide versus thalidomide based regimens as first-line therapy for patients with multiple myeloma. *Leuk Lymphoma* 2013;54(10):2219-25.

# Appendix E: Co-authorship of indirect comparison meta-analytic methods by country over time

Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000 to 2013. Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), while authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow).

## 2001

## 2002

## 2003

## 2004

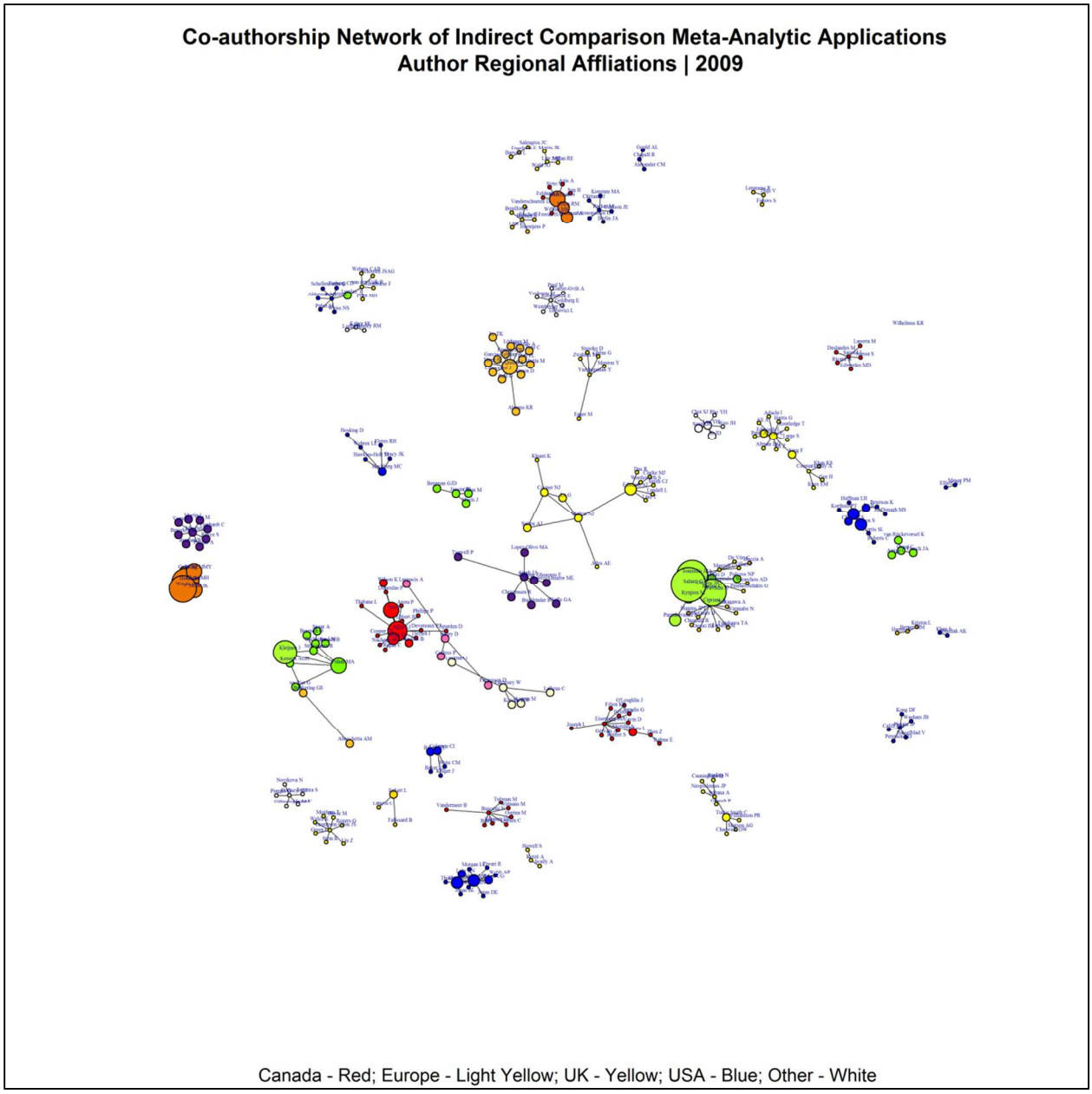
## 2005

## 2006

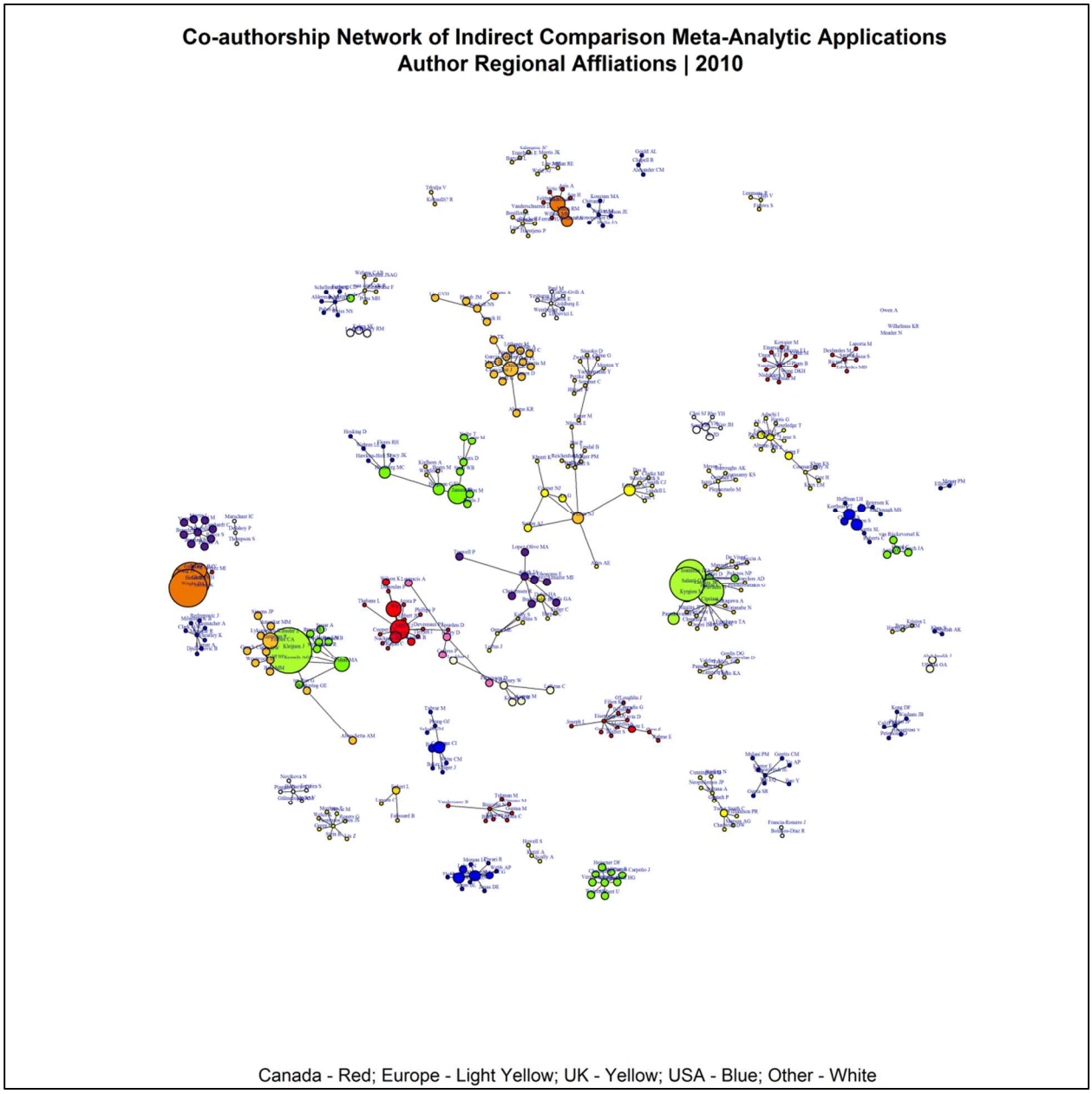
## 2007

## 2008

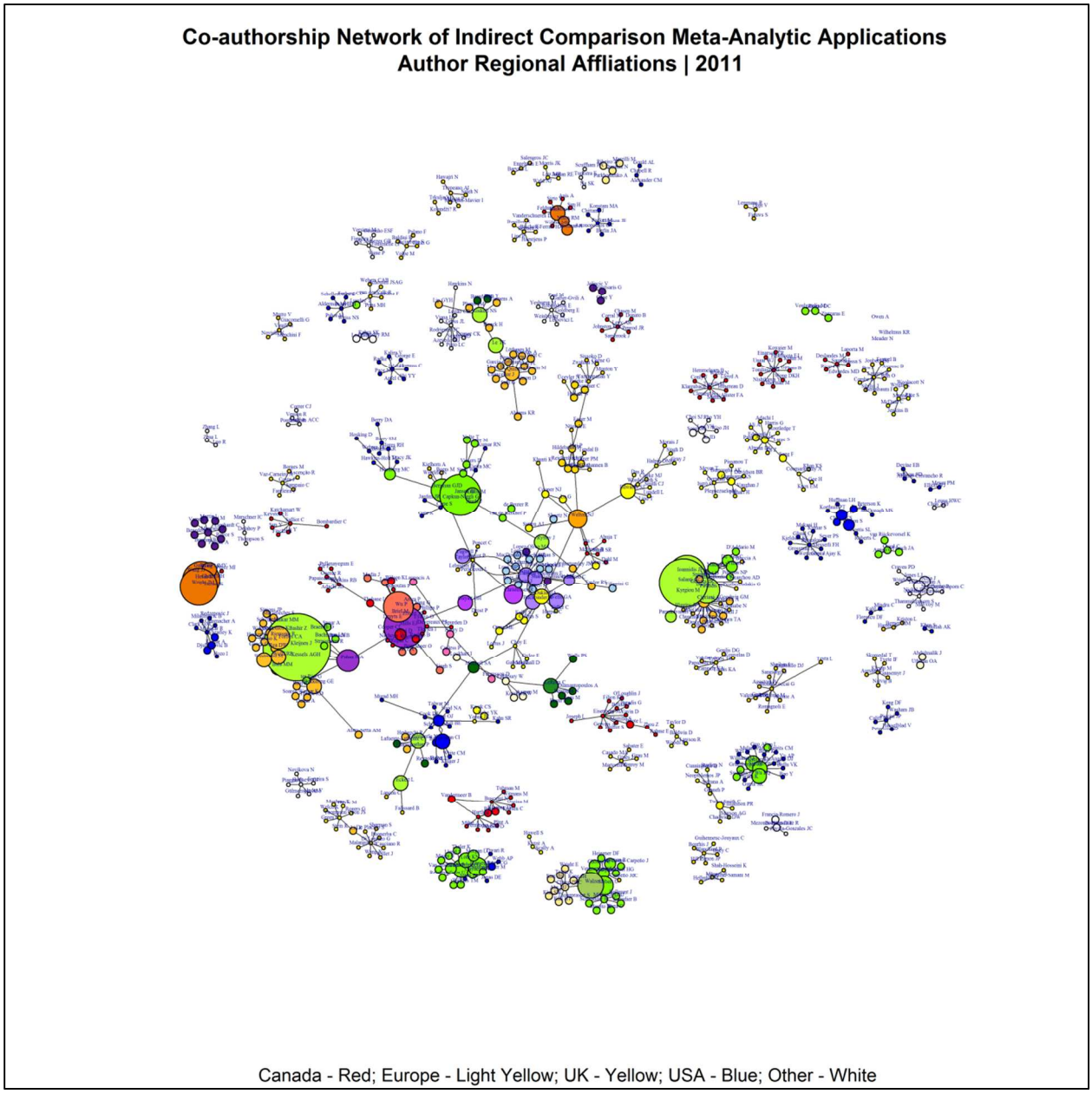
## 2009



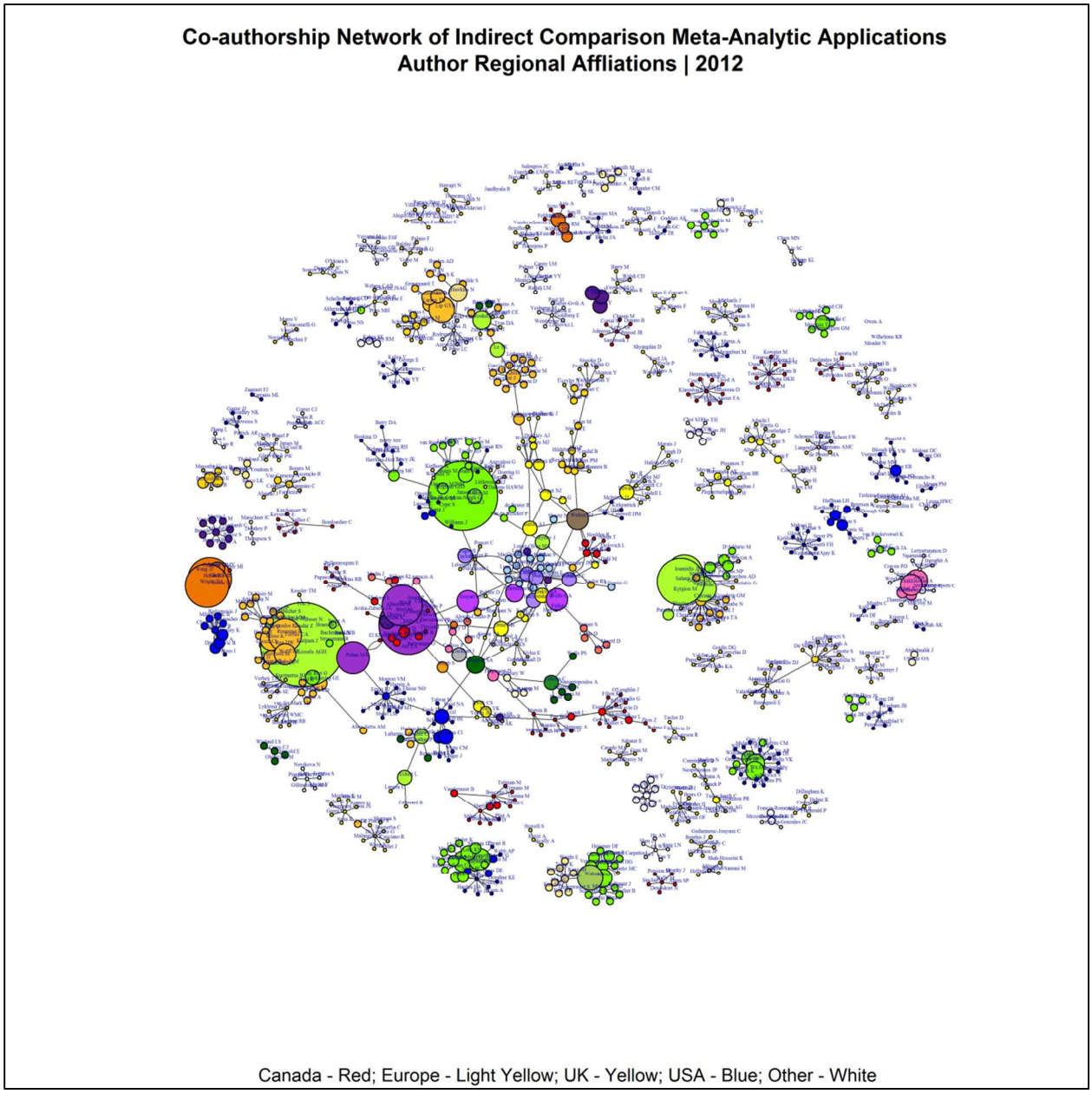
## 2010



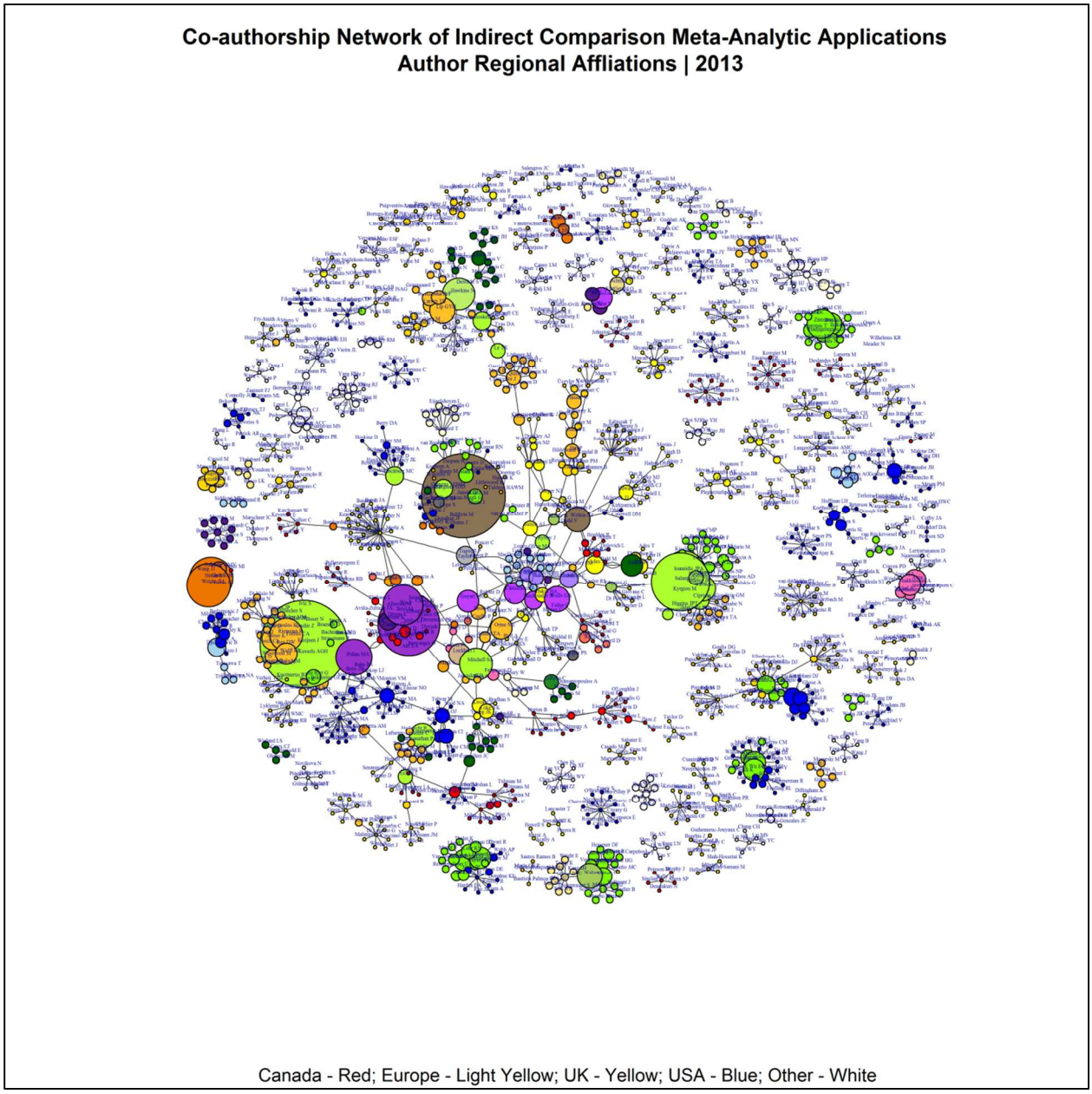
## 2011



## 2012



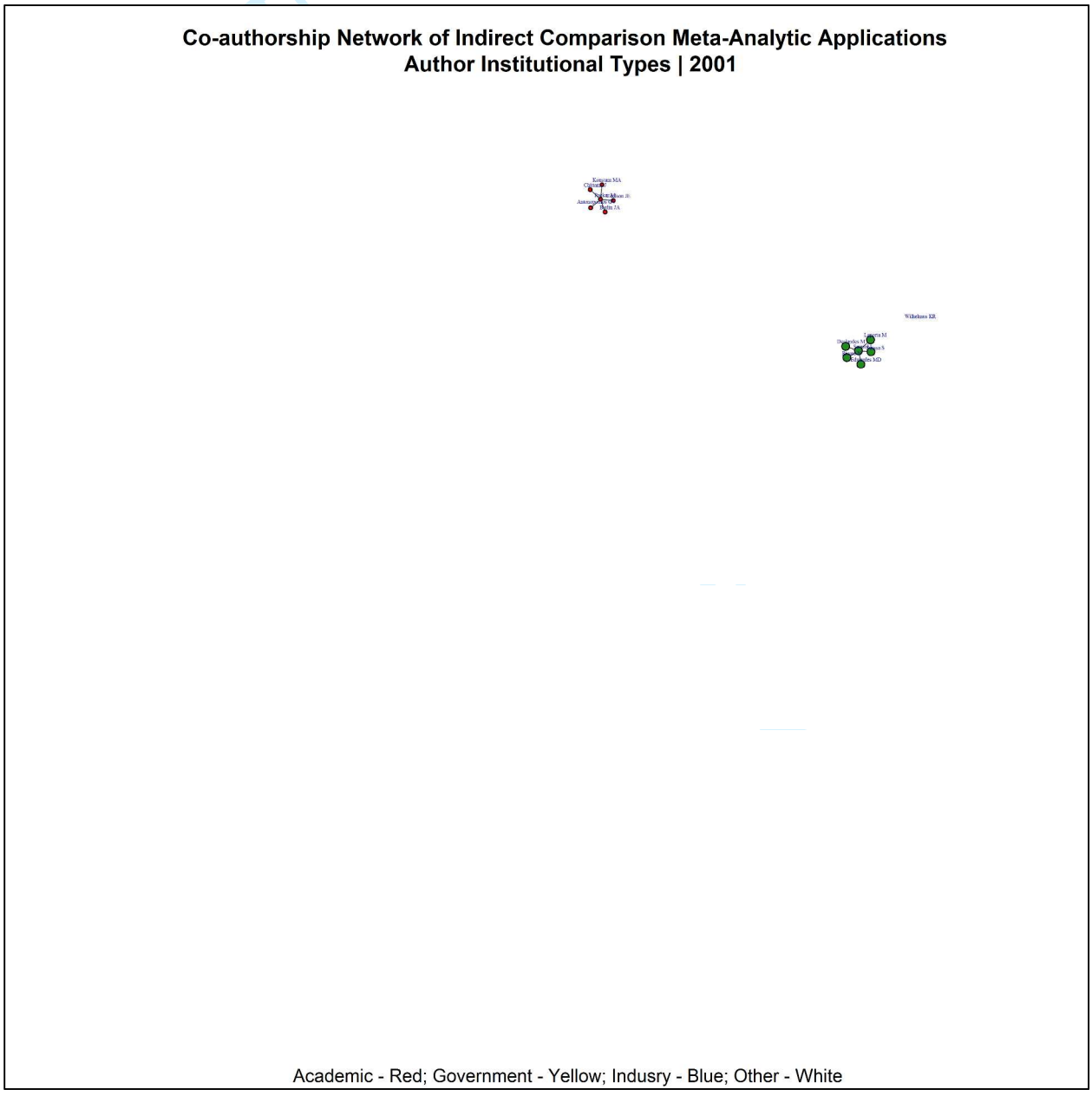
## 2013



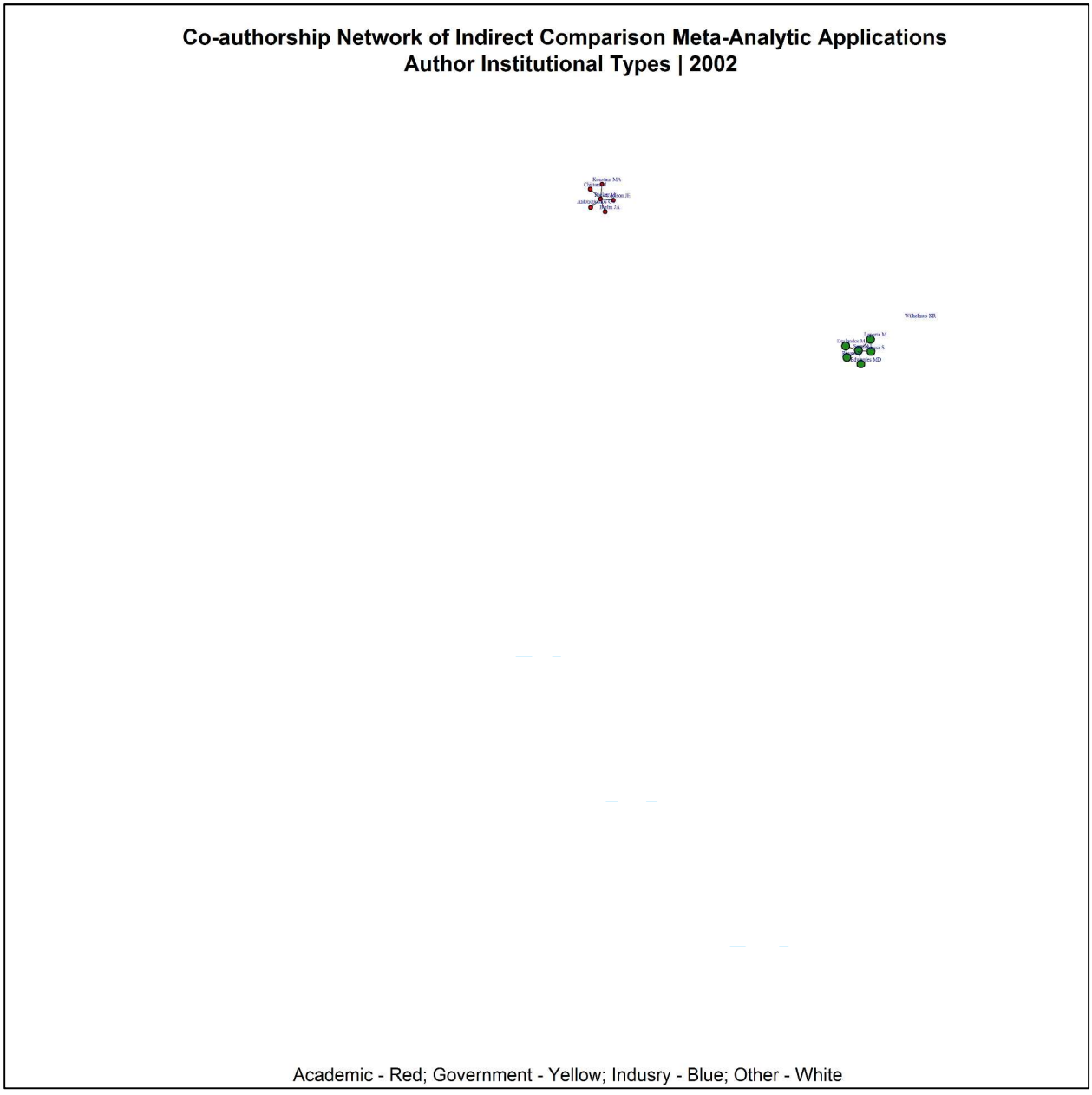
# Appendix F: Co-authorship of indirect comparison meta-analytic methods by affiliation type over time

Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliation types from academia and government were coloured orange (a combination of red and yellow), while authors on papers affiliated with academic, industry, and other were coloured light purple (a combination of red, blue, and white).

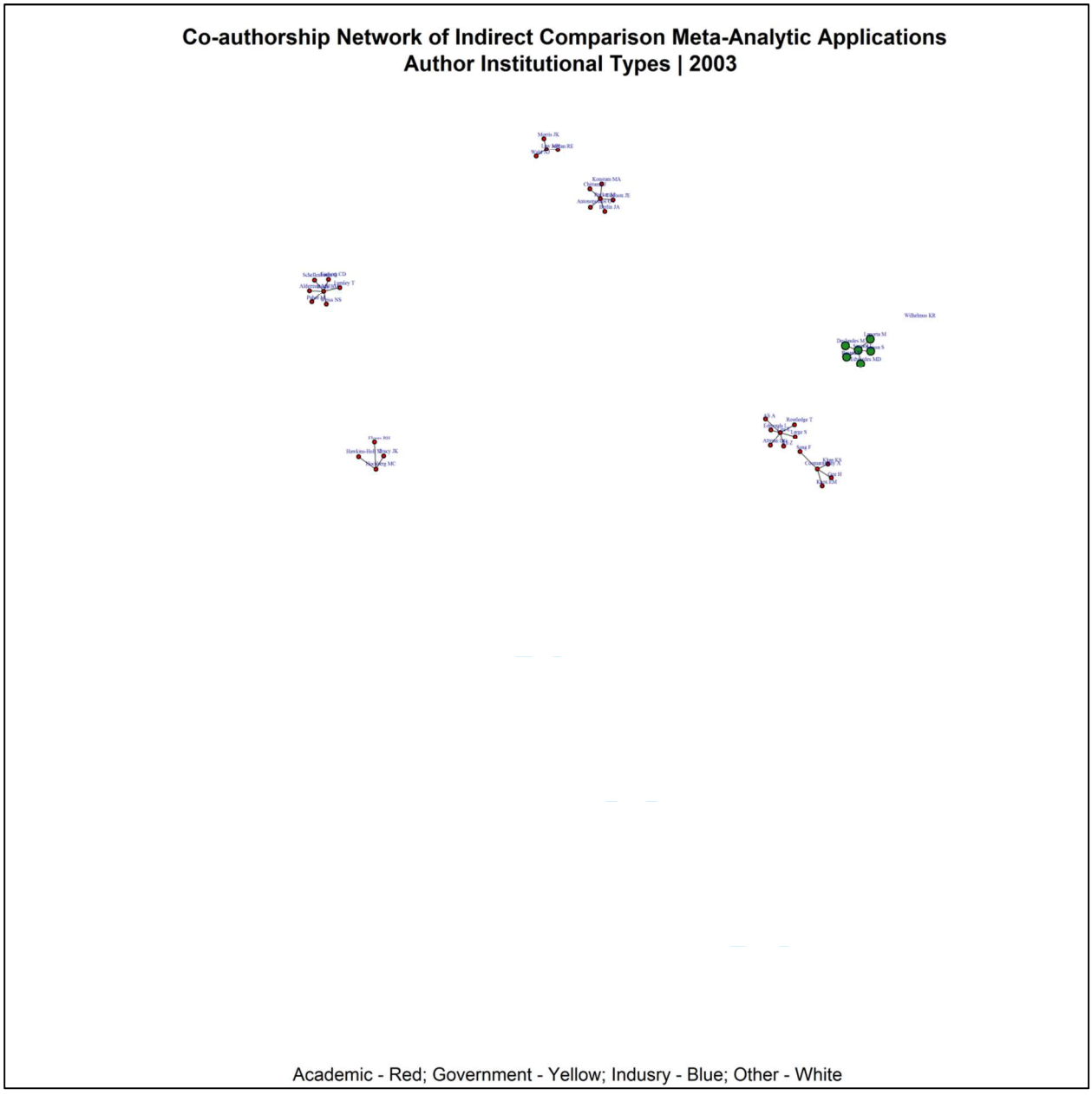
## 2001



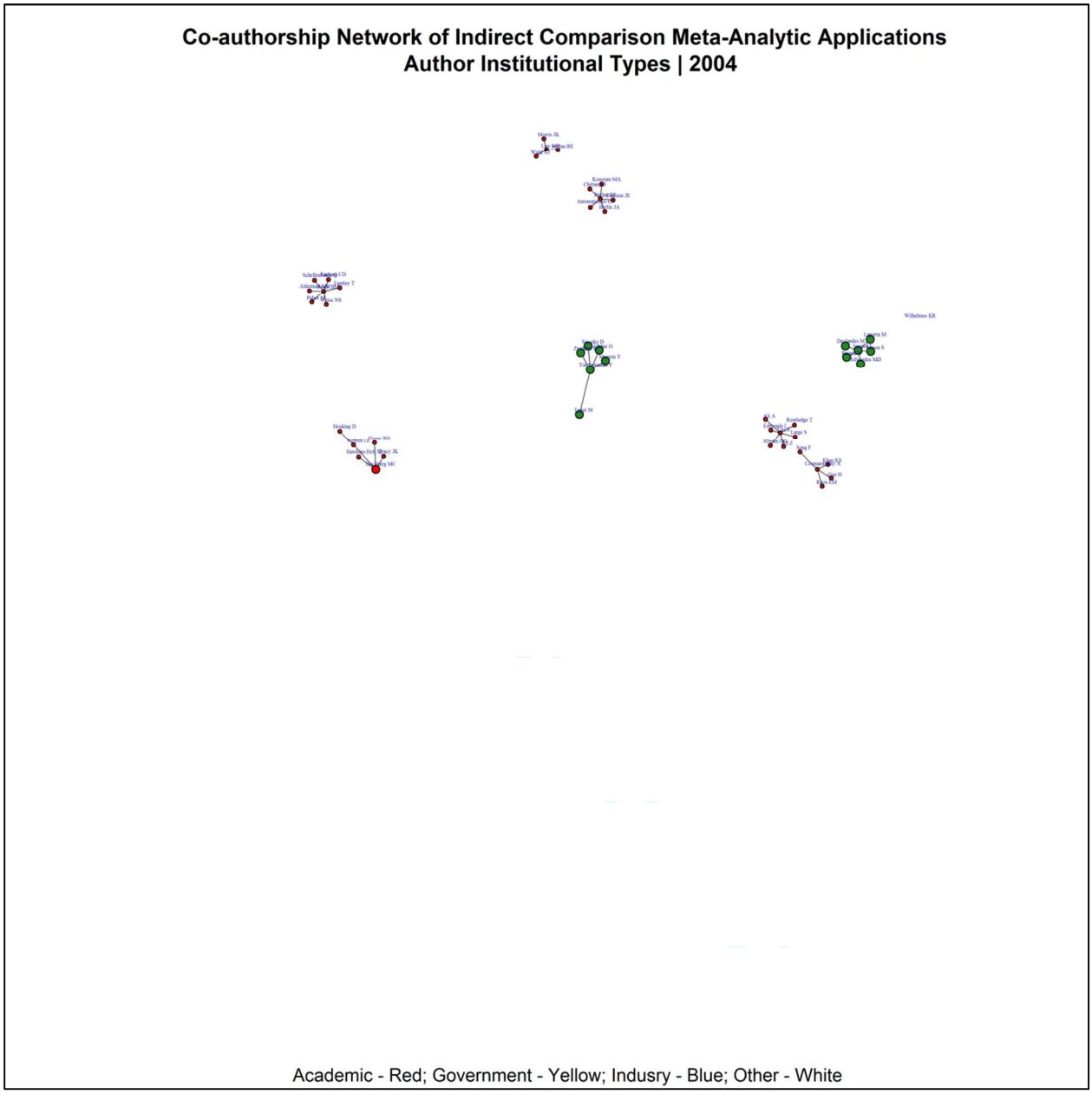
## 2002



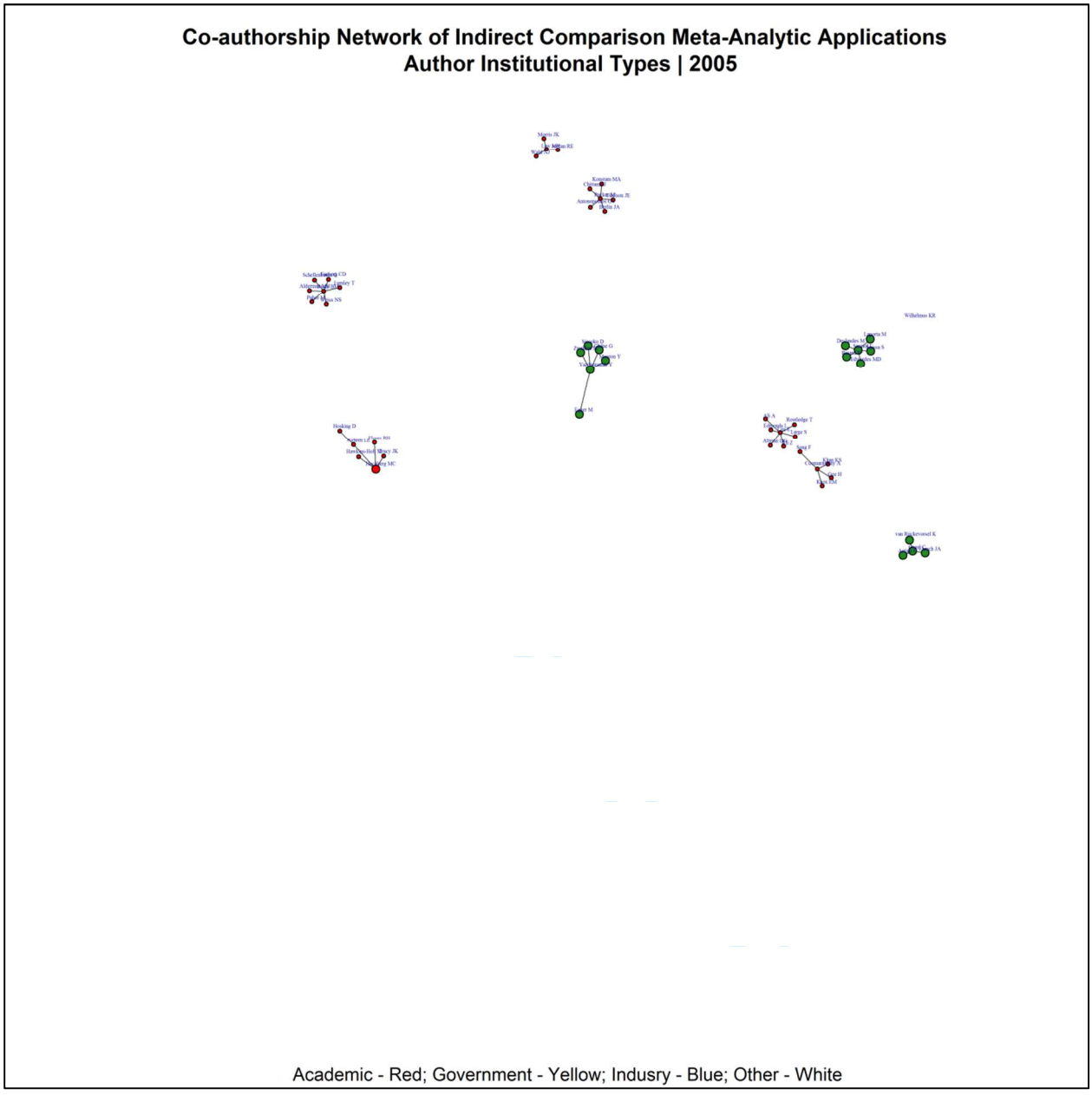
## 2003



## 2004



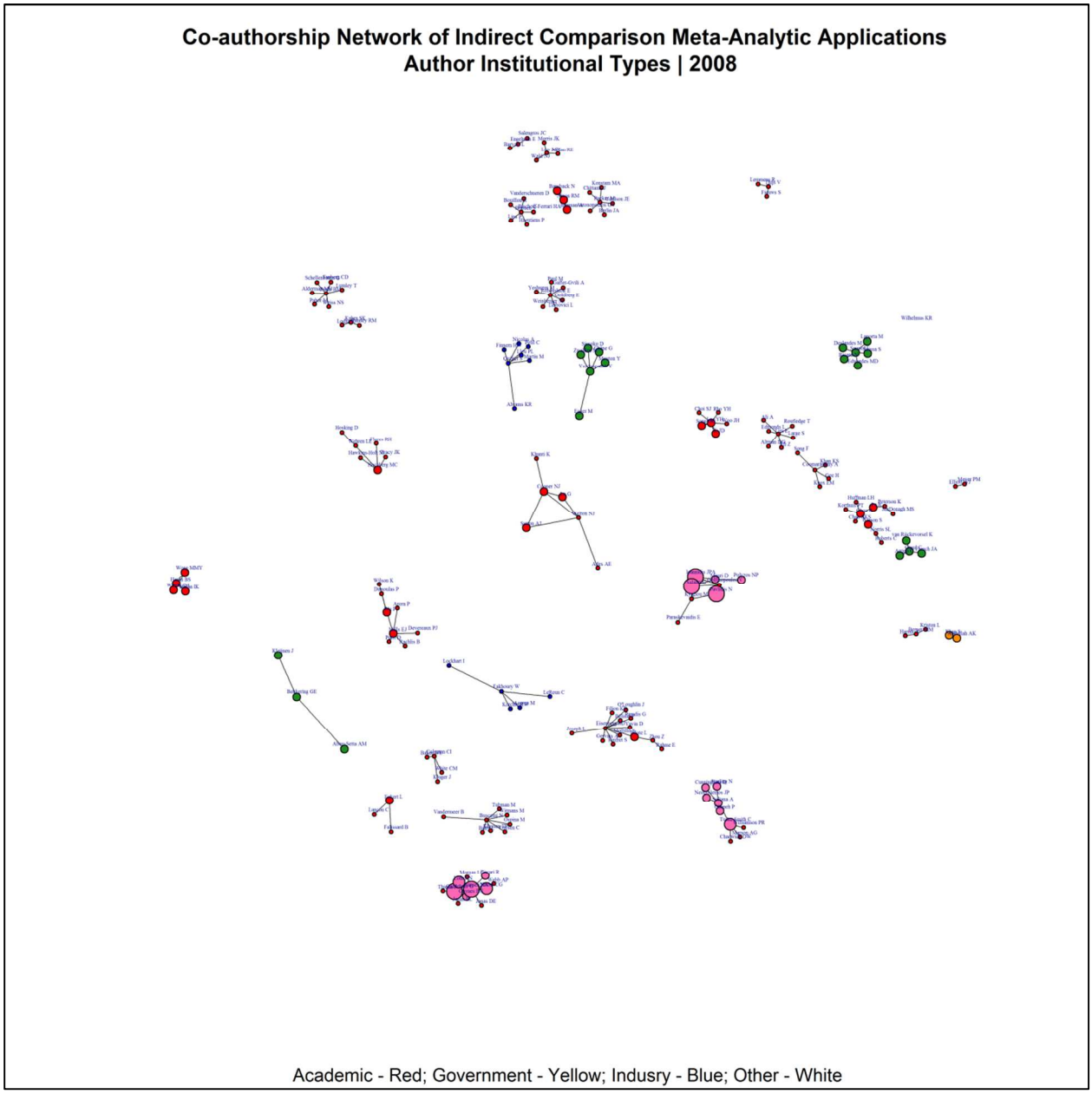
## 2005



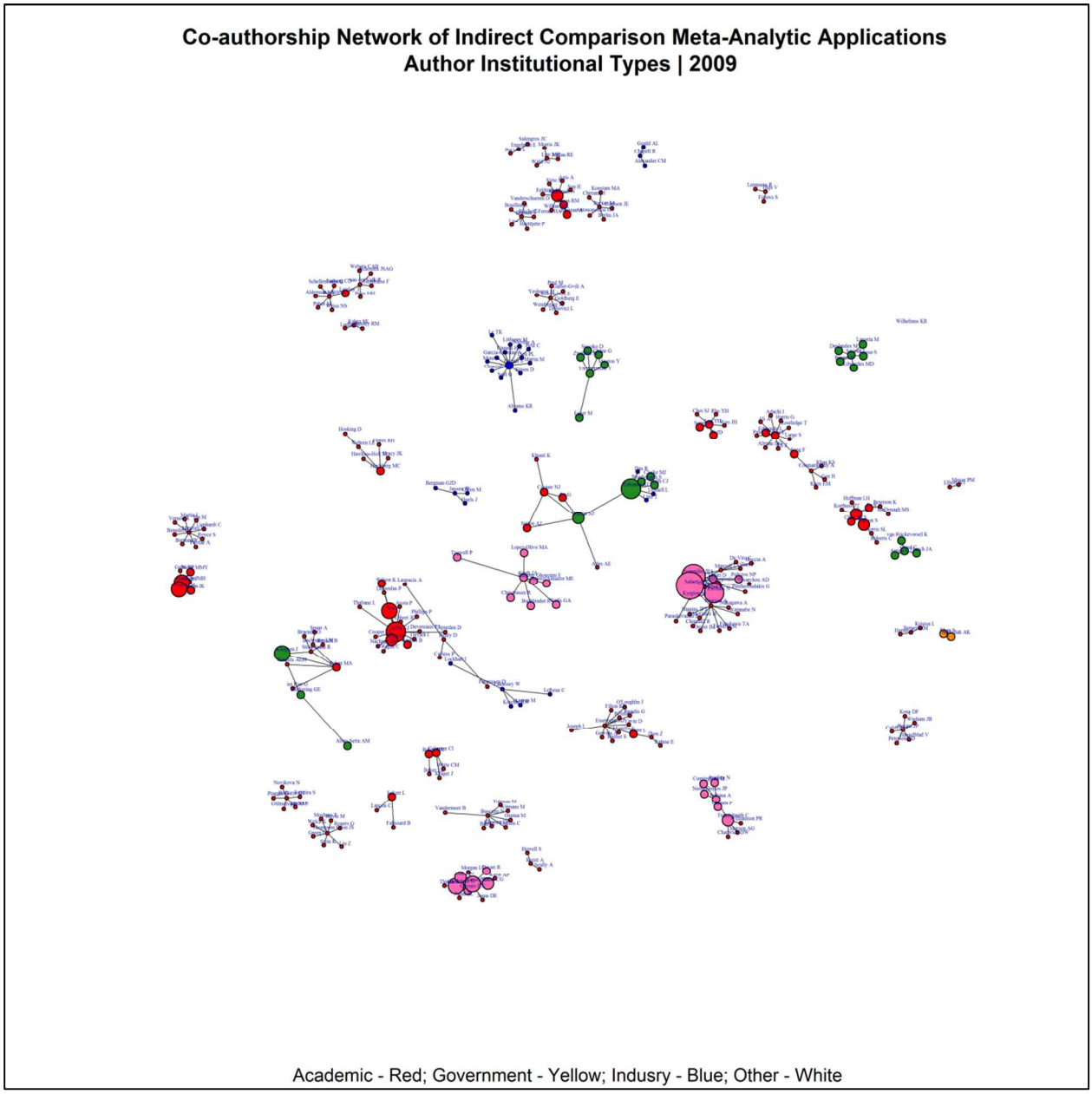
## 2006

## 2007

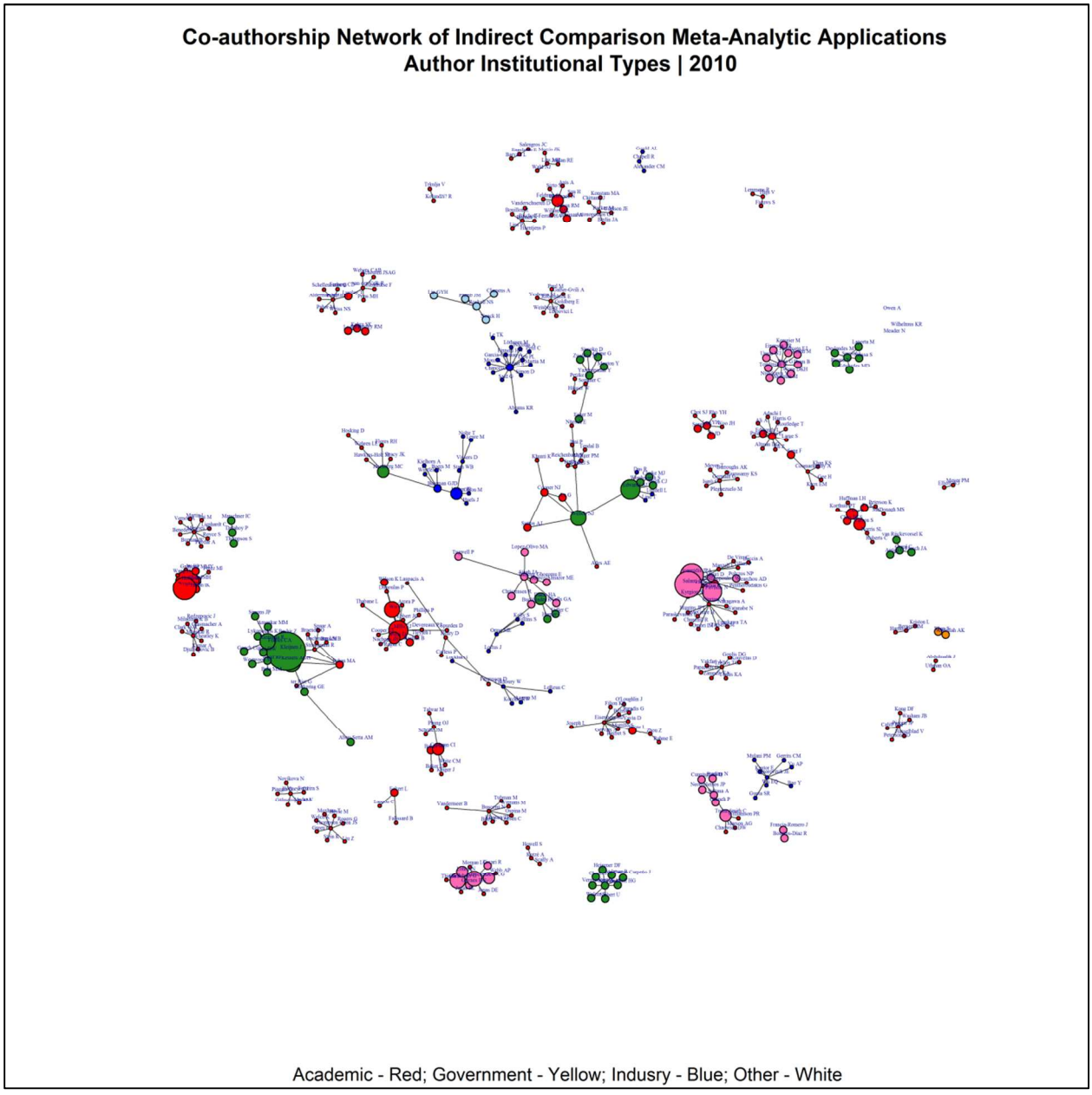
## 2008



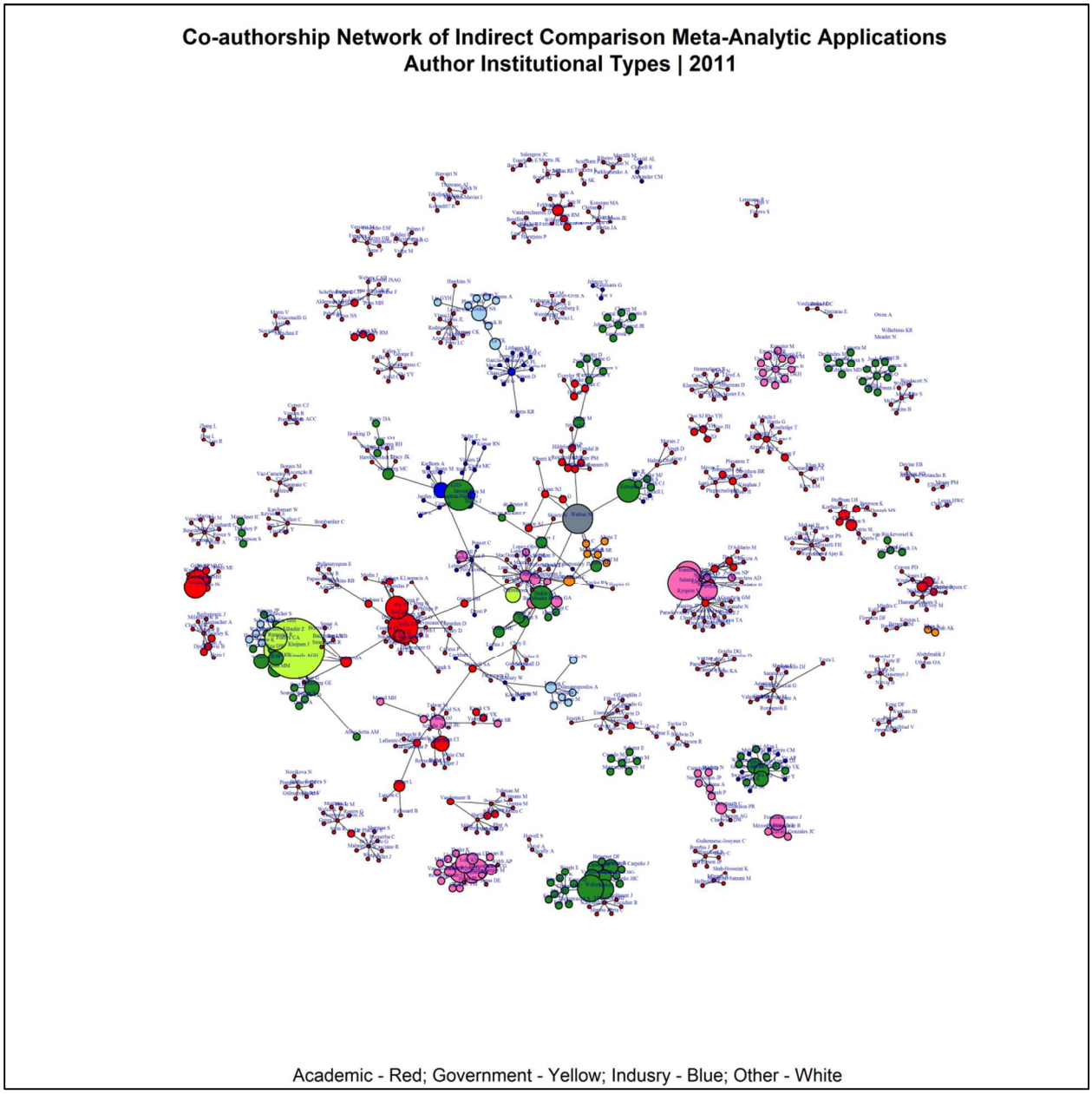
## 2009



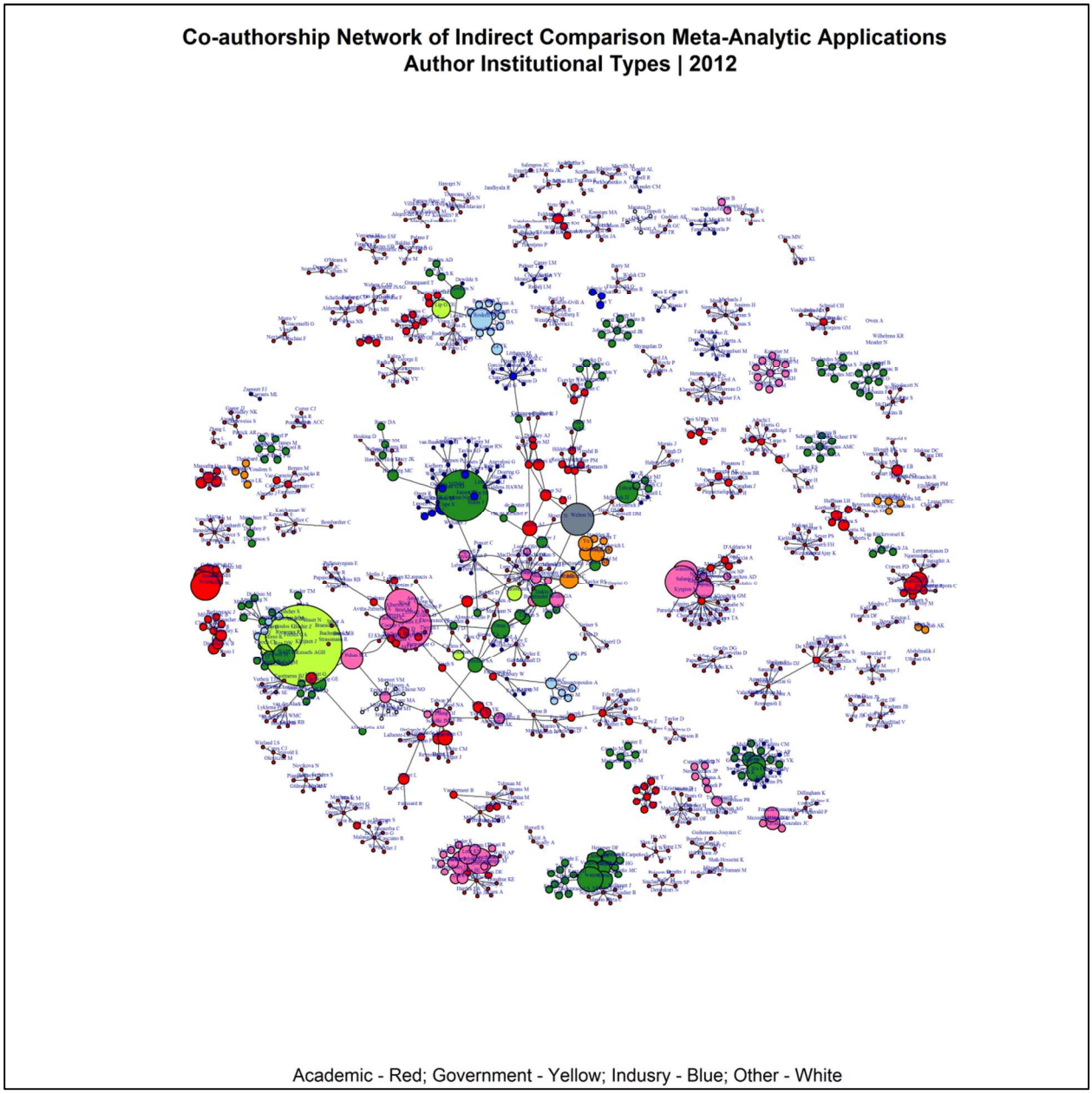
## 2010



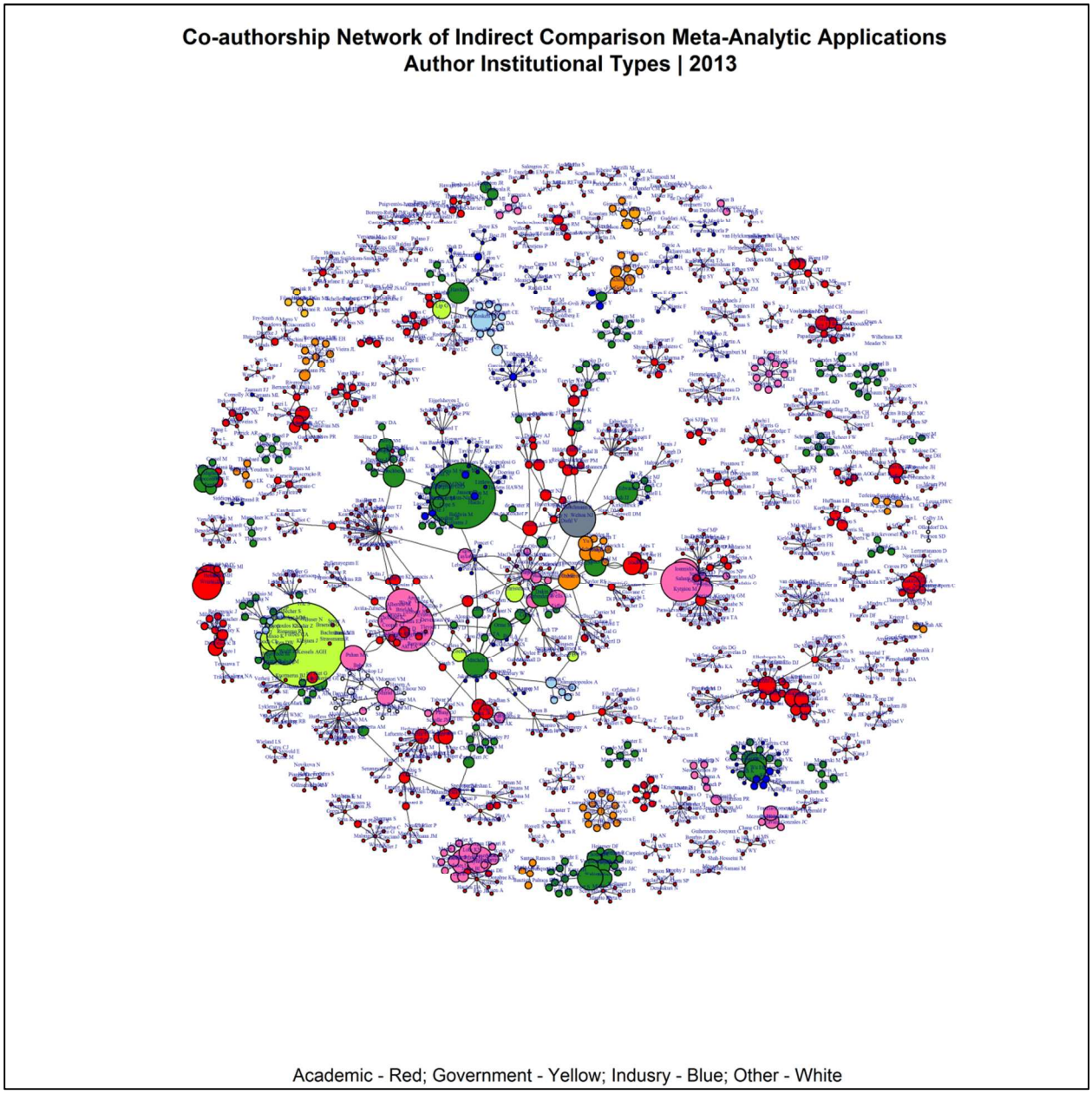
## 2011



## 2012



## 2013



BMJ Open

# History and Publication Trends in the Diffusion and Early Uptake of Indirect Comparison Meta-Analytic Methods to Study Drugs: Animated Co-Authorship Networks over Time

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-019110.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 22-Feb-2018 |
| Complete List of Authors: | Ban, Joann; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Tadrous, Mina; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Lu, Amy; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Cicinelli, Erin; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Cadarette, Suzanne; University of Toronto, Leslie Dan Faculty of Pharmacy |
| Primary Subject Heading: | Research methods |
| Secondary Subject Heading: | Communication |
| Keywords: | Diffusion of innovations, Indirect comparisons, Methodological innovation, Network meta-analysis, Social networks |
| | |

Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.

Supplemental Material 1.avi
Supplemental Material 2.avi

# History and Publication Trends in the Diffusion and Early Uptake of Indirect Comparison Meta-Analytic Methods to Study Drugs: Animated Co-Authorship Networks over Time

Joann K. Ban,[1] Mina Tadrous,[1] Amy X. Lu, [1] Erin A. Cicinelli,[1] Suzanne M. Cadarette[1]

[1]Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

**Correspondence to:** Mina Tadrous, Leslie L. Dan Pharmacy Building, University of Toronto, 144 College Street, Toronto, Ontario, M5S 3M2 Canada. Tel: 416-864-6060, E-mail: mina.tadrous@mail.utoronto.ca

**Conflict of Interest:** None related to this work.

**Word Count:** 3,925

**Subject Heading:** Research methods (primary), Communication (secondary)

**Keywords:** Diffusion of Innovations, Indirect Comparisons, Methodological Innovation, Network Meta-Analysis, Social Networks

## ABSTRACT

**Objective:** To characterize the early diffusion of indirect comparison meta-analytic methods to study drugs.

**Design:** Systematic literature synthesis.

**Data sources:** Cochrane Database of Systematic Reviews®, EMBASE®, MEDLINE®, Scopus®, and Web of Science®.

**Study selection:** English language papers that used indirect comparison meta-analytic methods to study the efficacy or safety of three or more interventions, where at least one was a drug.

**Data extraction:** The number of publications and authors were plotted by year and type: methodological contribution, review, or empirical application. Author and methodological details were summarized for empirical applications, and animated co-authorship networks were created to visualize contributors by country and affiliation type (academia, industry, government, or other) over time.

**Results:** We identified 477 papers (74 methodological contributions, 42 reviews, and 361 empirical applications) by 1,689 distinct authors from 1997 to 2013. Prior to 2002, only three applications were published, with contributions from the United States (n=2) and Canada (n=1). The number of applications gradually increased annually with rapid uptake between 2011 and 2013 (n=254, 71%). Early diffusion occurred primarily in Europe with the first application credited to the United Kingdom in 2003. Application spread to other European countries in 2005, and may have been supported by regulatory requirements for drug approval. By the end of 2013, contributions included 49% credited to Europe (22% United Kingdom, 27% other), 37% credited to North America (11% Canada, 26% United States), and 14% from other regions.

**Conclusion:** Indirect comparison meta-analytic methods are an important innovation for health research. Although Canada and the United States were the first to apply these methods, Europe led their diffusion. The increase in uptake of these methods may have been facilitated by acceptance by regulatory agencies, which are calling for more comparative drug effect data to assist in drug accessibility and reimbursement decisions.

**Abstract word count:** 296 (MAX 300 WORDS)

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our paper walks through the development and history of indirect comparison meta-analytic methods and its early diffusion in the study of drugs using co-authorship networks. Our animated co-authorship networks are innovative by allowing the visualization of social structures and collaboration trends through authors and their connections with each other over time.
- Mapping contributions based on first and last authors may miss some important contributions by co-authors, yet including second authors had little impact in a prior study.
- An extensive systematic literature search was completed to identify all eligible English language papers that used indirect comparison meta-analytic methods to study drugs through to December 2013. This period of time permits assessment of early diffusion including 477 papers (361 empirical applications). However, some relevant papers may have been missed, such as non-English language papers and grey literature. In addition, our paper did not consider methodological and reporting quality, since focus was on early uptake by country and institutional affiliation. Our results set the stage for further research that may consider quality.

# INTRODUCTION

Randomized controlled trials (RCT) are essential for bringing novel pharmaceutical products to market. RCTs for drug approval typically compare new treatment efficacy to placebo and provide safety data for only common adverse effects. However, RCTs are often not powered to identify all important drug efficacy and safety endpoints and thus meta-analytic methods were developed. Meta-analysis is a statistical method that combines the results of two or more studies to evaluate the same intervention in comparison to a control such as placebo, to obtain a more precise estimate of the intervention's effects relative to that control [1-3]. The term *meta-analysis* was first coined by G. V. Glass in 1976, yet use of statistical methods to combine the results of multiple studies dates back to the early part of the 20$^{th}$ century, with early methodological techniques proposed by R. Fisher and W. Cochran in the 1930s [1, 2].

When completed using high quality RCTs, meta-analyses are regarded as providing the highest level of evidence [4]. However, traditional pairwise meta-analysis is limited by only being able to combine and estimate the benefits or harms of two treatments if they have been compared directly. In addition, meta-analysis cannot compare more than two treatments at a time [3, 5]. This presents a challenge to policy-makers, clinicians, and patients who often need to select the most optimal treatment from several competing options [6]. Indirect comparisons have been made informally using point estimates and 95% confidence intervals of treatments [7]. However, this informal approach does not provide a precise estimate of the relative difference between two treatments because the relative effects are not measured.

In 1997, the *adjusted indirect comparison* method was proposed by H. C. Bucher, as an innovative meta-analytic approach that utilizes indirect evidence to estimate the relative benefits and risks between two treatments [8]. Unlike traditional pairwise meta-analysis, adjusted indirect

comparisons estimate the relative effects of two treatments that have not been compared directly by leveraging results from each treatment that has been compared to a common comparator, such as a placebo [6, 8, 9]. However, the adjusted indirect comparison method ignores direct evidence, even when available. In 2002, *network meta-analysis* was proposed as an extension of the adjusted indirect comparison method that combines direct and indirect comparative data across several sets of pairwise treatment comparisons [5, 10]. The combination of direct and indirect data yields more precise effect estimates [6]. A similar method, coined *mixed treatment comparison*, was proposed in 2004 [11], and the term *multiple treatment meta-analysis* was also introduced to describe concepts of combining both direct and indirect evidence in 2005 [5], **Table 1**.

Indirect comparison meta-analytic methods have become valuable tools in clinical and policy decision making, and have thus, been rapidly adopted since their introduction [7, 12-14]. However, application of these methodological innovations varies widely [6, 12, 15]. Rogers' Diffusion of Innovations Model defines *diffusion* as the process by which an innovation is communicated across individuals within a social system, particularly during the initial stages of its use [16, 17]. Our study sought to characterize the early diffusion of indirect comparison meta-analytic methods used to study drugs [16]. We interpreted diffusion and uptake relative to the social system, by creating co-authorship networks to examine the speed of uptake (number of publications) and spread of these methods (collaboration between authors, authors' countries, and across institutions) over time.

## MATERIALS AND METHODS

We recently examined the diffusion of two confounder summary score methods and illustrate the importance of innovation attributes (**relative advantage, compatibility, simplicity, trialability,** and **observability**) and seminal author engagement on the uptake of methodological innovations using Rogers' Diffusion of Innovations Model [16]. In addition to innovation attributes, Rogers' Model identifies key aspects of the social system that may impact the rate of adoption [17]. In particular, a methodological innovation will have a quicker rate of adoption if members within the social system (e.g., researchers, clinicians, and policymakers) share similar system norms. For example, regulatory agencies make decisions for drug approval and formulary coverage. Regulatory agencies are therefore well-positioned to influence the uptake of methodological innovations that support the drug approval process. If novel methods become a requirement for drug approval, pharmaceutical companies, which share a vested interest in the drug approval process, may willingly adopt the methodological innovation in question. We examined the diffusion and early uptake of indirect comparison meta-analytic methods used to study drugs, and interpreted contributions by country and affiliation type using Rogers' Diffusion of Innovations Model.

### Systematic Search

We completed a systematic literature search to identify all papers that utilized indirect comparison meta-analytic methods to study drug effects in humans. We searched the Cochrane Database of Systematic Reviews®, EMBASE®, and MEDLINE® from their dates of inception to 31 December 2013 using keywords based on a recent search (**Appendix A Table A**) [18]. We then used SCOPUS® and Web of Science® to perform a citation search to identify papers that

referenced key seminal papers [8, 10], major methodological contributions [19-21], and reviews [7, 13-15, 22, 23] on indirect comparison meta-analytic methods [18].

All English language papers that used indirect meta-analytic methods to compare the clinical efficacy or safety of three or more interventions among humans were eligible if at least one intervention was a drug. We excluded abstracts, letters, commentaries, cost-effectiveness studies, overviews of systematic reviews, protocols, and papers with no identifiable authors. Papers that used informal indirect comparisons (e.g., simply compared point estimates with 95% confidence intervals) or did not clearly describe the techniques used to perform the indirect comparison in the title, abstract, introduction, or methods sections were also excluded. Two authors (JKB and MT) independently searched and screened all titles and abstracts for eligibility. Discrepancies following full text review were resolved by a third author (SMC).

The number of papers and cumulative authors were plotted by calendar year and type: methodological contribution, review paper, or empirical application; and important social system events (e.g., publication of seminal papers) were added to the graph. We then focused exclusively on empirical applications. A proportional Venn diagram was used to illustrate the yield of each database search strategy that contributed to the identification of eligible empirical applications. We abstracted: author(s), journal, year of publication, area of study, primary outcomes (efficacy, safety, or both), first and last author institutional affiliations, terminology used to describe methods, and presence and details of network diagrams. If no primary outcome was explicitly stated, all outcomes were considered primary. When multiple diagrams were present, the total number of unique comparators across all network diagrams was taken. Two authors (JKB and EAC) abstracted all the data, and another (MT) verified the data.

## Co-Authorship Network of Empirical Applications

An Excel macro™ was used to generate a co-authorship matrix from author names downloaded into Microsoft Excel 2010 from Endnote X5 (Thomson Reuters, 2011). Names of authors presented in multiple forms were collapsed into the most common presentation or, in the event of a tie, the one with more initials. Publication (authors and order) and paper characteristics (country and institutional type ascribed) were imported into R®, version 3.3.1 (R Foundation for Statistical Computing, 2016), leveraging RStudio®, version 0.99.887 (RStudio, Inc., 2009), to generate directed co-authorship networks, and identify components. Co-authorship networks depict authors as "nodes" with "ties" between nodes denoting co-authorship. Directed co-authorship networks clarify network structure by sending "ties" depicted as arrows, from first authors to co-authors. A component is a group of authors connected directly as co-authors on the same paper, or indirectly through a mutual co-author on separate papers. A disconnected co-authorship network is based on the total number of components. The more components found in a co-authorship network, the more disconnected authors are from each other as a result of isolated publishing. Institutional affiliations and corresponding countries of the first and last authors of each empirical application were used to ascribe credit to each application and the network [16]. Institutions were categorized by country and type (academia, government, industry, or other). Node size was created proportional to the number of publications by that author. Node colour was created, first based on country affiliation attributed to each paper, and second based on institutional type. The networks were animated by calendar year of publication to visualize growth in application and contributions over time.

## Patient and Public Involvement

No patients or the public were involved in the development and design of this research.

# RESULTS

## Systematic Search

We identified 477 eligible papers: 74 methodological contributions (**Appendix B**), 42 review papers (**Appendix C**), and 361 empirical applications (**Appendix D**), **Figure 1**; published by 1,691 distinct authors between 1997 and 2013. A steady increase in the number of eligible papers was seen over time, and proportionally more were published in recent years, **Figure 2**. Focusing exclusively on the 361 empirical applications, the keyword search strategy identified most applications (n=314, 87%; 30% unique). EMBASE® identified the most (n=282, 78%; 6% unique), followed by MEDLINE® (n=239, 66%; 3% unique), and relatively few were identified by the Cochrane Database of Systematic Reviews® (n=20, 6%; <1% unique), **Appendix A Figure A**. The citation search identified an additional 47 (13%) papers outside keyword searches, **Appendix A Figure B**.

The indirect comparison meta-analytic applications were published in 188 different journals. The most common areas of study were cardiovascular disorders (22%), cancers (12%), musculoskeletal disorders (12%), infectious diseases (10%), and psychiatry (9%), **Table 2**. Sixty-nine percent of primary outcomes assessed therapeutic efficacy, 25% assessed efficacy and drug safety, and 6% assessed drug safety alone. Of the 361 empirical applications, only 161 (45%) published network diagrams illustrating the direct or indirect comparisons. The median number of interventions compared was 7 (interquartile range of 5-10, min=3, max=145). The most common terminology used was network meta-analysis (38%), followed by mixed treatment comparison (26%), Bucher's method (24%), and adjusted indirect comparison (21%). The sum of these percentages is greater than 100% due to an overlap in the terminology used. More

specifically, 18% (n=65) of all eligible empirical applications used two or more terms to describe the methods used.

## Co-Authorship Network of Empirical Applications

**Figure 3 (A: country, B: affiliation)** summarizes the final co-authorship networks, and **Appendix E-F** maps the growth of each network by country affiliation and institution type over time. The largest component included 143 (40%) papers and 567 (37%) authors, including innovators Guyatt GH, Lu G, and Ades AE, **Appendix D1-143**. Of the remaining 128 components, ninety (70%) included only a single paper (25% of all applications made up single-paper components), demonstrating a relatively disconnected network.

Early application of these methods started in 2000, with three papers published by 2002 [24-26]; and each referencing the innovator paper [8]. Authors were from Canada (red) and the United States (blue), and published in isolation of each other, **Appendix E**. In 2003, five papers were published in isolation of each other, with two credited to the United States (blue), and three credited to the United Kingdom (yellow). The majority referenced innovator Bucher [8], yet one paper referenced innovator Lumley [10]. By 2004, an increase in collaboration between authors from different countries was noted, with the first multi-paper component (France) published in 2004, and the first single-paper component with institutional affiliations from two countries (United States and Belgium) published in 2005. By 2006, another 13 papers were published: 11 papers referenced innovator Bucher with institutional affiliations credited to many countries worldwide (Belgium, Canada, France, Germany, India, United States), and two papers referenced two innovator papers [10, 11], with one paper credited to the United States, the United Kingdom, and Greece, and the other credited to the United Kingdom. From 2007 to 2013, we noted an increase in the number of applications published over time, with fastest uptake noted

in 2011, and an increase in authors publishing from a broad range of countries depicted by the increase in colours observed in the animated networks (**Appendix E-F** and **Supplemental Files 1-2**). In particular, a rapid increase in collaboration between authors was noted in 2009, as demonstrated by the merging of smaller components into larger components. Europe led the diffusion with node colours of yellow (United Kingdom), light yellow (all other Europe), and combinations of yellow with other primary colours comprising the majority of nodes in the co-authorship network.

Overall, institutional credit was given to 358 unique institutions around the world: 77% of contributions came from academic institutions, 18% from industry, 1% from government, and 4% from other institutions, **Table 3**. Europe led the diffusion with 49% of credited papers (22% United Kingdom, 27% other); 37% were credited to North America (26% United States, 11% Canada), and 14% to other regions.

## DISCUSSION

Indirect comparison meta-analytic methods are an important methodological innovation that has become valuable in providing comparative drug effect data in the absence of head-to-head trials. In this paper, we found that uptake was concentrated primarily in Europe (49%) with further contributions from North America (37%). Despite initial development from Canada (1997) and the United States (2002) [8, 10], our results are not surprising given that refined methods were published by core innovators from the Universities of Bristol and Washington [10, 11]. Early use of indirect comparison meta-analytic applications predominated from the United Kingdom, and may have been the result of an increase in demand by the United Kingdom government for more comparative effectiveness research to assist with clinical practice guideline development and to guide drug funding decisions. Indeed, the need for clinical practice guideline development was one of the major reasons for the establishment of the National Institute for Health and Clinical Excellence (NICE) in 1999 [27], which has since become a world leader in providing guidance on the clinical- and cost-effectiveness of new and established health technologies (including drugs). NICE decisions are made by independent committees of researchers, clinicians, industry and lay representatives; and have included innovator Ades, and early adopters from the NICE Guidelines Technical Support Unit, University of Bristol [5, 20, 28-30].

The steady increase in the use of indirect comparison meta-analytic methods, and effective diffusion to Europe and North America, may also be partially explained by consideration of the five key innovation attributes described in Rogers' Diffusion of Innovations Model (**relative advantage, compatibility, simplicity, trialability,** and **observability**) [16]. The Multi-Parameter Evidence Synthesis (MPES) Research Group (from which the NICE Guidelines Technical Support Unit is based) has offered introductory short-courses and workshops to

facilitate understanding and application of these methods to health economists, statisticians, and policy-makers worldwide in collaboration with other academic institutions in the United Kingdom (Universities of Sheffield and York) since 2002 (**observability, simplicity, trialability**) [30]. Active workshops demonstrating the use of this methodological innovation likely provided a vehicle for peer observation to occur, so that the results and benefits of using this innovation were visible to potential adopters (**observability**). The provision of sample datasets and statistical code, as well as the integration of these methods into established software and software packages, may have also eased the use of these methods (**simplicity**), and allowed potential adopters the chance to try using these methods with direct guidance from the innovators and early adopters themselves (**trialability**). In addition, the MPES Research Group published tutorials and case-studies highlighting the advantages of using pairwise, indirect comparison, and network meta-analyses for evidence synthesis (**advantage**), and highlighting the validity of these methods to inform clinical and policy decision-making (**compatibility**) [28, 31-34]. We noted rapid uptake since 2011, coinciding with the publication of guidelines and reviews on these methods by health technology assessment and reimbursement agencies (e.g., Canadian Agency for Drugs and Technologies in Health, Hauté Autorité de Santé, Institute for Quality and Efficiency in Health Care, Pharmaceutical Benefits Advisory Committee, and Scottish Medicines Consortium) from many countries around the world [19, 35-40].

Given the economic pressure on payers to better allocate healthcare resources, many regulatory agencies have been calling for the use of comparative effectiveness research to assist in drug accessibility and reimbursement decisions [39, 40]. In addition, applications focused on drug efficacy tie into payer demands for more cost-effectiveness analyses of newly marketed drugs in comparison with competing or existing therapies. For example, the Canadian Agency

for Drugs and Technologies in Health (CADTH) has published guidance documents to facilitate best practices in the use of indirect comparison meta-analytic methods to assess clinical and economic value of drugs and other health technologies in Canada, including how to best incorporate these methods to inform clinical parameters in these types of evaluations [19, 41]. Consequently, many pharmaceutical companies and contract research organizations have started to apply these methods. For example, the International Society for Pharmaceutical Outcomes Research Indirect Comparisons Good Research Practice Task Force adopted methods and statistical code from the MPES Research Group to publish a two-part report to guide researchers, clinicians, and policy-makers on good research practices for indirect comparisons; given its value and increasing acceptance by regulatory agencies [6, 15]. Co-authors mainly comprised of research experts from pharmaceutical companies and contract research organization (including J. P. Jansen who collaborated with innovator A. E. Ades and co-authors from the MPES Research Group), which may have helped disseminate use of these methods into industry. In addition, publication of this report may partially explain rapid and large uptake from 2011 since co-authors from the two-part report were from multiple countries (Belgium, Canada, the Netherlands, the United Kingdom, the United States). We believe that this observation may have been a response to requests by these agencies, as we noted collaboration with core innovators from academia, and an increase in the number of industry-sponsored applications published from 2009.

Our findings demonstrated rapid increase in the use of indirect comparison meta-analytic methods in recent years, with contributions increasing worldwide. With 70% (n=90) of the co-authorship network comprised of single paper components; and 81% (n=1,121) of authors having published only a single paper; use of indirect comparison meta-analytic methods has indeed

spread to many distinct research groups. However, uptake of these methods has been diffuse and highly disconnected when compared to the diffusion and early uptake of other methodological innovations [16], since many authors are publishing in isolation of each other (i.e., smaller, single paper components). In a prior study that examined the diffusion and early uptake of two confounder summary scores (the disease risk score and high-dimensional propensity score), only 19% and 11% of all eligible applications made up single paper components in their respective co-authorship networks in comparison with 25% of all indirect comparison meta-analytic applications [16]. Rapid and widespread use by academics, and more recently, government and industry, suggests that use of these methods has become diffuse and are no longer in the early stages of adoption, but rather, mainstream and accepted methods. As we also noted a lack of standardization in the terminology used to describe the indirect comparison meta-analytic methods used, we encourage use of the term, *network meta-analysis*, as it is clearer than mixed treatment or multiple treatments meta-analysis, which may be assumed to indicate the concomitant administration of two or more drug therapies (e.g., adjuvant therapy).

Our results are subject to some limitations. First, our analysis limited the co-authorship of empirical applications to English language papers identified in select bibliographic databases: the Cochrane Database of Systematic Reviews®, EMBASE®, MEDLINE®, Scopus®, and Web of Science®. The limitation of our search to these databases may have resulted in missed articles that were published in other languages, or identifiable in other bibliographic databases, such as Google Scholar®, JSTOR®, Pubmed®, and RevMan5®. Articles that did not clearly describe the techniques used to perform these methods were also excluded, since we could not assume that these methods were used. While we acknowledge that this may have resulted in the exclusion of some applications, we included articles that clearly described these methods in the

title, abstract, introduction, or methods sections to allow for as much inclusion as possible. Consequently, we believe that our systematic search is both comprehensive and robust, as this is the largest and only search completed to date that examines the diffusion of indirect comparison meta-analytic methods in the study of drugs. However, it is worth noting that the term *matching-adjusted indirect comparison*, an extension of the adjusted indirect comparison which was introduced in 2010 and uses individual patient data from single-comparator-RCTs to adjust for differences in patient characteristics across studies was not considered in our analysis [42]. However, 6 eligible papers were published using this term, and we expect to see an increase in the future.

Secondly, our study only ascribed country and institutional credit to the first and last author of each paper. Although the first (principal) and last (often senior) authors traditionally contribute the most, and thus receive the most credit, for papers in the biomedical sciences, other co-authors in the authorship order may also help drive use of novel methods. Consequently, mapping contributions based on first and last authors may have resulted in missed contributions by other co-authors. Nonetheless, inclusion of the second authors in a previous study that examined the diffusion of two confounder summary scores found little impact on country and institutional credit [16].

Finally, our work did not examine the quality of eligible empirical articles, or explore the correlation and impact of early diffusion on the quality of indirect comparison meta-analytic methods. Given the large number of authors who published in isolation of each other, it is possible that the degree of interconnectedness between authors in the network may have influenced the quality of eligible applications, as inconsistencies in methodological and reporting quality of indirect comparison meta-analytic methods have been documented [18]. Similar to

traditional pairwise meta-analysis; limitations related to the quality of the search conducted, quality and heterogeneity of studies included, and publication bias; can all influence the quality of the study. Uniquely, indirect comparison meta-analytic methods have additional limitations that should be accounted for, such as issues with transitivity and inconsistency of networks, as well as the presentation of results [43]. A recent systematic review of network meta-analyses in clinical research demonstrated improvement in methodological and reporting quality over time [44]. However, we acknowledge that this is an important area of future research that should be explored.

In conclusion, prior research identified challenges with integrating new statistical methods into practice [45, 46]. We recently identified the importance of considering the five innovation attributes from Rogers' Diffusion of Innovations Model to facilitate knowledge translation of new methods for rapid integration [16]. In this paper, we used indirect comparison meta-analytic methods to examine the impact of social systems on the diffusion of novel methods. We demonstrated rapid adoption by effective consideration of innovation attributes by innovators, and rapid adoption due to collaboration between innovators from the United Kingdom and a large number of early adopters from many countries around the world. Although speculative, and while there are likely multiple reasons for the relatively rapid adoption of these methods, we believe that adoption by government agencies may have contributed to more rapid uptake, and is worth noting; though further research should be explored. We believe that the social system can play a major role in facilitating the adoption of innovative methods, here through regulation, and by the increase in demand by government for more comparative effectiveness research. As many health technology assessment and regulatory agencies have started to call for more evidence synthesis methods to assist in drug accessibility and

reimbursement decisions [40], use of indirect comparison meta-analytic methods has become more widely accepted, and will likely continue to be a key tool for policy decision making. We encourage authors of novel methods to consider the five innovation attributes when integrating new methods into practice (**relative advantage, compatibility, simplicity, trialability,** and **observability**), with emphasis on early collaboration with potential adopters, such as government regulatory bodies.

## ACKNOWLEDGEMENTS

No specific funding was received to support this work. Joann K. Ban was supported in part by a Canadian Institute of Health Research (CIHR) Program in Drug Safety and Effectiveness Cross-Disciplinary Training. Mina Tadrous was supported in part by a CIHR Frederick Banting and Charles Best Canada Graduate Scholarship (GSD-11342). Erin A. Cicinelli was supported in part by a CIHR Health Professional Student Research Award.

This research was presented at the Canadian Association for Health Services and Policy Research (CAHSPR) Annual Conference in Toronto, ON, Canada, May 2016, and at the International Conference on Pharmacoepidemiology and Therapeutic Risk Management (ICPE) in Dublin, Ireland, August 2016. Participation at CAHSPR was supported by a CAHSPR Student Travel Bursary, and participation at ICPE was supported by an ICPE Travel Scholarship, the Leslie Dan Faculty of Pharmacy Student Experience Fund, and a University of Toronto School of Graduate Studies Conference Grant.

Authors thank Dave Dubins, PhD for initial work in creating Excel macros for co-authorship matrix generation; and Gina Matesic, MLIS for helping with search strategies.

# REFERENCES

[1] Friedman HP, Goldberg JD. Meta-analysis: an introduction and point of view. *Hepatology*. 1996;23:917-28.
[2] O'Rourke K. An historical perspective on meta-analysis: dealing quantitatively with varying study results. *J R Soc Med*. 2007;100:579-82.
[3] Jansen JP, Naci H. Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect modifiers. *BMC Med*. 2013;11:159.
[4] Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg*. 2011;128:305-10.
[5] Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ*. 2005;331:897-900.
[6] Jansen JP, Fleurence R, Devine B, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. *Value Health*. 2011;14:417-28.
[7] Edwards SJ, Clarke MJ, Wordsworth S, et al. Indirect comparisons of treatments based on systematic reviews of randomised controlled trials. *Int J Clin Pract*. 2009;63:841-54.
[8] Bucher HC, Guyatt GH, Griffith LE, et al. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol*. 1997;50:683-91.
[9] Song F, Altman DG, Glenny AM, et al. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ*. 2003;326:472.
[10] Lumley T. Network meta-analysis for indirect treatment comparisons. *Stat Med*. 2002;21:2313-24.
[11] Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med*. 2004;23:3105-24.
[12] Lee AW. Review of mixed treatment comparisons in published systematic reviews shows marked increase since 2009. *J Clin Epidemiol*. 2014;67:138-43.
[13] Song F, Loke YK, Walsh T, et al. Methodological problems in the use of indirect comparisons for evaluating healthcare interventions: survey of published systematic reviews. *BMJ*. 2009;338:b1147.
[14] Donegan S, Williamson P, Gamble C, et al. Indirect comparisons: a review of reporting and methodological quality. *PLoS One*. 2010;5:e11054.
[15] Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. *Value Health*. 2011;14:429-37.
[16] Cadarette SM, Ban JK, Consiglio GP, et al. Diffusion of Innovations model helps interpret the comparative uptake of two methodological innovations: co-authorship network analysis and recommendations for integration of novel methods in practice. *J Clin Epidemiol*. 2017;84:150-160.
[17] Rogers EM. Diffusion of Innovations. Fifth ed. Toronto: Free Press; 2003.
[18] Bafeta A, Trinquart L, Seror R, et al. Analysis of the systematic reviews process in reports of network meta-analyses: methodological systematic review. *BMJ*. 2013;347:f3675.
[19] Wells GA, Sultan SA, Chen L, et al. Indirect Evidence: Indirect Treatment Comparisons in Meta-Analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.

[20] Lu G, Ades AE, Sutton AJ, et al. Meta-analysis of mixed treatment comparisons at multiple follow-up times. *Stat Med*. 2007;26:3681-99.
[21] Salanti G, Higgins JP, Ades AE, et al. Evaluation of networks of randomized trials. *Stat Methods Med Res*. 2008;17:279-301.
[22] Glenny AM, Altman DG, Song F, et al. Indirect comparisons of competing interventions. *Health Technol Assess*. 2005;9:1-134, iii-iv.
[23] Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol*. 2011;64:163-71.
[24] Wilhelmus KR. The treatment of herpes simplex virus epithelial keratitis. *Trans Am Ophthalmol Soc*. 2000;98:505-32.
[25] Packer M, Antonopoulos GV, Berlin JA, et al. Comparative effects of carvedilol and metoprolol on left ventricular ejection fraction in heart failure: results of a meta-analysis. *Am Heart J*. 2001;141:899-907.
[26] Sauriol L, Laporta M, Edwardes MD, et al. Meta-analysis comparing newer antipsychotic drugs for the treatment of schizophrenia: evaluating the indirect approach. *Clin Ther*. 2001;23:942-56.
[27] Chalkidou K. Comparative effectiveness review within the U.K.'s National Institute for Health and Clinical Excellence. Issue Brief (Commonw Fund). 2009;59:1-11.
[28] Caldwell DM, Welton NJ, Ades AE. Mixed treatment comparison analysis provides internally coherent treatment effect estimates based on overviews of reviews and can reveal inconsistency. *J Clin Epidemiol*. 2010;63:875-82.
[29] Dias S, Welton NJ, Caldwell DM, et al. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med*. 2010;29:932-44.
[30] University of Bristol. Multi-parameter Evidence Synthesis Research. Multi-parameter Evidence Synthesis Research Group | School of Social and Community Medicine | University of Bristol. 2017. http://www.bristol.ac.uk/social-community-medicine/centres/cresyda/mpes/ (accessed 23 Jul 2017).
[31] Dias S, Sutton AJ, Ades AE, et al. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making*. 2013;33:607-17.
[32] Sutton A, Ades AE, Cooper N, et al. Use of indirect and mixed treatment comparisons for technology assessment. *Pharmacoeconomics*. 2008;26:753-67.
[33] Dias S, Sutton AJ, Welton NJ, et al. Evidence synthesis for decision making 3: heterogeneity--subgroups, meta-regression, bias, and bias-adjustment. *Med Decis Making*. 2013;33:618-40.
[34] Dias S, Welton NJ, Sutton AJ, et al. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making*. 2013;33:641-56.
[35] Haute Autorité de Santé. Indirect Comparisons: Methods and Validity. Saint-Denis: Haute Autorité de Santé; 2009.
[36] Indirect Comparisons Working Group. Report of the Indirect Comparisons Working Group to the Pharmaceutical Benefits Advisory Committee: assessing indirect comparisons. Canberra: Australian Government Department of Health and Ageing; 2013.

[37] Pharmaceutical Benefits Advisory Committee. Guidelines for Preparing Submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Australian Government Department of Health and Ageing; 2008.
[38] National Institute for Health and Care Excellence. Guide to the Methods of Technology Appraisal 2013, Process and Method Guides. National Institute for Healh and Care Excellence; 2013.
[39] Lebioda A, Gasche D, Dippel FW, et al. Relevance of indirect comparisons in the German early benefit assessment and in comparison to HTA processes in England, France and Scotland. *Health Econ Rev*. 2014;4:31.
[40] Laws A, Kendall R, Hawkins N. A comparison of national guidelines for network meta-analysis. *Value Health*. 2014;17:642-54.
[41] Use of Network Meta-Analysis to Inform Clinical Parameters in Economic Evaluation. Ottawa: Canadian Agency for Drugs and Technologies in Health.
[42] Signorovitch JE, Wu EQ, Yu AP, et al. Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept. *Pharmacoeconomics*. 2010;28:935-45.
[43] Cipriani A, Higgins JP, Geddes JR, et al. Conceptual and technical challenges in network meta-analysis. *Annals Intern Med*. 2013 ;159 :130-7.
[44] Petropoulou M, Nikolakopoulou A, Veroniki AA, et al. Bibliographic study showed improving statistical methodology of network meta-analyses published between 1999 and 2015. *J Clin Epidemiol*. 2017;82:20-28.
[45] Altman DG, Goodman SN. Transfer of technology from statistical journals to the biomedical literature. Past trends and future predictions. *JAMA*. 1994;272:129-32.
[46] Pullenayegum EM, Platt RW, Barwick M, et al. Knowledge translation in biostatistics: a survey of current practices, preferences, and barriers to the dissemination and uptake of new statistical methods. *Stat Med*. 2016;35:805-18.
[47] Institute for Quality and Efficiency in Health Care. General Methods (Version 4.1). Cologne: Institute for Quality and Efficiency in Health Care; 2013.

# In-Text Figures and Tables

## Tables

**Table 1:** Timeline of Meta-analytic Methodological Innovations

| Innovation | Year | Innovators | Institution | Country | Description |
|---|---|---|---|---|---|
| Traditional Pairwise Meta-Analysis [1] | 1904 | Pearson K | University College London | UK | Combines direct evidence from multiple RCTs comparing the same intervention and comparator (e.g., placebo) to strengthen the intervention's effect estimate relative to that comparator. |
| | 1935 | Fisher R | Rothamsted Experimental Station | UK | |
| | 1937 | Cochran W | Rothamsted Experimental Station | UK | |
| | 1976 | Glass GV | University of Colorado | USA | |
| Adjusted Indirect Comparison [8] | 1997 | Bucher HC<br>Guyatt GH<br>Griffith LE<br>Walter SD | McMaster University | Canada | Combines odds ratios from multiple RCTs comparing one of two interventions of interest to a common comparator (e.g. placebo) to estimate the effects of two interventions that have not been compared directly. |
| Network Meta-Analysis* [10] | 2002 | Lumley T | University of Washington | USA | Combines direct and indirect data from multiple RCTs to compare several sets of pairwise treatment comparisons. |
| Mixed Treatment Comparison* [11] | 2004 | Lu G<br>Ades AE | University of Bristol | UK | |

RCT: randomized controlled trials, UK: United Kingdom, USA: United States of America

* To our knowledge, Caldwell et al. (2005) introduced the term *multiple treatments meta-analysis* to describe the concept of combining direct and indirect evidence to compare multiple treatments connected by a network of RCTs, as seen in both methods [5].

**Table 2:** Characteristics of empirical indirect comparison meta-analytic applications in the study of drugs, n=361

| Characteristics | N | % |
|---|---|---|
| **Area of Study** | | |
| Blood Disorders | 1 | 0.3 |
| Cancers | 45 | 12.5 |
| Cardiovascular Disorders | 79 | 21.9 |
| Dermatology/Skin Disorders | 11 | 3.0 |
| Endocrine/Metabolic Disorders | 18 | 5.0 |
| Gastrointestinal Disorders | 8 | 2.2 |
| Genitourinary Disorders | 4 | 1.1 |
| Infectious Diseases | 36 | 10.0 |
| Musculoskeletal Disorders | 45 | 12.5 |
| Neurologic Disorders | 21 | 5.8 |
| Ophthalmic Disorders | 6 | 1.7 |
| Pain | 20 | 5.5 |
| Pregnancy | 4 | 1.1 |
| Psychiatric Disorders | 31 | 8.6 |
| Renal Disorders | 2 | 0.6 |
| Respiratory Disorders | 16 | 4.4 |
| Sexual Health | 6 | 1.7 |
| Surgery | 8 | 2.2 |
| **Primary Outcome** | | |
| Efficacy Only | 249 | 69.0 |
| Safety Only | 23 | 6.4 |
| Both Efficacy and Safety | 89 | 24.6 |
| **Terminology** | | |
| Adjusted Indirect Comparison | 75 | 20.8 |
| Bucher's Method | 88 | 24.4 |
| Indirect Comparison | 45 | 12.5 |
| Matching-Adjusted Indirect Comparison | 6 | 1.7 |
| Mixed Treatment Comparison | 95 | 26.3 |
| Multiple Treatments Meta-Analysis | 29 | 8.0 |
| Network Meta-Analysis | 137 | 38.0 |
| **Network Diagram(s)** | 161 | 44.6 |
| Interventions* | | |
| 3 | 7 | 4.3 |
| 4 | 16 | 9.9 |
| 5 | 23 | 14.3 |
| 6 | 24 | 14.9 |

| | | |
|---|---|---|
| 7 | 18 | 11.2 |
| 8 | 17 | 10.6 |
| 9 | 14 | 8.7 |
| 10-19 | 30 | 18.6 |
| 20+ | 12 | 7.4 |

* Based on the total number of interventions studied, indicated in the network diagram(s) published, n=161.

**Table 3:** Institutional affiliations by country (n=35) and institution type (n=7) for the entire indirect comparison meta-analytic applications network

| Institution | First and Last Author Credit (%) |
|---|---|
| **Country** | |
| Australia | 2.0 |
| Belgium | 1.7 |
| Brazil | 2.4 |
| Canada | 11.3 |
| China | 3.0 |
| France | 3.0 |
| Germany | 3.6 |
| Greece | 1.9 |
| India | 1.0 |
| Italy | 4.7 |
| Netherlands | 3.8 |
| Spain | 1.8 |
| Switzerland | 2.5 |
| Taiwan | 1.7 |
| United Kingdom | 22.1 |
| United States of America | 26.0 |
| Other* | 7.4 |
| **Type** | |
| **Academic** | **77.4** |
| School | 56.4 |
| Hospital | 21.0 |
| **Government** | **1.5** |
| **Industry** | **17.5** |
| Contract Research Organization | 11.3 |
| Pharmaceutical Company | 6.2 |
| **Other** | **3.6** |
| Independent Research Groups | 1.1 |
| Non-profit Organizations | 2.4 |
| Trade Associations | 0.1 |

* Institutional affiliations from other countries with <1% first and last author credit each (Austria, Bahrain, Cameroon, Croatia, Denmark, Hong Kong, Ireland, Israel, Japan, New Zealand, Nigeria, Norway, Peru, Poland, Portugal, Saudi Arabia, South Africa, South Korea, and Thailand).

## Figure Captions

**Figure 1:** Flow diagram of systematic search results.

**Figure 2:** Number of publications on indirect comparison meta-analytic methods by year of publication, n=477. Methodological contributions (checkered bar), review papers (horizontal stripes), and empirical applications (solid). Cumulative number of unique authors represented by the solid grey line, n=1689. [†]Innovators by seminal publication: Bucher et al. 1997 (Canada) [8]; Lumley (USA) 2002 [10]; Lu and Ades 2004 (UK) [11]. Early adopters: [§]government-sponsored academic groups and health technology and reimbursement assessment agencies (National Institute for Health and Clinical Excellence Guidelines Technical Support Unit 2002 (UK) [30]; Pharmaceutical Benefits Advisory Committee 2005 (Australia) [36, 37]; Canadian Agency for Drugs and Technologies in Health 2009 (Canada) [19]; Haute Autorité de Santé 2009 (France) [35]; Institute for Quality and Efficiency in Health Care 2013 (Germany) [47]); [#]independent research organizations: Indirect Treatment Comparisons Good Research Practices Task Force 2011 (Canada, The Netherlands, USA, UK) [6, 15].

**Figure 3:** Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. The lines represent the relationships (co-authorship) between authors, with arrows directed from first author to co-authors of each paper. Node size is proportional to the number of published articles.

**A.** Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), while authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow).

**B.** Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliation types from academia and government were coloured orange (a combination of red and yellow), while authors on papers affiliated with academic, industry, and other were coloured light purple (a combination of red, blue, and white).

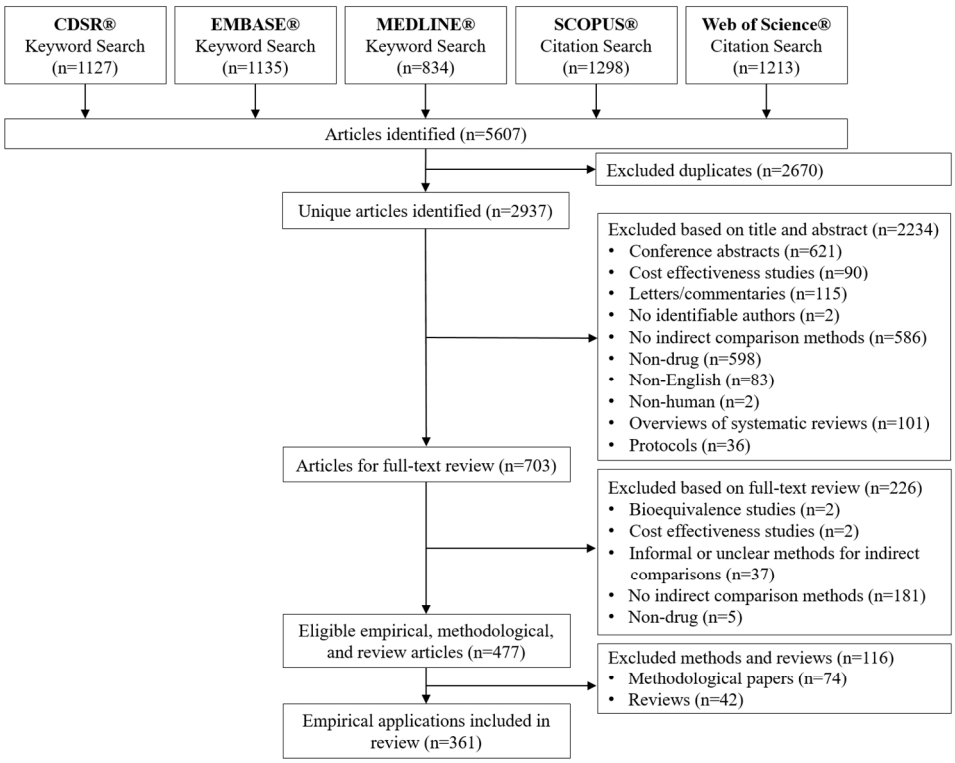



Figure 1: Flow diagram of systematic search results.

135x106mm (300 x 300 DPI)

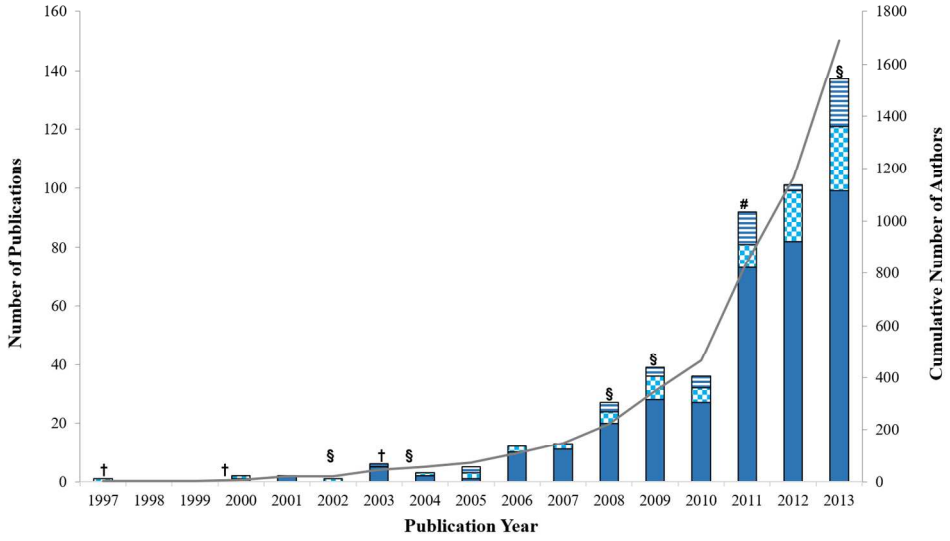
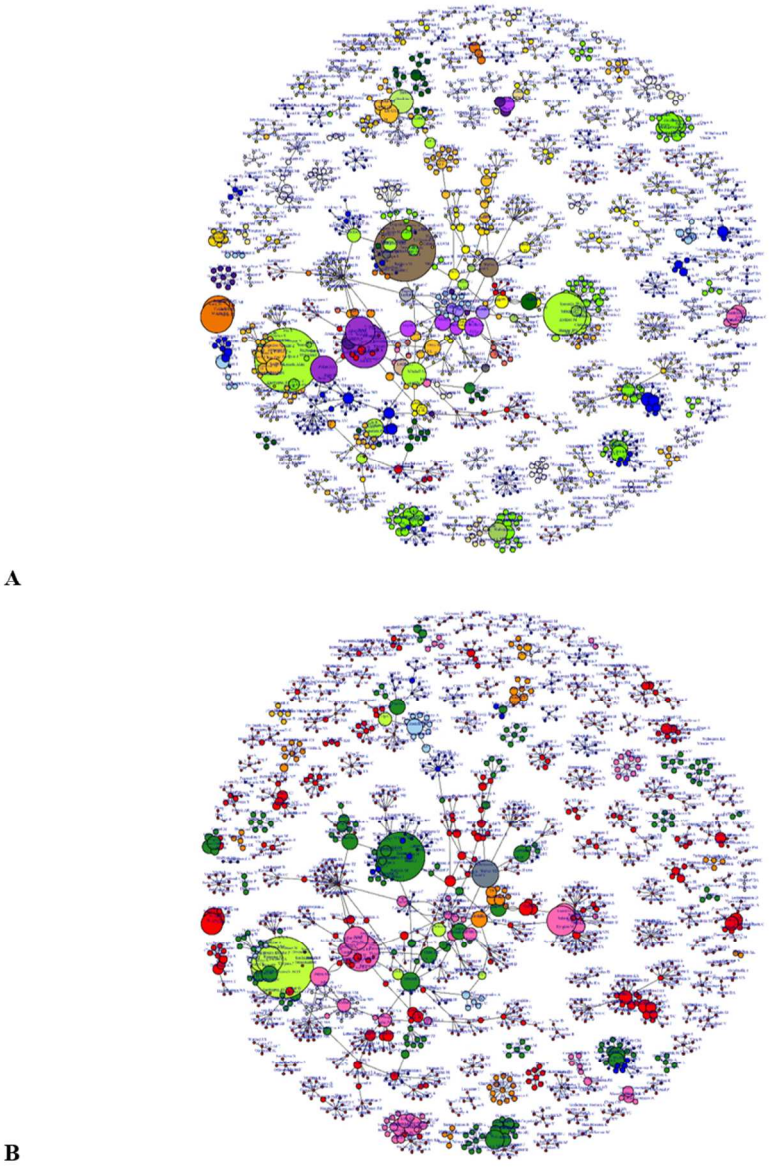



Figure 2: Number of publications on indirect comparison meta-analytic methods by year of publication, n=477. Methodological contributions (checkered bar), review papers (horizontal stripes), and empirical applications (solid). Cumulative number of unique authors represented by the solid grey line, n=1689. †Innovators by seminal publication: Bucher et al. 1997 (Canada) [8]; Lumley (USA) 2002 [10]; Lu and Ades 2004 (UK) [11]. Early adopters: §government-sponsored academic groups and health technology and reimbursement assessment agencies (National Institute for Health and Clinical Excellence Guidelines Technical Support Unit 2002 (UK) [30]; Pharmaceutical Benefits Advisory Committee 2005 (Australia) [36, 37]; Canadian Agency for Drugs and Technologies in Health 2009 (Canada) [19]; Haute Autorité de Santé 2009 (France) [35]; Institute for Quality and Efficiency in Health Care 2013 (Germany) [47]); #independent research organizations: Indirect Treatment Comparisons Good Research Practices Task Force 2011 (Canada, The Netherlands, USA, UK) [6, 15].

144x79mm (300 x 300 DPI)



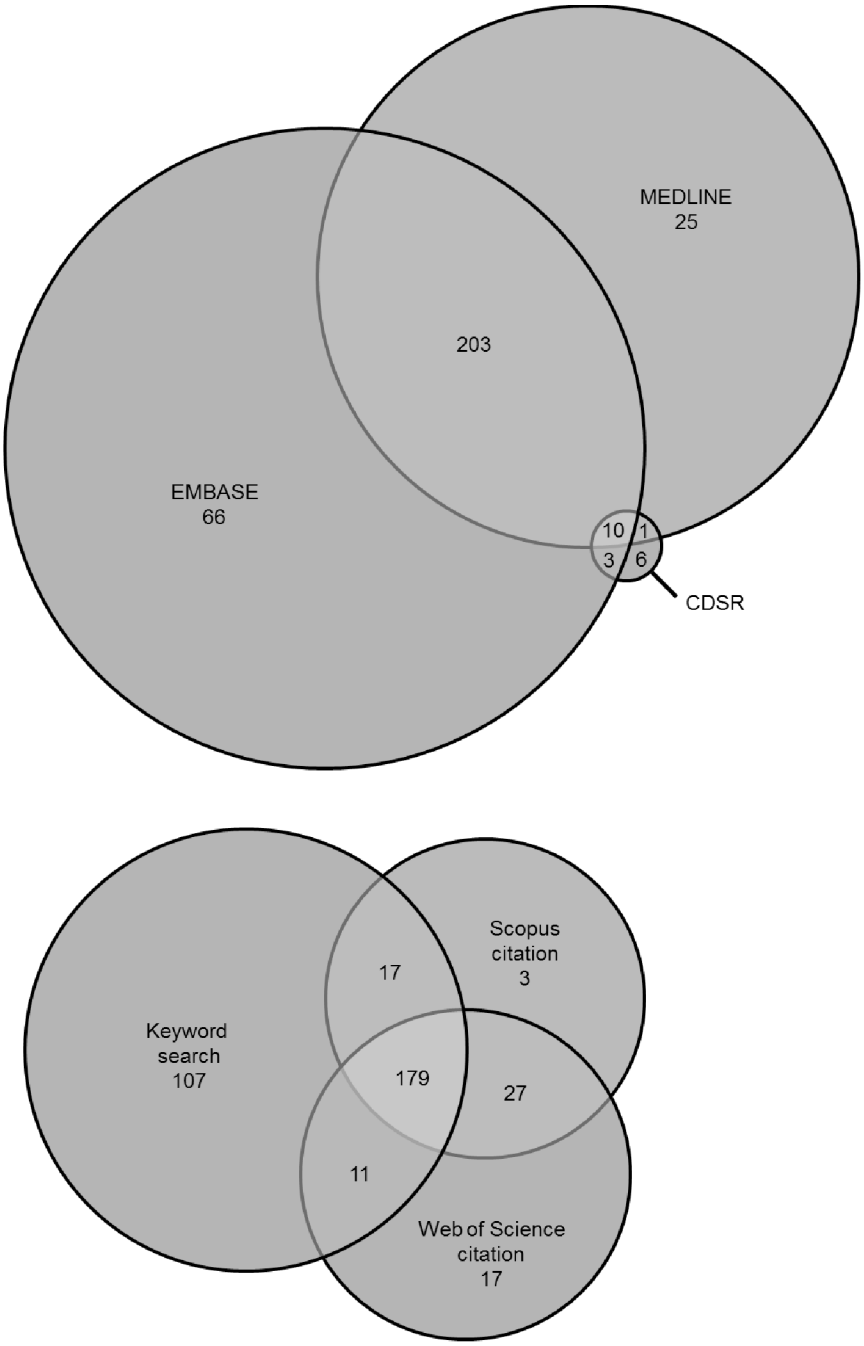

Caption : Figure 3: Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. The lines represent the relationships (co-authorship) between authors, with arrows directed from first author to co-authors of each paper. Node size is proportional to the number of published articles.‼ ┼ A. Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), while authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow). ‼ ┼ B. Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliation types from academia and government were coloured orange (a combination of red and yellow), while

authors on papers affiliated with academic, industry, and other were coloured light purple (a combination of red, blue, and white).

82x110mm (300 x 300 DPI)

# Appendix A: Systematic Literature Search

| **Appendix A Table A:** Systematic Literature Keyword Search | | | |
|---|---|---|---|
| **Databases:** | Cochrane Database of Systematic Reviews® | MEDLINE® | EMBASE® |
| **Limits:** | - Date of inception to 31 December 2013 | - Date of inception to 31 December 2013<br>- English language<br>- Humans<br>- Publication types: meta-analysis, systematic reviews | |
| **Keywords:** | "network meta-analysis" OR "network meta-regression" OR "multiple treatment meta-analysis" OR "multiple treatments meta-analysis" OR "mixed treatment comparison" OR "mixed treatment comparisons" OR "mixed treatment" OR "mixed treatments" OR "multiple treatment" OR "multiple treatments" OR "treatment network" OR "treatment networks" OR "multiple comparison" OR "multiple comparisons" OR "indirect comparison" OR "indirect comparisons" OR "overview of reviews" OR "umbrella review" OR "overview of systematic reviews" OR "overview of meta-analyses" OR "multiple systematic reviews" OR "multiple meta-analyses" OR "overview of Cochrane reviews" OR "multiple Cochrane reviews" OR "overview of Cochrane" | | |



# Appendix B: List of references of identified methodological contributions of indirect comparison meta-analytic methods

[B1] Achana FA, Cooper NJ, Dias S, Lu G, Rice SJ, Kendrick D, et al. Extending methods for investigating the relationship between treatment effect and baseline risk from pairwise meta-analysis to network meta-analysis. *Stat Med* 2013; 32(5):752-71.

[B2] Ades AE, Mavranezouli I, Dias S, Welton NJ, Whittington C, Kendall T. Network meta-analysis with competing risk outcomes. *Value Health* 2010;13(8):976-83.

[B3] Ballesteros, J. Orphan comparisons and indirect meta-analysis: a case study on antidepressant efficacy in dysthymia comparing tricyclic antidepressants, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors by using general linear models. *J Clin Psychpharmacol* 2005;25(2):127-31.

[B4] Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol* 1997;50(6):683-91.

[B5] Caldwell DM, Welton NJ, Ades AE. Mixed treatment comparison analysis provides internally coherent treatment effect estimates based on overviews of reviews and can reveal inconsistency. *J Clin Epidemiol* 2010;63(8):875-82.

[B6] Chaimani A, Vasiliadis HS, Pandis N, Schmid CH, Welton NJ, Salanti G. Effects of study precision and risk of bias in networks of interventions: a network meta-epidemiological study. *Int J Epidemiol* 2013;42(4):1120-131.

[B7] Chaimani A, Higgins JP, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One* 2013;8(10):e76654.

[B8] Chootrakool H, Shi JQ, Yue R. Meta-analysis and sensitivity analysis for multi-arm trials with selection bias. *Stat Med* 2011;30(11):1183-98.

[B9] Chung H, Lumley T. Graphical exploration of network meta-analysis data: the use of multidimensional scaling. *Clin Trials* 2008;5(4):301-7.

[B10] Cooper NJ, Sutton AJ, Morris D, Ades AE, Welton NJ. Addressing between-study heterogeneity and inconsistency in mixed treatment comparisons: application to stroke prevention treatments in individuals with non-rheumatic atrial fibrillation. *Stat Med* 2009;28(14):1861-81.

[B11] Cooper NJ, Peters J, Lai MC, Juni P, Wandel S, Palmer S, et al. How valuable are multiple treatment comparison methods in evidence-based health-care evaluation? *Value Health* 2011;14(2):371-80.

[B12] Cope S, Jansen JP. Quantitative summaries of treatment effect estimates obtained with network meta-analysis of survival curves to inform decision-making. *BMC Med Res Methodol* 2013;13:147.

[B13] Del Giovane C, Vacchi L, Mavridis D, Filippini G, Salanti G. Network meta-analysis models to account for variability in treatment definitions: application to dose effects. *Stat Med* 2013;32(1):25-39.

[B14] Dias S, Welton NJ, Caldwell DM, Ades AE. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med* 2010;29:932-44.

[B15] Dias S, Welton NJ, Marinho VCC, Salanti G, Higgins JPT, Ades AE. Estimation and adjustment of bias in randomized evidence by using mixed treatment comparison meta-analysis. *J R Statist Soc A* 2010;173(3):613-29.

[B16] Ding Y, Fu H. Bayesian indirect and mixed treatment comparisons across longitudinal time points. *Stat Med* 2013;32(15):2613-28.

[B17] Donegan S, Williamson P, D'Alessandro U, Tudur Smith C. Assessing the consistency assumption by exploring treatment by covariate interactions in mixed treatment comparison meta-analysis: individual patient-level covariates versus aggregate trial-level covariates. *Stat Med* 2012;31(29):3840-57.

[B18] Donegan S, Williamson P, D'Alessandro U, Garner P, Smith CT. Combining individual patient data and aggregate data in mixed treatment comparison meta-analysis: individual patient data may be beneficial if only for a subset of trials. *Stat Med* 2013;32(6):914-30.

[B19] Druyts E, Thorlund K, Humphreys S, Lion M, Cooper CL, Mills EJ. Interpreting discordant indirect and multiple treatment comparison meta-analyses: an evaluation of direct acting antivirals for chronic hepatitis C infection. *Clin Epidemiol* 2013;5(1):173-183.

[B20] Eckermann S, Coory M, Willan AR. Indirect comparison: relative risk fallacies and odds solution. *J Clin Epidemiol* 2009;62:1031-6.

[B21] Fu H, Price KL, Nilsson ME, Ruberg SJ. Identifying potential adverse events dose-response relationships via Bayesian indirect and mixed treatment comparison models. *J Biopharm Stat* 2013;23(1):26-42.

[B22] Griffin S, Bojke L, Main C, Palmer S. Incorporating direct and indirect evidence using bayesian methods: an applied case study in ovarian cancer. *Value Health* 2006;9(2):123-31.

[B23] Gross JL, Rogers J, Polhamus D, Gillespie W, Friedrich C, Gong Y, et al. A novel model-based meta-analysis to indirectly estimate the comparative efficacy of two medications: an example using DPP-4 inhibitors, sitagliptin and linagliptin, in treatment of type 2 diabetes mellitus. *BMJ Open* 2013;3(3):e001844.

[B24] Gwaza L, Gordon J, Welink J, Potthast H, Hansson H, Stahl M, et al. Statistical approaches to indirectly compare bioequivalence between generics: a comparison of methodologies employing artemether/lumefantrine 20/120 mg tablets as prequalified by WHO. *Eur J Clin Pharmacol* 2012;68(12):1611-8.

[B25] Hawkins N, Scott DA, Woods B. How far do you go? Efficient searching for indirect evidence. *Med Decis Making* 2009;29(3):273-81.

[B26] Hawkins N, Scott DA, Woods BS, Thatcher N. No study left behind: a network meta-analysis in non-small-cell lung cancer demonstrating the importance of considering all relevant data. *Value Health* 2009;12(6):996-1003.

[B27] Hong H, Carlin BP, Shamliyan TA, Wyman JF, Ramakrishnan R, Sainfort F, et al. Comparing Bayesian and frequentist approaches for multiple outcome mixed treatment comparisons. *Med Decis Making* 2013;33(5):702-14.

[B28] Jansen JP, Cope S. Meta-regression models to address heterogeneity and inconsistency in network meta-analysis of survival outcomes. *BMC Med Res Method* 2012;12:152.

[B29] Jansen JP, Schmid CH, Salanti G. Directed acyclic graphs can help understand bias in indirect and mixed treatment comparisons. *J Clin Epidemiol* 2012;65(7):798-807.

[B30] Jansen JP. Network meta-analysis of survival data with fractional polynomials. *BMC Med Res Methodol* 2011;11:61.

[B31] König J, Krahn U, Binder H. Visualizing the flow of evidence in network meta-analysis and characterizing mixed treatment comparisons. *Stat Med* 2013;32(30): 5414-29.

[B32] Krahn U, Binder H, König J. A graphical tool for locating inconsistency in network meta-analyses. *BMC Med Res Methodol* 2013;13(1):35.

[B33] Lee C, Hunsche E, Balshaw R, Kong SX, Scnitzer TJ. Need for common internal controls when assessing the relative efficacy of pharmacologic agents using a meta-analytic approach: Case study of cyclooxygenase 2-selective inhibitors for the treatment of osteoarthritis. *Arthritis Rheum* 2005;53(4):510-8.

[B34] Lu G, Ades A. Modeling between-trial variance structure in mixed treatment comparisons. *Biostatistics* 2009;10(4):792-805.

[B35] Lu G, Ades AE. Assessing evidence inconsistency in mixed treatment comparisons. *JASA* 2006;101(474):447-459.

[B36] Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med* 2004;23(20):3105-24.

[B37] Lu G, Ades AE, Sutton AJ, Cooper NJ, Briggs AH, Caldwell DM. Meta-analysis of mixed treatment comparisons at multiple follow-up times. *Stat Med* 2007;26(20):3681-99.

[B38] Lumley T. Network meta-analysis for indirect treatment comparisons. *Stat Med* 2002;21(16):2313-24.

[B39] Lunn D, Barrett J, Sweeting M, Thompson S. Fully Bayesian hierarchical modelling in two stages, with application to meta-analysis. *J R Stat Soc C Appl Stat* 2013;62(4):551-72.

[B40] Madan J, Stevenson MD, Cooper KL, Ades AE, Whyte S, Akehurst R. Consistency between direct and indirect trial evidence: is direct evidence always more reliable? *Value Health* 2011;14(6):953-60.

[B41] Mavridis D, Sutton A, Cipriani A, Salanti G. A fully Bayesian application of the Copas selection model for publication bias extended to network meta-analysis. *Stat Med* 2013;32(1):51-66.

[B42] Mills EJ, Ghement I, O'Regan C, Thorlund K. Estimating the power of indirect comparisons: a simulation study. *PLoS One* 2011;6(1):e16237.

[B43] Mills EJ, Kanters S, Thorlund K, Chaimani A, Veroniki AA, Ioannidis JP. The effects of excluding treatments from network meta-analyses: survey. *BMJ* 2013;347:f5195.

[B44] Mills, E.J., K. Thorlund, and J.P.A. Ioannidis, Calculating additive treatment effects from multiple randomized trials provides useful estimates of combination therapies. *J Clin Epidemiol* 2012;65(12):1282-8.

[B45] Norton EC, Miller MM, Wang JJ, Coyne K, Kleinman LC. Rank reversal in indirect comparisons. *Value Health* 2012;15(8):1137-40.

[B46] O'Regan C, Ghement I, Eyawo O, Guyatt GH, Mills EJ. Incorporating multiple interventions in meta-analysis: an evaluation of the mixed treatment comparison with the adjusted indirect comparison. *Trials* 2009;10:86.

[B47] Piepho HP, Williams ER, Madden LV. The use of two-way linear mixed models in multitreatment meta-analysis. *Biometrics* 2012;68(4):1269-77.

[B48] Price MJ, Welton NJ, Ades AE. Parameterization of treatment effects for meta-analysis in multi-state Markov models. *Stat Med* 2011;30(2):140-51.

[B49] Salanti G, Dias S, Welton NJ, Ades AE, Golfinopoulos V, Kyrgiou M, et al. Evaluating novel agent effects in multiple-treatments meta-regression. *Stat Med* 2010;29(23):2369-83.

[B50] Salanti G, Higgins JP, Ades AE, Ioannidis JP. Evaluation of networks of randomized trials. *Stat Methods Med Res* 2008;17(3):279-301.

[B51] Salanti G, Kavvoura FK, Ioannidis JP. Exploring the geometry of treatment networks. *Ann Intern Med* 2008;148(7):544-53.

[B52] Salanti G, Marinho V, Higgins JP. A case study of multiple-treatments meta-analysis demonstrates that covariates should be considered. *J Clin Epidemiol* 2009;62(8):857-64.

[B53] Saramago P, Sutton AJ, Cooper NJ, Manca A. Mixed treatment comparisons using aggregate and individual participant level data. *Stat Med* 2012;31(28):3516-36.

[B54] Schmidli H, Wandel S, Neuenschwander B. The network meta-analytic-predictive approach to non-inferiority trials. *Stat Methods Med Res* 2013;22(2):219-40.

[B55] Schmitz S, Adams R, Walsh C. The use of continuous data versus binary data in MTC models: a case study in rheumatoid arthritis. *BMC Med Res Methodol* 2012;12:167.

[B56] Signorovitch JE, Sikirica V, Erder MH, Xie J, Lu M, Hodgkins PS, et al. Matching-adjusted indirect comparisons: a new tool for timely comparative effectiveness research. *Value Health* 2012;15(6):940-7.

[B57] Song F, Glenny AM, Altman DG, Indirect comparison in evaluating relative efficacy illustrated by antimicrobial prophylaxis in colorectal surgery. *Control Clin Trials* 2000;21(5):488-97.

[B58] Song F, Xiong T, Parekh-Bhurke S, Loke YK, Sutton AJ, Eastwood AJ, et al. Inconsistency between direct and indirect comparisons of competing interventions: meta-epidemiological study. *BMJ* 2011;343:d4909.

[B59] Song F, Clark A, Bachmann MO, Maas J. Simulation evaluation of statistical properties of methods for indirect and mixed treatment comparisons. *BMC Med Res Methodol* 2012;12:138.

[B60] Song F, Harvey I, Lilford R. Adjusted indirect comparison may be less biased than direct comparison for evaluating new pharmaceutical interventions. *J Clin Epidemiol* 2008;61(5):455-63.

[B61] Spineli LM, Higgins JP, Cipriani A, Leucht S, Salanti G. Evaluating the impact of imputations for missing participant outcome data in a network meta-analysis. *Clin Trials* 2013;10(3):378-88.

[B62] Thorlund K, Mills E. Stability of additive treatment effects in multiple treatment comparison meta-analysis: a simulation study. *Clin Epidemiol* 2012;4(1):75-85.

[B63] Thorlund K, Mills EJ. Sample size and power considerations in network meta-analysis. *Syst Rev* 2012;1(1):41.

[B64] Thorlund K, Thabane L, Mills EJ. Modelling heterogeneity variances in multiple treatment comparison meta-analysis - are informative priors the better solution? *BMC Med Res Methodol* 2013;13:2.

[B65] Trinquart L, Abbé A, Ravaud P. Impact of reporting bias in network meta-analysis of antidepressant placebo-controlled trials. *PLoS One* 2012;7(4):e35219.

[B66] Trinquart L, Chatellier G, Ravaud P. Adjustment for reporting bias in network meta-analysis of antidepressant trials. *BMC Med Res Methodol* 2012;12:150.

[B67] van Valkenhoef G, Tervonen T, de Brock B, Hillege H. Algorithmic parameterization of mixed treatment comparisons. *Stat Comput* 2012;22(5):1099-111.

[B68] van Valkenhoef G, Tervonen T, Zhao J, de Brock B, Hillege HL, Postmus D. Multicriteria benefit-risk assessment using network meta-analysis. *J Clin Epidemiol* 2012;65(4):394-403.

[B69] Vandermeer BW, Buscemi N, Liang Y, Witmans M. Comparison of meta-analytic results of indirect, direct, and combined comparisons of drugs for chronic insomnia in adults: a case study. *Med Care* 2007;45(10):S166-72.

[B70] Veroniki AA, Vasiliadis HS, Higgins JP, Salanti G. Evaluation of inconsistency in networks of interventions. *Int J Epidemiol* 2013;42(1):332-45.

[B71] Wei YH, Higgins JP. Bayesian multivariate meta-analysis with multiple outcomes. *Stat Med* 2013;32(17):2911-34.

[B72] Wells GA, Sultan SA, Chen L, Khan M, Coyle D. Indirect Evidence: Indirect Treatment Comparisons in Meta-analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2009.

[B73] White IR. Multivariate random-effects meta-regression: updates to mvmeta. *Stata J* 2011;11(2):255-70.

[B74] Xiong T, Parekh-Bhurke S, Loke YK, Abdelhamid A, Sutton AJ, Eastwood AJ, et al. Overall similarity and consistency assessment scores are not sufficiently accurate for predicting discrepancy between direct and indirect comparison estimates. *J Clin Epidemiol* 2013;66(2):184-91.

# Appendix C: List of references of identified reviews of indirect comparison meta-analytic methods

[C1] Ades AE, Madan J, Welton NJ. Indirect and mixed treatment comparisons in arthritis research. *Rheumatology* 2011;50 Suppl 4:iv5-9.

[C2] Bafeta A, Trinquart L, Seror R, Ravaud P. Analysis of the systematic reviews process in reports of network meta-analyses: methodological systematic review. *BMJ* 2013;347:f3675.

[C3] Buti J, Glenny AM, Worthington HV, Nieri M, Baccini M. Network meta-analysis of randomised controlled trials: direct and indirect treatment comparisons. *Eur J Oral Implantol* 2011;4(1):55-62.

[C4] Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005;331:897-900.

[C5] Caro JJ, Ishak KJ. No head-to-head trial? Simulate the missing arms. *Pharmacoeconomics* 2010;28(10):957-67.

[C6] Carpiuc KT, Rosti G, Castagnetti F, Treur M, Stephens J. Indirect comparisons of second-generation tyrosine kinase inhibitors in CML: case study using baseline population characteristics. *Onco Targets Ther* 2010;3:205-10.

[C7] Cepeda MS, Fife D, Lobanov V, Sutton A. Can soccer predictions boost the use of indirect comparison to assess the safety of drugs? *Open Drug Saf J* 2011;2(1):25-8.

[C8] Chu J, Sloan CE, Freedberg KA, Yazdanpanah Y, Losina E. Drug efficacy by direct and adjusted indirect comparison to placebo: an illustration by Mycobacterium avium complex prophylaxis in HIV. *AIDS Res Ther* 2011;8:14.

[C9] Cipriani A, Higgins JP, Geddes JR, Salanti G. Conceptual and technical challenges in network meta-analysis. *Ann Intern Med* 2013;159(2):130-7.

[C10] Cipriani A, Barbui C, Rizzo C, Salanti G. What is a multiple treatments meta-analysis? *Epidemiol Psychiatr Sci* 2012;21(2):151-3.

[C11] Cooper NJ, Spiegelhalter D, Bujkiewicz S, Dequen P, Sutton AJ. Use of implicit and explicit bayesian methods in health technology assessment. *Int J Technol Assess Health Care* 2013;29(3):336-42.

[C12] Dias S, Sutton AJ, Ades AE, Welton NJ. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making* 2013;33(5):607-17.

[C13] Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making* 2013;33(5):641-56.

[C14] Dias S, Welton NJ, Sutton AJ, Ades AE. Evidence synthesis for decision making 5: the baseline natural history model. *Med Decis Making* 2013;33(5):657-70.

[C15] Donegan S, Williamson P, Gamble C, Tudur-Smith C. Indirect comparisons: a review of reporting and methodological quality. *PLoS One* 2010;5(11):e11054.

[C16] Edwards SJ, Clarke MJ, Wordsworth S, Borrill J. Indirect comparisons of treatments based on systematic reviews of randomised controlled trials. *Int J Clin Pract* 2009;63:841-54.

[C17] Gartlehner G, Moore CG. Direct versus indirect comparisons: a summary of the evidence. *Int J Technol Assess Health Care* 2008;24:170-7.

[C18] Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R, et al. Indirect comparisons of competing interventions. *Health Technol Assess* 2005;9(26):1-134, iii-iv.

[C19] Harenberg J, Weiss C. Clinical trials with new oral anticoagulants. Additive value of indirect comparisons also named network meta-analyses. *Hamostaseologie* 2013;33(1):62-70.

[C20] Hoaglin DC, Hawkins N, Jansen JP, Scott DA, Itzler R, Cappelleri JC, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. *Value Health* 2011;14(4):429-37.

[C21] Ioannidis JP. Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. *CMAJ* 2009;181(8):488-93.

[C22] Jansen JP, Naci H. Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect modifiers. *BMC Med* 2013;11(1):159.

[C23] Jansen JP, Crawford B, Bergman G, Stam W. Bayesian meta-analysis of multiple treatment comparisons: an introduction to mixed treatment comparisons. *Value Health* 2008;11(5):956-64.

[C24] Jansen JP, Fleurence R, Devine B, Itzler R, Barrett A, Hawkins N, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. *Value Health* 2011;14(4):417-28.

[C25] Jones B, Roger J, Lane PW, Lawton A, Fletcher C, Cappelleri JC, et al. Statistical approaches for conducting network meta-analysis in drug development. *Pharm Stat* 2011;10(6): 523-31.

[C26] Mavridis D, Salanti G. A practical introduction to multivariate meta-analysis. *Stat Methods Med Res* 2013;22(2):133-58.

[C27] Mills EJ, Ioannidis JP, Thorlund K, Schünemann HJ, Puhan MA, Guyatt GH. How to use an article reporting a multiple treatment comparison meta-analysis. *JAMA* 2012;308(12):1246-53.

[C28] Mills EJ, Bansback N, Ghement I, Thorlund K, Kelly S, Puhan MA, et al. Multiple treatment comparison meta-analyses: a step forward into complexity. *Clin Epidemiol* 2011;3(1):193-202.

[C29] Mills EJ, Thorlund K, Ioannidis JP. Demystifying trial networks and network meta-analysis. *BMJ* 2013;346:f2914.

[C30] Naci H, O'Connor AB. Assessing comparative effectiveness of new drugs before approval using prospective network meta-analyses. *J Clin Epidemiol* 2013;66(8):812-6.

[C31] Naci H, Fleurence R. Using indirect evidence to determine the comparative effectiveness of prescription drugs: do benefits outweigh risks? *Health Outcomes Res Med* 2011;2(4):e241-9.

[C32] Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol* 64(2):163-71.

[C33] Schacht A, Dyachkova Y, Walton RJ. Critical evaluation of mixed treatment comparison meta-analyses using examples assessing antidepressants and opioid detoxification treatments. Int *J Methods Psychiatr Res* 2013;22(2):166-74.

[C34] Senn S, Gavini F, Magrez D, Scheen A. Issues in performing a network meta-analysis. *Stat Methods Med Res* 2013;22(2):169-89.

[C35] Snapinn S, Jiang Q. Indirect comparisons in the comparative efficacy and non-inferiority settings. *Pharm Stat* 2011;10(5):420-6.

[C36] Sobieraj DM, Cappelleri JC, Baker WL, Phung OJ, White CM, Coleman CI. Methods used to conduct and report Bayesian mixed treatment comparisons published in the medical literature: a systematic review. *BMJ Open* 2013;3(7):e003111.

[C37] Song F, Loke YK, Walsh T, Glenny AM, Eastwood AJ, Altman DG. Methodological problems in the use of indirect comparisons for evaluating healthcare interventions: survey of published systematic reviews. *BMJ* 2009;338:b1147.

[C38] Song F, Altman DG, Glenny AM, Deeks JJ. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ* 2003;326(7387):472-5.

[C39] Sutton A, Ades AE, Cooper N, Abrams K. Use of indirect and mixed treatment comparisons for technology assessment. *Pharmacoeconomics* 2008;26(9):753-67.

[C40] Tan SH, Bujkiewicz S, Sutton A, Dequen P, Cooper N. Presentational approaches used in the UK for reporting evidence synthesis using indirect and mixed treatment comparisons. *J Health Serv Res Policy* 2013;18(4):224-32.

[C41] Thorlund K, Druyts E, Aviña-Zubieta JA, Wu P, Milles EJ. Why the findings of published multiple treatment comparison meta-analyses of biologic treatments for rheumatoid arthritis are

different: an overview of recurrent methodological shortcomings. *Ann Rheum Dis* 2013;72(9): 1524-35.

[C42] Woods BS, Hawkins N, Scott DA. Network meta-analysis on the log-hazard scale, combining count and hazard ratio statistics accounting for multi-arm trials: a tutorial. *BMC Med Res Methodol* 2010;10:54.

# Appendix D: List of references of identified empirical applications of indirect comparison meta-analytic methods

Component 1: D1-143
Component 2: D144-152
Component 3: D153-160
Component 4: D161-166
Component 5: D167-171
Component 6: D172-176
Component 7: D177-181
Component 8: D182-186
Component 9: D187-191
Component 10: D192-196
Component 11: D197-200
Component 12: D201-204
Component 13: D205-208
Component 14: D209-212
Component 15: D213-216
Component 16: D217-220
Component 17: D221-224
Component 18: D225-227
Component 19: D228-230
Component 20: D231-233
Component 21: D234-235
Component 22: D236-237
Component 23: D238-239
Component 24: D240-241
Component 25: D242-243
Component 26: D244-245
Component 27: D246-247
Component 28: D248-249
Component 29: D250-251
Component 30: D252-253
Component 31: D254-255
Component 32: D256-257
Component 33: D258-259
Component 34: D260-261
Component 35: D262-263
Component 36: D264-265
Component 37: D266-267
Component 38: D268-269
Component 39: D270-271
Component 40: D272
Component 41: D273
Component 42: D274

Component 43: D275
Component 44: D276
Component 45: D277
Component 46: D278
Component 47: D279
Component 48: D280
Component 49: D281
Component 50: D282
Component 51: D283
Component 52: D284
Component 53: D285
Component 54: D286
Component 55: D287
Component 56: D288
Component 57: D289
Component 58: D290
Component 59: D291
Component 60: D292
Component 61: D293
Component 62: D294
Component 63: D295
Component 64: D296
Component 65: D297
Component 66: D298
Component 67: D299
Component 68: D300
Component 69: D301
Component 70: D302
Component 71: D303
Component 72: D304
Component 73: D305
Component 74: D306
Component 75: D307
Component 76: D308
Component 77: D309
Component 78: D310
Component 79: D311
Component 80: D312
Component 81: D313
Component 82: D314
Component 83: D315
Component 84: D316
Component 85: D317
Component 86: D318
Component 87: D319
Component 88: D320

Component 89: D321
Component 90: D322
Component 91: D323
Component 92: D324
Component 93: D325
Component 94: D326
Component 95: D327
Component 96: D328
Component 97: D329
Component 98: D330
Component 99: D331
Component 100: D332
Component 101: D333
Component 102: D334
Component 103: D335
Component 104: D336
Component 105: D337
Component 106: D338
Component 107: D339
Component 108: D340
Component 109: D341
Component 110: D342
Component 111: D343
Component 112: D344
Component 113: D345
Component 114: D346
Component 115: D347
Component 116: D348
Component 117: D349
Component 118: D350
Component 119: D351
Component 120: D352
Component 121: D353
Component 122: D354
Component 123: D355
Component 124: D356
Component 125: D357
Component 126: D358
Component 127: D359
Component 128: D360
Component 129: D361

[D1] Akbar A, Abu Dayyeh BK, Baron TH, Wang Z, Altayar O, Murad MH. Rectal nonsteroidal anti-inflammatory drugs are superior to pancreatic duct stents in preventing pancreatitis after endoscopic retrograde cholangiopancreatography: a network meta-analysis. *Clin Gastroenterol Hepatol* 2013;11(7):778-83.

[D2] Akshintala VS, Hutfless SM, Colantuoni E, Kim KJ, Khashab MA, Li T, et al. Systematic review with network meta-analysis: pharmacological prophylaxis against post-ERCP pancreatitis. *Aliment Pharmacol Ther* 2013;38(11-12):1325-37.

[D3] Alberton M, Wu P, Druyts E, Briel M, Mills EJ. Adverse events associated with individual statin treatments for cardiovascular disease: an indirect comparison meta-analysis. *QJM* 2012;105(2):145-57.

[D4] Alonso-Coello P, Zhou Q, Guyatt G. Home-monitoring of oral anticoagulation vs. dabigatran. An indirect comparison. *Thromb Haemost* 2012;108(4):647-53.

[D5] Baker WL, Baker EL, Coleman CI. Pharmacologic treatments for chronic obstructive pulmonary disease: a mixed-treatment comparison meta-analysis. *Pharmacotherapy* 2009;29(8): 891-905.

[D6] Baker WL, Phung OJ. Systematic review and adjusted indirect comparison meta-analysis of oral anticoagulants in atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2012;5(5):711-9.

[D7] Bekkering GE, Abou-Setta AM, Kleijnen J. The application of quantitative methods for identifying and exploring the presence of bias in systematic reviews: PDE-5 inhibitors for erectile dysfunction. *Int J Impot Res* 2008;20(3):264-77.

[D8] Bekkering GE, Soares-Weiser K, Reid K, Kessels AG, Dahan A, Treede RD, et al. Can morphine still be considered to be the standard for treating chronic pain? A systematic review including pair-wise and network meta-analyses. *Curr Med Res Opin* 2011;27(7):1477-91.

[D9] Bergman GJ, Hochberg MC, Boers M, Wintfeld N, Kielhorn A, Jansen JP. Indirect comparison of tocilizumab and other biologic agents in patients with rheumatoid arthritis and inadequate response to disease-modifying antirheumatic drugs. *Semin Arthritis Rheum* 2010;39(6):425-41.

[D10] Berry SM, Broglio KR, Berry DA. Addressing the incremental benefit of histamine dihydrochloride when added to interleukin-2 in treating acute myeloid leukemia: a Bayesian meta-analysis. *Cancer Invest* 2011;29(4):293-9.

[D11] Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet* 2013;382(9894):769-79.

[D12] Bottomley JM, Taylor RS, Ryttov J. The effectiveness of two-compound formulation calcipotriol and betamethasone dipropionate gel in the treatment of moderately severe scalp psoriasis: a systematic review of direct and indirect evidence. *Curr Med Res Opin* 2011;27(1):251-68.

[D13] Buscemi N, Vandermeer B, Friesen C, Bialy L, Tubman M, Ospina M, et al. The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs. *J Gen Intern Med* 2007;22(9):1335-50.

[D14] Buser N, Ivic S, Kessler TM, Kessels AG, Bachmann LM. Efficacy and adverse events of antimuscarinics for treating overactive bladder: network meta-analyses. *Eur Urol* 2012;62(6):1040-60.

[D15] Castellucci LA, Cameron C, Le Gal G, Rodger MA, Coyle D, Wells PS, et al. Efficacy and safety outcomes of oral anticoagulants and antiplatelet drugs in the secondary prevention of venous thromboembolism: systematic review and network meta-analysis. *BMJ* 2013;347:f5133.

[D16] Choy E, Marshall D, Gabriel ZL, Mitchell SA, Gylee E, Dakin HA. A systematic review and mixed treatment comparison of the efficacy of pharmacological treatments for fibromyalgia. *Semin Arthritis Rheum* 2011;41(3):335-45.e6.

[D17] Cipriani A, Furukawa TA, Salanti G, Geddes JR, Higgins JP, Churchill R, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* 2009;373(9665):746-58.

[D18] Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, et al. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. *Lancet* 2011;378(9799):1306-15.

[D19] Cohen A, Drost P, Marchant N, Mitchell S, Orme M, Rublee D, et al. The efficacy and safety of pharmacological prophylaxis of venous thromboembolism following elective knee or hip replacement: systematic review and network meta-analysis. *Clin Appl Thromb Hemost* 2012;18(6):611-27.

[D20] Coleman CI, Baker WL, Kluger J, White CM. Antihypertensive medication and their impact on cancer incidence: a mixed treatment comparison meta-analysis of randomized controlled trials. *J Hypertens* 2008;26(4):622-9.

[D21] Cooper CL, Druyts E, Thorlund K, Nachega JB, El Khoury AC, O'Regan C, et al. Boceprevir and telaprevir for the treatment of chronic hepatitis C genotype 1 infection: an indirect comparison meta-analysis. *Ther Clin Risk Manag* 2012;8:105-30.

[D22] Cooper C, Lester R, Thorlund K, Druyts E, El Khoury AC, Yaya S, et al. Direct-acting antiviral therapies for hepatitis c genotype 1 infection: a multiple treatment comparison meta-analysis. *QJM* 2013;106(2):153-63.

[D23] Cooper NJ, Sutton AJ, Lu G, Khunti K. Mixed comparison of stroke prevention treatments in individuals with nonrheumatic atrial fibrillation. Arch Intern Med 2006;166(12):1269-75.

[D24] Cope S, Cupkun-Niggli G, Gale R, Jardim JR, Jansen JP. Comparative efficacy of indacaterol 150 mug and 300 mug versus fixed-dose combinations of formoterol + budesonide or salmeterol + fluticasone for the treatment of chronic obstructive pulmonary disease - a network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2011;6(1):329-44.

[D25] Cope S, Zhang J, Williams J, Jansen JP. Efficacy of once-daily indacaterol 75 μg relative to alternative bronchodilators in COPD: a study level and a patient level network meta-analysis. BMC Pulm Med 2012;12:29.

[D26] Cope S, Kraemer M, Zhang J, Capkun-Niggli G, Jansen JP. Efficacy of indacaterol 75 mug versus fixed-dose combinations of formoterol-budesonide or salmeterol-fluticasone for COPD: a network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2012;7:415-20.

[D27] Cope S, Capkun-Ziggli G, Gale R, Lassen C, Owen R, Ouwens MJ, et al. Efficacy of once-daily indacaterol relative to alternative bronchodilators in COPD: a patient-level mixed treatment comparison. *Value Health* 2012;15(3):524-33.

[D28] Cope S, Donohue JF, Jansen JP, Kraemer M, Capkun-Niggli G, Baldwin M, et al. Comparative efficacy of long-acting bronchodilators for COPD: a network meta-analysis. *Respir Res* 2013;14:100.

[D29] Cope S, Ouwens MJ, Jansen JP, Schmid P. Progression-free survival with fulvestrant 500 mg and alternative endocrine therapies as second-line treatment for advanced breast cancer: a network meta-analysis with parametric survival models. *Value Health* 2013;16(2):403-17.

[D30] Dakin H, Fidler C, Harper H. Mixed treatment comparison meta-analysis evaluating the relative efficacy of nucleos(t)ides for treatment of nucleos(t)ide-naive patients with chronic hepatitis B. *Value Health* 2010;13(8):934-45.

[D31] Dakin HA, Welton NJ, Ades AE, Collins S, Orme M, Kelly S. Mixed treatment comparison of repeated measurements of a continuous endpoint: an example using topical treatments for primary open-angle glaucoma and ocular hypertension. *Stat Med* 2011;30(20):2511-35.

[D32] Dequen P, Lorigan P, Jansen JP, van Baardewijk M, Ouwens MJ, Kotapati S. Systematic review and network meta-analysis of overall survival comparing 3 mg/kg ipilimumab with alternative therapies in the management of pretreated patients with unresectable stage III or IV melanoma. *Oncologist* 2012;17(11):1376-85.

[D33] Dunkley AJ, Charles K, Gray LJ, Camosso-Stefinovic J, Davies MJ, Khunti K. Effectiveness of interventions for reducing diabetes and cardiovascular disease risk in people with metabolic syndrome: systematic review and mixed treatment comparison meta-analysis. *Diabetes Obes Metab* 2012;14(7):616-25.

[D34] Eckert L, Falissard B. Using meta-regression in performing indirect-comparisons: Comparing escitalopram with venlafaxine XR. *Curr Med Res Opin* 2006;22(11):2313-21.

[D35] Eckert L, Lançon C. Duloxetine compared with fluoxetine and venlafaxine: use of meta-regression analysis for indirect comparisons. *BMC Psychiatry* 2006;6:30.

[D36] Edwards SJ, Lind T, Lundell L, Das R. Systematic review: standard- and double-dose proton pump inhibitors for the healing of severe erosive oesophagitis - a mixed treatment comparison of randomized controlled trials. *Aliment Pharmacol Ther* 2009;30(6):547-56.

[D37] Edwards SJ, Smith CJ. Tolerability of atypical antipsychotics in the treatment of adults with schizophrenia or bipolar disorder: a mixed treatment comparison of randomized controlled trials. *Clin Ther* 2009;31:1345-59.

[D38] Edwards SJ, Clarke MJ, Wordsworth S, Welton NJ. Carbapenems versus other beta-lactams in the treatment of hospitalised patients with infection: a mixed treatment comparison. *Curr Med Res Opin* 2009;25(1):251-61.

[D39] Eisenberg MJ, Fillion KB, Yavin D, Bélisle P, Mottillo S, Joseph L, et al. Pharmacotherapies for smoking cessation: a meta-analysis of randomized controlled trials. *CMAJ* 2008;179(2):135-44.

[D40] Fakhoury W, Lockhart I, Kotchie RW, Aagren M, LeReun C. Indirect comparison of once daily insulin detemir and glargine in reducing weight gain and hypoglycaemic episodes when administered in addition to conventional oral anti-diabetic therapy in patients with type-2 diabetes. *Pharmacology* 2008;82(2):156-63.

[D41] Filippini G, Del Giovane C, Vacchi L, D'Amico R, Di Pietrantonj C, Beecher D, et al. Immunomodulators and immunosuppressants for multiple sclerosis: a network meta-analysis. *Cochrane Database of Syst Rev* 2013;6;CD008933.

[D42] Fox BD, Kahn SR, Langleben D, Eisenberg MJ, Shimony A. Efficacy and safety of novel oral anticoagulants for treatment of acute venous thromboembolism: direct and adjusted indirect meta-analysis of randomised controlled trials. *BMJ* 2012;345:e7498.

[D43] Freemantle N, Lafuente-Lafuente C, Mitchell S, Eckert L, Reynolds M. Mixed treatment comparison of dronedarone, amiodarone, sotalol, flecainide, and propafenone, for the management of atrial fibrillation. *Europace* 2011;13(3):329-45.

[D44] Freemantle N, Tharmanathan P, Herbrecht R. Systematic review and mixed treatment comparison of randomized evidence for empirical, pre-emptive and directed treatment strategies for invasive mould disease. *J Antimicrob Chemother* 2011;66 Suppl 1:i25-35.

[D45] Freemantle N, Cooper C, Diez-Perez A, Gitlin M, Radcliffe H, Shepherd S, et al. Results of indirect and mixed treatment comparison of fracture efficacy for osteoporosis treatments: a meta-analysis. *Osteoporos Int* 2013;24(1):209-17.

[D46] Golfinopoulos V, Salanti G, Pavlidis N, Ioannidis JP. Survival and disease-progression benefits with treatment regimens for advanced colorectal cancer: a meta-analysis. *Lancet Oncol* 2007;8(10):898-911.

[D47] Golfinopoulos V, Pentheroudakis G, Salanti G, Nearchou AD, Ioannidis JP, Pavlidis N. Comparative survival with diverse chemotherapy regimens for cancer of unknown primary site: multiple-treatments meta-analysis. *Cancer Treat Rev* 2009;35(7):570-3.

[D48] Gray LJ, Cooper N, Dunkley A, Warren FC, Ara R, Abrams K, et al. A systematic review and mixed treatment comparison of pharmacological interventions for the treatment of obesity. *Obes Rev* 2012;13(6):483-98.

[D49] Guyot P, Taylor P, Christensen R, Pericleous L, Poncet C, Lebmeier M, et al. Abatacept with methotrexate versus other biologic agents in treatment of patients with active rheumatoid arthritis despite methotrexate: a network meta-analysis. *Arthritis Res Ther* 2011;13(6):R204.

[D50] Haas DM, Caldwell DM, Kirkpatrick P McIntosh JJ, Welton NJ. Tocolytic therapy for preterm delivery: systematic review and network meta-analysis. *BMJ* 2012;345:e6226.

[D51] Halpin DM, Gray J, Edwards SJ, Morais J, Singh D. Budesonide/formoterol vs. salmeterol/fluticasone in COPD: a systematic review and adjusted indirect comparison of pneumonia in randomised controlled trials. *Int J Clin Pract* 2011;65(7):764-74.

[D52] Harenberg J, Marx S, Diener HC, Lip GY, Marder VJ, Wehling M, et al. Comparison of efficacy and safety of dabigatran, rivaroxaban and apixaban in patients with atrial fibrillation using network meta-analysis. *Int Angiol* 2012;31(4):330-9.

[D53] Harenberg J, Marx S, Dahl OE, Marder VJ, Schulze A, Wehling M, et al. Interpretation of endpoints in a network meta-analysis of new oral anticoagulants following total hip or total knee replacement surgery. *Thromb Haemost* 2012;108(5):903-12.

[D54] Hartling L, Fernandes RM, Bialy L, Milne A, Johnson D, Plint A, et al. Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis. *BMJ* 2011;342:d1714.

[D55] Häuser W, Petzke F, Sommer C. Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. *J Pain* 2010;11(6):505-21.

[D56] Häuser W, Petzke F, Üçeyler N, Sommer C. Comparative efficacy and acceptability of amitriptyline, duloxetine and milnacipran in fibromyalgia syndrome: a systematic review with meta-analysis. *Rheumatology* 2011;50(3):532-43.

[D57] Henry D, Carless P, Fergusson D, Laupacis A. The safety of aprotinin and lysine-derived antifibrinolytic drugs in cardiac surgery: a meta-analysis. *CMAJ* 2009;180(2):183-93.

[D58] Hochberg MC, Tracy JK, Hawkins-Holt M, Flores RH. Comparison of the efficacy of the tumour necrosis factor α blocking agents adalimumab, etanercept, and infliximab when added to methotrexate in patients with active rheumatoid arthritis. *Ann Rheum Dis* 2003;62 Supply 2:13-6.

[D59] Hochberg MC, Berry S, Broglio K, Rosenblatt L, Nadkarni A, Trivedi D, et al. Mixed treatment comparison of efficacy and tolerability of biologic agents in patients with rheumatoid arthritis. *Curr Med Res Opin* 2013;29(10):1213-22.

[D60] Hopkins RB, Goeree R, Pullenayegum E, Adachi JD, Papaioannou A, Xie F, et al. The relative efficacy of nine osteoporosis medications for reducing the rate of fractures in post-menopausal women. *BMC Musculoskelet Disord* 2011;12:209.

[D61] Howell N, Senanayake E, Freemantle N, Pagano D. Putting the record straight on aprotinin as safe and effective: results from a mixed treatment meta-analysis of trials of aprotinin. *J Thorac Cardiovasc Surg* 2013;145(1):234-40.

[D62] Hutton B, Joseph L, Fergusson D, Mazer CD, Shapiro S, Tinmouth A. Risks of harms using antifibrinolytics in cardiac surgery: systematic review and network meta-analysis of randomised and observational studies. BMJ 2012;345:e5798.

[D63] Jansen JP, Bergman GJ, Huels J, Olson M. Prevention of vertebral fractures in osteoporosis: mixed treatment comparison of bisphosphonate therapies. *Curr Med Res Opin* 2009;25(8):1861-8.

[D64] Jansen JP, Bergman GJ, Huels J, Olson M. The efficacy of bisphosphonates in the prevention of vertebral, hip, and nonvertebral-nonhip fractures in osteoporosis: a network meta-analysis. *Semin Arthritis Rheum* 2011;40(4):275-84.e1-2.

[D65] Kinnaird T, Medic G, Casella G, Schiele F, Kaul U, Radke PW, et al. Relative efficacy of bivalirudin versus heparin monotherapy in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: a network meta-analysis. *J Blood Med* 2013;4:129-40.

[D66] Knottnerus BJ, Grigoryan L, Geerlings SE, Moll van Charante EP, Verheij TJ, Kessels AG, et al. Comparative effectiveness of antibiotics for uncomplicated urinary tract infections: network meta-analysis of randomized trials. *Fam Pract* 2012;29(6):659-70.

[D67] Krogh TP, Bartels EM, Ellingsen T, Stengaard-Pedersen K, Buchbinder R, Fredberg U, et al. Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network meta-analysis of randomized controlled trials. *Am J Sports Med* 2013;41(6):1435-46.

[D68] Kwok CS, Yeong JK, Loke YK. Meta-analysis: risk of fractures with acid-suppressing medication. *Bone* 2011;48(4):768-76.

[D69] Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, Loke YK. Risk of Clostridium difficile infection with acid suppressing drugs and antibiotics: meta-analysis. *Am J Gastroenterol* 2012;107(7):1011-9.

[D70] Kwok CS, Pradhan S, Yeong JK, Loke YK. Relative effects of two different enoxaparin regimens as comparators against newer oral anticoagulants: meta-analysis and adjusted indirect comparison. *Chest* 2013;144(2):593-600.

[D71] Kyrgiou M, Salanti G, Pavlidis N, Paraskevaidis E, Ioannidis JP. Survival benefits with diverse chemotherapy regimens for ovarian cancer: meta-analysis of multiple treatments. *J Natl Cancer Inst* 2006;98(22):1655-63.

[D72] Lanas A, Wu P, Medin J, Mills EJ. Low doses of acetylsalicylic acid increase risk of gastrointestinal bleeding in a meta-Analysis. *Clin Gastroenterol Hepatol* 2011;9(9):762-82.e6.

[D73] Lang SH, Manning N, Armstrong N, Misso K, Allen A, Di Nisio M, et al. Treatment with tirofiban for acute coronary syndrome (ACS): a systematic review and network analysis. *Curr Med Res Opin* 2012;28(3):351-70.

[D74] Larkin J, Paine A, Tumur I, Cappelleri JC, Healey PJ Sr, Foley G, et al. Second-line treatments for the management of advanced renal cell carcinoma: systematic review and meta-analysis. *Expert Opin Pharmacother* 2013;14(1):27-39.

[D75] Lereun C, Wells P, Diamantopoulos A, Rasul F, Lees M, Sengupta N. An indirect comparison, via enoxaparin, of rivaroxaban with dabigatran in the prevention of venous thromboembolism after hip or knee replacement. J Med Econ 2011;14(2):238-44.

[D76] Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, Richter F, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet* 2013;382(9896):951-62.

[D77] Lip GYH, Larsen TB, Skjøth F, Rasmussen LH. Indirect comparisons of new oral anticoagulant drugs for efficacy and safety when used for stroke prevention in atrial fibrillation. *J Am Coll Cardiol* 2012;60(8):738-46.

[D78] Littlewood KJ, Higashi K, Jansen JPO, Capkun-Niggli G, Balp MM, Doering G, et al. A network meta-analysis of the efficacy of inhaled antibiotics for chronic Pseudomonas infections in cystic fibrosis. *J Cyst Fibros* 2012;11(5):419-26.

[D79] Loke YK, Kwok CS. Dabigatran and rivaroxaban for prevention of venous thromboembolism - systematic review and adjusted indirect comparison. *J Clin Pharm Ther* 2011;36(1):111-24.

[D80] Manzoli L, Salanti G, De Vito C, Boccia A, Ioannidis JP, Villari P. Immunogenicity and adverse events of avian influenza A H5N1 vaccine in healthy adults: multiple-treatments meta-analysis. *Lancet Infect Dis* 2009;9(8):482-92.

[D81] Manzoli L, De Vito C, Salanti G, D'Addario M, Villari P, Ioannidis JP. Meta-analysis of the immunogenicity and tolerability of pandemic influenza A 2009 (H1N1) vaccines. PLoS One 2011;6(9):e24384.

[D82] Mauri D, Polyzos NP, Salanti G, Pavlidis N, Ioannidis JP. Multiple-treatments meta-analysis of chemotherapy and targeted therapies in advanced breast cancer. *J Natl Cancer Inst* 2008;100(24):1780-91.

[D83] McIntosh B, Cameron C, Singh SR, Yu C, Ahuja T, Welton NJ, et al. Second-line therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed-treatment comparison meta-analysis. *Open Med* 2011;5(1):35-48.

[D84] McIntosh B, Cameron C, Singh SR, Yu C, Dolovich L, Houlden R. Choice of therapy in patients with type 2 diabetes inadequately controlled with metformin and a sulphonylurea: a systematic review and mixed-treatment comparison meta-analysis. *Open Med* 2012;6(2):e62-74.

[D85] Meissner K, Fässler M, Rücker G, Kleijnen J, Hróbjartsson A, Schneider A, et al. Differential effectiveness of placebo treatments: a systematic review of migraine prophylaxis. *JAMA Intern Med* 2013;173(21):1941-51.

[D86] Mills EJ, Rachlis B, Wu P, Devereaux PJ, Arora P, Perri D. Primary prevention of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients. *J Am Coll Cardiol* 2008;52(22):1769-81.

[D87] Mills EJ, Perri D, Cooper C, Nachega JB, Wu P, Tleyjeh I, et al. Antifungal treatment for invasive Candida infections: a mixed treatment comparison meta-analysis. *Ann Clin Microbiol Antimicrob* 2009;8:23.

[D88] Mills EJ, Rachlis B, O'Regan C, Thabane L, Perri D. Metastatic renal cell cancer treatments: an indirect comparison meta-analysis. *BMC Cancer* 2009;9:34.

[D89] Mills EJ, Wu P, Spurden D, Ebbert JO, Wilson K. Efficacy of pharmacotherapies for short-term smoking abstinance: a systematic review and meta-analysis. Harm Reduct J 2009;6:25.

[D90] Mills EJ, Druyts E, Ghement I, Puhan MA. Pharmacotherapies for chronic obstructive pulmonary disease: a multiple treatment comparison meta-analysis. *Clin Epidemiol* 2011;3(1):107-29.

[D91] Mills EJ, Wu P, Chong G, Ghement I, Singh S, Akl EA, et al. Efficacy and safety of statin treatment for cardiovascular disease: a network meta-analysis of 170,255 patients from 76 randomized trials. *QJM* 2011;104(2):109-24.

[D92] Mills EJ, Wu P, Lockhart I, Thorlund K, Phuan M, Ebbert JO. Comparisons of high-dose and combination nicotine replacement therapy, varenicline, and bupropion for smoking cessation: a systematic review and multiple treatment meta-analysis. *Ann Med* 2012;44(6):588-97.

[D93] Mitchell SA, Simon TA, Raza S, Jakouloff D, Orme ME, Lockhart I, et al. The efficacy and safety of oral anticoagulants in warfarin-suitable patients with nonvalvular atrial fibrillation: systematic review and meta-analysis. *Clin Appl Thromb Hemost* 2013;19(6):619-31.

[D94] Murad MH, Drake MT, Mullan RJ, Mauck KF, Stuart LM, Lane MA, et al. Clinical review. Comparative effectiveness of drug treatments to prevent fragility fractures: a systematic review and network meta-analysis. *J Clin Endocrinol Metab* 2012;97(6):1871-80.

[D95] Naci H, Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ* 2013;347:f5577.

[D96] Naci H, Brugts JJ, Ades T. Comparative tolerability and harms of individual statins: a study-level network meta-analysis of 246 955 participants from 135 randomized, controlled trials. *Circ Cardiovasc Qual Outcomes* 2013;6(4):390-9.

[D97] Naci H, Brugts JJ, Fleurence R, Tsoi B, Toor H, Ades AE. Comparative benefits of statins in the primary and secondary prevention of major coronary events and all-cause mortality: a network meta-analysis of placebo-controlled and active-comparator trials. *Eur J Prev Cardiol* 2013;20(4):641-57.

[D98] Naci H, Brugts JJ, Fleurence R, Ades AE. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. *Eur J Prev Cardiol* 2013;20(4):658-70.

[D99] Naci H, Brugts JJ, Fleurence R, Ades AE. Comparative effects of statins on major cerebrovascular events: a multiple-treatments meta-analysis of placebo-controlled and active-comparator trials. *QJM* 2013;106(4):299-306.

[D100] Naudet F, Millet B, Charlier P, Reymann JM, Maria AS, Falissard B. Which placebo to cure depression? A thought-provoking network meta-analysis. *BMC Med* 2013;11(1):230.

[D101] Navarese EP, Buffon A, Andreotti F, Kozinski M, Welton N, Fabiszak T, et al. Meta-analysis of impact of different types and doses of statins on new-onset diabetes mellitus. *Am J Cardiol* 2013;111(8):1123-30.

[D102] Nüesch E, Häuser W, Bernardy K, Barth J, Jüni P. Comparative efficacy of pharmacological and non-pharmacological interventions in fibromyalgia syndrome: network meta-analysis. *Ann Rheum Dis* 2013;72(6):955-62.

[D103] Orme M, Collins S, Dakin H, Kelly S, Loftus J. Mixed treatment comparison and meta-regression of the efficacy and safety of prostaglandin analogues and comparators for primary open-angle glaucoma and ocular hypertension. *Curr Med Res Opin* 2010;26(3):511-28.

[D104] Orme ME, Macgilchrist KS, Mitchell S, Spurden D, Bird A. Systematic review and network meta-analysis of combination and monotherapy treatments in disease-modifying antirheumatic drug-experienced patients with rheumatoid arthritis: analysis of American college of Rheumatology criteria scores 20, 50, and 70. *Biologics* 2012;6:429-64.

[D105] Phung OJ, Scholle JM, Talwar M, Coleman CI. Effect of noninsulin antidiabetic drugs added to metformin therapy on glycemic control, weight gain, and hypoglycemia in type 2 diabetes. *JAMA* 2010;303(14):1410-8.

[D106] Phung OJ, Kahn SR, Cook DJ, Murad MH. Dosing frequency of unfractionated heparin thromboprophylaxis: a meta-analysis. *Chest* 2011;140(2):374-81.

[D107] Phung OJ, Sood NA, Sill BE, Coleman CI. Oral anti-diabetic drugs for the prevention of Type 2 diabetes. *Diabet Med* 2011;28(8):948-64.

[D108] Puhan MA, Bachmann LM, Kleijnen J, Ter Riet G, Kessels AG. Inhaled drugs to reduce exacerbations in patients with chronic obstructive pulmonary disease: a network meta-analysis. *BMC Med* 2009;7:2.

[D109] Quilici S, Abrams KR, Nicolas A, Martin M, Petit C, Lleu PL, et al. Meta-analysis of the efficacy and tolerability of pramipexole versus ropinirole in the treatment of restless legs syndrome. *Sleep Med* 2008;9(7):715-26.

[D110] Quilici S, Chancellor J, Löthgren M, Simon D, Said G, Le TK, et al. Meta-analysis of duloxetine vs. pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain. *BMC Neurol* 2009;9:6.

[D111] Rashiq S, Vandermeer B, Abou-Setta AM, Beaupre LA, Jones CA, Dryden DM. Efficacy of supplemental peripheral nerve blockade for hip fracture surgery: multiple treatment comparison. *Can J Anesth* 2013;60(3):230-43.

[D112] Rasmussen LH, Larsen TB, Graungaard T, Skjøth F, Lip GY. Primary and secondary prevention with new oral anticoagulant drugs for stroke prevention in atrial fibrillation: indirect comparison analysis. *BMJ* 2012;345:e7097.

[D113] Riemsma R, Simons JP, Bashir Z, Gooch CL, Kleijnen J. Systematic Review of topotecan (Hycamtin) in relapsed small cell lung cancer. *BMC Cancer* 2010;10:436.

[D114] Riemsma R, Forbes CA, Kessels A, Lykopoulos K, Amonkar MM, Rea DW, et al. Systematic review of aromatase inhibitors in the first-line treatment for hormone sensitive advanced or metastatic breast cancer. *Breast Cancer Res Treat* 2010;123(1):9-24.

[D115] Riemsma R, Forbes C, Harker J, Worthy G, Misso K, Schäfer M, et al. Systematic review of tapentadol in chronic severe pain. *Curr Med Res Opin* 2011;27(10):1907-30.

[D116] Riemsma R, Forbes CA, Amonkar MM, Lykopoulos K, Diaz JR, Kleijnen J, et al. Systematic review of lapatinib in combination with letrozole compared with other first-line treatments for hormone receptor positive(HR+) and HER2+ advanced or metastatic breast cancer(MBC). *Curr Med Res Opin* 2012;28(8):1263-79.

[D117] Roskell NS, Lip GY, Noack H, Clemens A, Plumb JM. Treatments for stroke prevention in atrial fibrillation: a network meta-analysis and indirect comparisons versus dabigatran etexilate. *Thromb Haemost* 2010;104(6):1106-15.

[D118] Roskell NS, Beard SM, Zhao Y, Le TK. A meta-analysis of pain response in the treatment of fibromyalgia. *Pain Pract* 2011;11(6):516-27.

[D119] Roskell NS, Zimovetz EA, Rycroft CE, Eckert BJ, Tyas DA. Annualized relapse rate of first-line treatments for multiple sclerosis: a meta-analysis, including indirect comparisons versus fingolimod. *Curr Med Res Opin* 2012;28(5):767-80.

[D120] Salliot C, Finckh A, Katchamart W, Lu Y, Sun Y, Bombardier C, et al. Indirect comparisons of the efficacy of biological antirheumatic agents in rheumatoid arthritis in patients with an inadequate response to conventional disease-modifying antirheumatic drugs or to an anti-tumour necrosis factor agent: a meta-analysis. *Ann Rheum Dis* 2011;70(2):266-71.

[D121] Singh JA, Christensen R, Wells GA, Suarez-Almazor ME, Buchbinder R, Lopez-Olivo MA, et al. A network meta-analysis of randomized controlled trials of biologics for rheumatoid arthritis: a Cochrane overview. *CMAJ* 2009;181(11):787-96.

[D122] Singh JA, Wells GA, Christensen R, Tanjong Ghogomu E, Maxwell L, Macdonald JK, et al. Adverse effects of biologics: a network meta-analysis and Cochrane overview. *Cochrane Database Syst Rev* 2011;(2):CD008794.

[D123] Skoetz N, Trelle S, Rancea M, Haverkamp H, Diehl V, Engert A, et al. Effect of initial treatment strategy on survival of patients with advanced-stage Hodgkin's lymphoma: a systematic review and network meta-analysis. *Lancet Oncol* 2013;14(10):943-52.

[D124] Snedecor SJ, Sudharshan L, Cappelleri JC, Sadosky A, Desai R, Jalundhwala YJ, et al. Systematic review and comparison of pharmacologic therapies for neuropathic pain associated with spinal cord injury. *J Pain Res* 2013;6:539-47.

[D125] Stam WB, Jansen J, Taylor S. Efficacy of etoricoxib, celecoxib, lumiracoxib, non-selective NSAIDs, and acetaminophen in osteoarthritis: a mixed treatment comparison. *Open Rheumatol J* 2012;6(1):6-20.

[D126] Steiner S, Moertl D, Chen L, Coyle D, Wells GA. Network meta-analysis of prasugrel, ticagrelor, high- and standard-dose clopidogrel in patients scheduled for percutaneous coronary interventions. *Thromb Haemost* 2012;108(2):318-27.

[D127] Strassmann R, Bausch B, Spaar A, Kleijnen J, Braendli O, Puhan MA. Smoking cessation interventions in COPD: a network meta-analysis of randomised trials. *Eur Respir J* 2009;34(3):634-40.

[D128] Sundaresh V, Brito JP, Wang Z, Prokop LJ, Stan MN, Murad MH, et al. Comparative effectiveness of therapies for graves' hyperthyroidism: a systematic review and network meta-Analysis. *J Clin Endocrinol Metab* 2013;98(9):3671-7.

[D129] Thorlund K, Druyts E, Aviña-Zubieta JA, Mills EJ. Anti-tumor necrosis factor (TNF) drugs for the treatment of psoriatic arthritis: an indirect comparison meta-analysis. *Biologics* 2012;6:417-27.

[D130] Trelle S, Reichenbach S, Wandel S, Hildebrand P, Tschannen B, Villiger PM, et al. Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. *BMJ* 2011;342:c7086.

[D131] van de Kerkhof P, de Peuter R, Ryttov J, Jansen JP. Mixed treatment comparison of a two-compound formulation (TCF) product containing calcipotriol and betamethasone dipropionate with other topical treatments in psoriasis vulgaris. *Curr Med Res Opin* 2011;27(1): 225-38.

[D132] van der Mark LB, Lyklema PH, Geskus RB, Mohrs J, Bindels PJ, van Aalderen WM, et al. A systematic review with attempted network meta-analysis of asthma therapy recommended for five to eighteen year olds in GINA steps three and four. *BMC Pulm Med* 2012;12:63.

[D133] Vieira MC, Kumar RN, Jansen JP. Comparative effectiveness of efavirenz, protease inhibitors, and raltegravir-based regimens as first-line treatment for HIV-infected adults: a mixed treatment comparison. *HIV Clin Trials* 2011;12(4):175-89.

[D134] Vissers D, Stam W, Nolte T, Lenre M, Jansen J. Efficacy of intranasal fentanyl spray versus other opioids for breakthrough pain in cancer. *Curr Med Res Opin* 2010;26(5):1037-45.

[D135] Wandel S, Jüni P, Tendal B, Nüesch E, Villiger PM, Welton NJ, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ* 2010;341:c4675.

[D136] Wehren LE, Hosking D, Hochberg MC. Putting evidence-based medicine into clinical practice: comparing anti-resorptive agents for the treatment of osteoporosis. *Curr Med Res Opin* 2004;20(4):525-31.

[D137] Welton NJ, Cooper NJ, Ades AE, Lu G, Sutton AJ. Mixed treatment comparison with multiple outcomes reported inconsistently across trials: evaluation of antivirals for treatment of influenza A and B. *Stat Med* 2008;27(27):5620-39.

[D138] Wolff RF, Bala MM, Westwood M, Kessels AG, Kleijnen J. 5% lidocaine medicated plaster in painful diabetic peripheral neuropathy (DPN): a systematic review. *Swiss Med Wkly* 2010;140(21-22):297-306.

[D139] Wolff RF, Bala MM, Westwood M, Kessels AG, Kleijnen J. 5% lidocaine-medicated plaster vs other relevant interventions and placebo for post-herpetic neuralgia (PHN): a systematic review. *Acta Neurol Scand* 2011;123(5):295-309.

[D140] Wolff RF, Aune D, Truyers C, Hernandez AV, Misso K, Riemsma R, et al. Systematic review of efficacy and safety of buprenorphine versus fentanyl or morphine in patients with chronic moderate to severe pain. *Curr Med Res Opin* 2012;28(5):833-45.

[D141] Wu P, Wilson K, Dimoulas P, Mills EJ. Effectiveness of smoking cessation therapies: a systematic review and meta-analysis. *BMC Public Health* 2006;6:300.

[D142] Yazdanpanah Y, Sissoko D, Egger M, Mouton Y, Zwahlen M, Chêne G. Clinical efficacy of antiretroviral combination therapy based on protease inhibitors or non-nucleoside analogue reverse transcriptase inhibitors: indirect comparison of controlled trials. *BMJ* 2004;328(7434):249.

[D143] Zhou Z, Rahme E, Pilote L. Are statins created equal? Evidence from randomized trials of pravastatin, simvastatin, and atorvastatin for cardiovascular disease prevention. *Am Heart J* 2006;151(2):273-81.

[D144] Biondi-Zoccai G, Lotrionte M, Agostoni P, Abbate A, Romagnoli E, Sangiorgi G, et al. Adjusted indirect comparison meta-analysis of prasugrel versus ticagrelor for patients with acute coronary syndromes. *Int J Cardiol* 2011;150(3):325-31.

[D145] Biondi-Zoccai G, Malavasi V, D'Ascenzo F, Abbate A, Agostoni P, Lotrionte M, et al. Comparative effectiveness of novel oral anticoagulants for atrial fibrillation: evidence from pair-wise and warfarin-controlled network meta-analyses. *HSR Proc Intensive Care Cardiovasc Anesth* 2013;5(1):40-54.

[D146] Chatterjee S, Biondi-Zoccai G, Abbate A, D'Ascenzo F, Castagno D, Van Tassell B, et al. Benefits of beta blockers in patients with heart failure and reduced ejection fraction: network meta-analysis. *BMJ* 2013;346:f55.

[D147] Chatterjee S, Sardar P, Biondi-Zoccai G, Kumbhani DJ. New oral anticoagulants and the risk of intracranial hemorrhage: traditional and Bayesian meta-analysis and mixed treatment comparison of randomized trials of new oral anticoagulants in atrial fibrillation. *JAMA Neurol* 2013;70(12):1486-90.

[D148] Chatterjee S, Ghose A, Sharma A, Guha G, Mukherjee D, Frankel R. Comparing newer oral anti-platelets prasugrel and ticagrelor in reduction of ischemic events-evidence from a network meta-analysis. *J Thromb Thrombolysis* 2013;36(3):223-32.

[D149] Chatterjee S, Sardar P, Mukherjee D, Lichstein E, Aikat S. Timing and route of amiodarone for prevention of postoperative atrial fibrillation after cardiac surgery: a network regression meta-analysis. *Pacing Clin Electrophysiol* 2013;36(8):1017-23.

[D150] Landoni G, Greco T, Biondi-Zoccai G, Nigro Neto C, Febres D, Pintaudi M, et al. Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery. *Br J Anaesth* 2013;111(6):886-96.

[D151] Sardar P, Chatterjee S, Wu WC, Lichstein E, Ghosh J, Aikat S, Muhkerjee D. New oral anticoagulants are not superior to warfarin in secondary prevention of stroke or transient ischemic attacks, but lower the risk of intracranial bleeding: insights from a meta-analysis and indirect treatment comparisons. *PLoS One* 2013;8(10):e77694.

[D152] Testa L, Agnifili M, Latini RA, Mattioli R, Lanotte S, De Marco F, et al. Adjusted indirect comparison of new oral anticoagulants for stroke prevention in atrial fibrillation. *QJM* 2012;105(10):949-57.

[D153] Chen JM, Heran BS, Wright JM. Blood pressure lowering efficacy of diuretics as second-line therapy for primary hypertension. *Cochrane Database Syst Rev* 2009;(4):CD007187.

[D154] Chen JM, Heran BS, Perez MI, Wright JM. Blood pressure lowering efficacy of beta-blockers as second-line therapy for primary hypertension. *Cochrane Database Syst Rev* 2010;(1):CD007185.

[D155] Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin converting enzyme (ACE) inhibitors for primary hypertension. *Cochrane Database Syst Rev* 2008;(4):CD003823.

[D156] Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin receptor blockers for primary hypertension. *Cochrane Database Syst Rev* 2008;(4):CD003822.

[D157] Heran BS, Galm BP, Wright JM. Blood pressure lowering efficacy of alpha blockers for primary hypertension. *Cochrane Database Syst Rev* 2009;(4):CD004643.

[D158] Heran BS, Chen JM, Wang JJ, Wright JM. Blood pressure lowering efficacy of potassium-sparing diuretics (that block the epithelial sodium channel) for primary hypertension. *Cochrane Database Syst Rev* 2010;(1):CD008167.

[D159] Heran BS, Galm BP, Wright JM. Blood pressure lowering efficacy of alpha blockers for primary hypertension. *Cochrane Database Syst Rev* 2012;(8):CD004643.

[D160] Heran BS, Chen JM, Wang JJ, Wright JM. Blood pressure lowering efficacy of potassium-sparing diuretics (that block the epithelial sodium channel) for primary hypertension. Cochrane Database Syst Rev 2012;(11):CD008167.

[D161] Dewilde S, Hawkins N. Investigating incoherence gives insight: clopidogrel is equivalent to extended-release dipyridamole plus aspirin in secondary stroke prevention. *J Clin Epidemiol* 2012;65(8):835-45.

[D162] Gross JL, Kramer CK, Leitão CB, Hawkins N, Viana LV, Schaan BD, et al. Effect of antihyperglycemic agents added to metformin and a sulfonylurea on glycemic control and weight gain in type 2 diabetes: a network meta-analysis. *Ann Intern Med* 2011;154(10):672-9.

[D163] Khan N, Shah D, Tongbram V, Verdian L, Hawkins N. The efficacy and tolerability of perampanel and other recently approved anti-epileptic drugs for the treatment of refractory partial onset seizure: a systematic review and Bayesian network meta-analysis. *Curr Med Res Opin* 2013;29(8):1001-13.

[D164] Mealing S, Barcena L, Hawkins N, Clark J, Eaton V, Hirji I, Davis C. The relative efficacy of imatinib, dasatinib and nilotinib for newly diagnosed chronic myeloid leukemia: a systematic review and network meta-analysis. *Exp Hematol Oncol* 2013;2(1):5.

[D165] Reich K, Burden AD, Eaton JN, Hawkins NS. Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials. *Br J Dermatol* 2012;166(1):179-88.

[D166] Scott DA, Boye KS, Timlin L, Clark JF, Best JH. A network meta-analysis to compare glycaemic control in patients with type 2 diabetes treated with exenatide once weekly or liraglutide once daily in comparison with insulin glargine, exenatide twice daily or placebo. *Diabetes Obes Metab* 2013;15(3):213-23.

[D167] Desai RJ, Hansen RA, Rao JK, Wilkins TM, Harden EA, Yuen A, et al. Mixed treatment comparison of the treatment discontinuations of biologic disease-modifying antirheumatic drugs in adults with rheumatoid arthritis. *Ann Pharmacother* 2012;46(11):1491-505.

[D168] Gartlehner G, Hansen RA, Jonas BL, Thieda P, Lohr KN. The comparative efficacy and safety of biologics for the treatment of rheumatoid arthritis: a systematic review and metaanalysis. *J Rheumatol* 2006;33(12):2398-408.

[D169] Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, et al. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. *Ann Intern Med* 2011;155(11):772-85.

[D170] Hansen RA, Gartlehner G, Webb AP, Morgan LC, Moore CG, Jonas DE. Efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease: a systematic review and meta-analysis. *Clin Interv Aging* 2008;3(2):211-25.

[D171] Hansen RA, Gaynes BN, Gartlehner G, Moore CG, Tiwari R, Lohr KN. Efficacy and tolerability of second-generation antidepressants in social anxiety disorder. *Int Clin Psychopharmacol* 2008;23(3):170-9.

[D172] Signorovitch JE, Wu EQ, Yu AP, Gerrits CM, Kantor E, Bao Y, et al. Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept. *Pharmacoeconomics* 2010;28(10):935-45.

[D173] Signorovitch JE, Wu EQ, Swallow E, Kantor E, Fan L, Gruenberger JB. Comparative efficacy of vildagliptin and sitagliptin in Japanese patients with type 2 diabetes mellitus: a matching-adjusted indirect comparison of randomized trials. *Clin Drug Investig* 2011;31(9):665-74.

[D174] Signorovitch JE, Wu EQ, Betts KA, Parikh K, Kantor E, Guo A, et al. Comparative efficacy of nilotinib and dasatinib in newly diagnosed chronic myeloid leukemia: a matching-adjusted indirect comparison of randomized trials. *Curr Med Res Opin* 2011;27(6):1263-71.

[D175] Signorovitch J, Erder MH, Xie J, Sikirica V, Lu M, Hodgkins PS, Wu EQ. Comparative effectiveness research using matching-adjusted indirect comparison: an application to treatment with guanfacine extended release or atomoxetine in children with attention-deficit/hyperactivity disorder and comorbid oppositional defiant disorder. *Pharmacoepidemiol Drug Saf* 2012;21 Suppl 2:130-7.

[D176] Sikirica V, Findling RL, Signorovitch J, Erder MH, Dammerman R, Hodgkins P, et al. Comparative efficacy of guanfacine extended release versus atomoxetine for the treatment of attention-deficit/hyperactivity disorder in children and adolescents: applying matching-adjusted indirect comparison methodology. *CNS Drugs* 2013;27(11):943-53.

[D177] Ribeiro RA, Ziegelmann PK, Duncan BB, Stella SF, da Costa Vieira JL, Restelatto LM, et al. Impact of statin dose on major cardiovascular events: a mixed treatment comparison meta-analysis involving more than 175,000 patients. *Int J Cardiol* 2013;166(2):431-9.

[D178] Rotta I, Ziegelmann PK, Otuki MF, Riveros BS, Bernardo NL, Correr CJ. Efficacy of topical antifungals in the treatment of dermatophytosis: a mixed-treatment comparison meta-analysis involving 14 treatments. *JAMA Dermatol* 2013;149(3):341-9.

[D179] Sanches AC, Correr CJ, Venson R, Pontarolo R. Revisiting the efficacy of long-acting insulin analogues on adults with type 1 diabetes using mixed-treatment comparisons. *Diabetes Res Clin Pract* 2011;94(3):333-9.

[D180] Sanches ACC, Correr CJ, Venson R, Gonçalves PR, Garcia MM, Piantavini S, et al. Insulin analogues versus human insulin in type 1 diabetes: direct and indirect meta-analyses of efficacy and safety. *Braz J Pharm Sci* 2013;49(3):501-9.

[D181] Wiens A, Lenzi L, Venson R, Correr CJ, Rotta I, Pedroso ML, et al. Comparative efficacy of oral nucleoside or nucleotide analog monotherapy used in chronic hepatitis B: a mixed-treatment comparison meta-analysis. *Pharmacotherapy* 2013;33(2):144-51.

[D182] Anothaisintawee T, Attia J, Nickel JC, Thammakraisorn S, Numthavaj P, McEvoy M, et al. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. *JAMA* 2011;305(1):78-86.

[D183] Jones LJ, Craven PD, Attia J, Thakkinstian A, Wright I. Network meta-analysis of indomethacin versus ibuprofen versus placebo for PDA in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2011;96(1):F45-52.

[D184] Numthavaj P, Thakkinstian A, Dejthevaporn C, Attia J. Corticosteroid and antiviral therapy for Bell's palsy: a network meta-analysis. *BMC Neurol* 2011;11:1.

[D185] Thakkinstian A, Attia J, Anothaisintawee T, Nickel JC. α-blockers, antibiotics and anti-inflammatories have a role in the management of chronic prostatitis/chronic pelvic pain syndrome. *BJU Int* 2012;110(7):1014-22.

[D186] Vejakama P, Thakkinstian A, Lertrattananon D, Ingsathit A, Ngarmukos C, Attia J. Reno-protective effects of renin-angiotensin system blockade in type 2 diabetic patients: a systematic review and network meta-analysis. *Diabetologia* 2012;55(3):566-78.

[D187] Dranitsaris G, Jelincic V, Choe Y. Meta regression analysis to indirectly compare dalteparin to enoxaparin for the prevention of venous thromboembolic events following total hip replacement. *Thromb J* 2011;9(1):3.

[D188] Dranitsaris G, Jelincic V, Choe Y. Meta-regression analysis to indirectly compare prophylaxis with dalteparin or enoxaparin in patients at high risk for venous thromboembolic events. *Clin Appl Thromb Hemost* 2012;18(3):233-42.

[D189] Dranitsaris G, Schmitz S, Broom RJ. Small molecule targeted therapies for the second-line treatment for metastatic renal cell carcinoma: a systematic review and indirect comparison of safety and efficacy. *J Cancer Res Clin Oncol* 2013;139(11):1917-26.

[D190] Kieran J, Schmitz S, O'Leary A, Walsh C, Bergin C, Norris S, et al. The relative efficacy of boceprevir and telaprevir in the treatment of hepatitis C virus genotype 1. *Clin Infect Dis* 2013;56(2):228-35.

[D191] Schmitz S, Adams R, Walsh CD, Barry M, FitzGerald O. A mixed treatment comparison of the efficacy of anti-TNF agents in rheumatoid arthritis for methotrexate non-responders demonstrates differences between treatments: a Bayesian approach. *Ann Rheum Dis* 2012;71(2): 225-30.

[D192] Chou R, Fu R, Huffman LH, Korthuis PT. Initial highly-active antiretroviral therapy with a protease inhibitor versus a non-nucleoside reverse transcriptase inhibitor: discrepancies between direct and indirect meta-analyses. *Lancet* 2006;368(9546):1503-15.

[D193] Chou R, Carson S, Chan BK. Pegylated interferons for chronic hepatitis C virus infection: an indirect analysis of randomized trials. *J Viral Hepat* 2008;15(8):551-70.

[D194] Chou R, Carson S, Chan BK. Gabapentin versus tricyclic antidepressants for diabetic neuropathy and post-herpetic neuralgia: discrepancies between direct and indirect meta-analyses of randomized controlled trials. *J Gen Intern Med* 2009;24(2):178-88.

[D195] Norris SL, Carson S, Roberts C. Comparative effectiveness of pioglitazone and rosiglitazone in type 2 diabetes, prediabetes, and the metabolic syndrome: a meta-analysis. *Curr Diabetes Rev* 2007;3(2):127-40.

[D196] Peterson K, McDonagh MS, Fu R. Comparative benefits and harms of competing medications for adults with attention-deficit hyperactivity disorder: a systematic review and indirect comparison meta-analysis. *Psychopharmacology* 2008;197(1):1-11.

[D197] Chang JWC, Thongprasert S, Wright E, Tsang K, Kim HT, Ahn MJ, et al. An indirect comparison of bevacizumab plus cisplatin-gemcitabine and cisplatin plus pemetrexed treatment for patients with advanced first-line non-squamous non-small cell lung cancer in East Asia. *Asia Pac J Clin Oncol* 2011;7 Suppl 2:13-21.

[D198] Mickisch GHJ, Schwander B, Escudier B, Bellmunt J, Maroto Jp, Porta C, et al. Indirect treatment comparison of bevacizumab + interferon-α-2a vs tyrosine kinase inhibitors in first-line metastatic renal cell carcinoma therapy. *Clinicoecon Outcomes Res* 2011;3(1):19-27.

[D199] Nuijten M, Heigener DF, Bischoff HG, Chouaid C, Vergnenègre A, de Castro Carpeño J, et al. Effectiveness of bevacizumab- and pemetrexed-cisplatin treatment for patients with advanced non-squamous non-small cell lung cancer. *Lung Cancer* 2010;69 Suppl 1):S4-10.

[D200] Nuijten MJ, Aultman R, Carpeño Jde C, Vergnenègre A, Chouaid C, Walzer S, et al. An indirect comparison of the efficacy of bevacizumab plus carboplatin and paclitaxel versus pemetrexed with cisplatin in patients with advanced or recurrent non-squamous adenocarcinoma non-small cell lung cancer. *Curr Med Res Opin* 2011;27(11):2193-201.

[D201] Liao WC, Chien KL, Lin YL, Wu MS, Lin JT, Wang HP, et al. Adjuvant treatments for resected pancreatic adenocarcinoma: a systematic review and network meta-analysis. *Lancet Oncol* 2013;14(11):1095-103.

[D202] Liu SC, Tu YK, Chien MN, Chien KL. Effect of antidiabetic agents added to metformin on glycaemic control, hypoglycaemia and weight change in patients with type 2 diabetes: a network meta-analysis. *Diabetes Obes Metab* 2012;14(9):810-20.

[D203] Wu HY, Huang JW, Lin JH, Liao WC, Peng YS, Hung KY, et al. Comparative effectiveness of renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes: systematic review and bayesian network meta-analysis. *BMJ* 2013;347:f6008.

[D204] Wu MS, Tan SC, Xiong T. Indirect comparison of randomised controlled trials: comparative efficacy of dexlansoprazole vs. esomeprazole in the treatment of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2013;38(2):190-201.

[D205] Bakalos G, Miligkos M, Doxani C, Mpoulimari I, Rodopoulou P, Zintzaras E. Assessing the relative effectiveness and tolerability of treatments in small cell lung cancer: a network meta-analysis. *Cancer Epidemiol* 2013;37(5):675-82.

[D206] Hadjigeorgiou GM, Doxani C, Miligkos M, Ziakas P, Bakalos G, Papadimitriou D, et al. A network meta-analysis of randomized controlled trials for comparing the effectiveness and safety profile of treatments with marketing authorization for relapsing multiple sclerosis. *J Clin Pharm Ther* 2013;38(6):433-9.

[D207] Zintzaras E, Doxani Mprotsis T, Schmid CH, Hadjigeorgiou GM. Network analysis of randomized controlled trials in multiple sclerosis. *Clin Ther* 2012;34(4):857-69.e9.

[D208] Ziogas DC, Voulgarelis M, Zintzaras E. A network meta-analysis of randomized controlled trials of induction treatments in acute myeloid leukemia in the elderly. *Clin Ther* 2011;33(3):254-79.

[D209] Kumar A, Hozo I, Wheatley K, Djulbegovic B. Thalidomide versus bortezomib based regimens as first-line therapy for patients with multiple myeloma: a systematic review. *Am J Hematol* 2011;86(1):18-24.

[D210] Mhaskar R, Redzepovic J, Wheatley K, Clark OA, Miladinovic B, Glasmacher A, et al. Bisphosphonates in multiple myeloma. *Cochrane Database Syst Rev* 2010;(3):CD003188.

[D211] Mhaskar R, Redzepovic J, Wheatley K, Clark OA, Miladinovic B, Glasmacher A, et al., Bisphosphonates in multiple myeloma: a network meta-analysis. *Cochrane Database Syst Rev* 2012;(5):CD003188.

[D212] Terasawa T, Trikalinos NA, Djulbegovic B, Trikalinos TA. Comparative efficacy of first-line therapies for advanced-stage chronic lymphocytic leukemia: a multiple-treatment meta-analysis. *Cancer Treat Rev* 2013;39(4):340-9.

[D213] Cheng MM, Goulart B, Veenstra Dl, Blough DK, Devine EB. A network meta-analysis of therapies for previously untreated chronic lymphocytic leukemia. *Cancer Treat Rev* 2012;38(8):1004-11.

[D214] Devine EB, Alfonso-Cristancho R, Sullivan SD. Effectiveness of biologic therapies for rheumatoid arthritis: an indirect comparisons approach. *Pharmacotherapy* 2011;31(1):39-51.

[D215] Lin VW, Ringold S, Devine EB. Comparison of ustekinumab with other biological agents for the treatment of moderate to severe plaque psoriasis: a Bayesian network meta-analysis. *Arch Dermatol* 2012;148(12):1403-10.

[D216] Ney JP, Devine EB, Watanabe JH, Sullivan SD. Comparative efficacy of oral pharmaceuticals for the treatment of chronic peripheral neuropathic pain: meta-analysis and indirect treatment comparisons. *Pain Med* 2013;14(5):706-19.

[D217] Migliore A, Bizzi E, Broccoli S, Laganà B. Indirect comparison of etanercept, infliximab, and adalimumab for psoriatic arthritis: mixed treatment comparison using placebo as common comparator. *Clin Rheumatol* 2012;31(1):133-7.

[D218] Migliore A, Broccoli S, Massafra U, Bizzi E, Frediani B. Mixed-treatment comparison of anabolic (teriparatide and PTH 1-84) therapies in women with severe osteoporosis. *Curr Med Res Opin* 2012;28(3):467-73.

[D219] Migliore A, Broccoli S, Bizzi E, Laganà B. Indirect comparison of the effects of anti-TNF biological agents in patients with ankylosing spondylitis by means of a mixed treatment comparison performed on efficacy data from published randomised, controlled trials. *J Med Econ* 2012;15(3):473-80.

[D220] Migliore A, Broccoli S, Massafra U, Cassol M, Frediani B. Ranking antireabsorptive agents to prevent vertebral fractures in postmenopausal osteoporosis by mixed treatment comparison meta-analysis. *Eur Rev Med Pharmacol Sci* 2013;17(5):658-67.

[D221] Wilhelmus KR. The treatment of herpes simplex virus epithelial keratitis. *Trans Am Ophthalmol Soc* 2000;98:505-32.

[D222] Wilhelmus KR. Therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Reviews* 2007;(1):CD002898.

[D223] Wilhelmus KR. Therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev* 2008;(1):CD002898.

[D224] Wilhelmus KR. Antiviral treatment and other therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev* 2010;(12):CD002898.

[D225] Coomarasamy A, Knox EM, Gee H, Song F, Khan KS. Effectiveness of nifedipine versus atosiban for tocolysis in preterm labour: a meta-analysis with an indirect comparison of randomised trials. *BJOG* 2003;110(12):1045-9.

[D226] Lim E, Ali Z, Ali A, Routledge T, Edmonds L, Altman DG, et al. Indirect comparison meta-analysis of aspirin therapy after coronary surgery. *BMJ* 2003;327(7427):1309-11.

[D227] Lim E, Harris G, Patel A, Adachi I, Edmonds L, Song F. Preoperative versus postoperative chemotherapy in patients with resectable non-small cell lung cancer systematic review and indirect comparison meta-analysis of randomized trials. *J Thorac Oncol* 2009;4(11): 1380-8.

[D228] Bansback N, Sizto S, Sun H, Feldman S, Willian MK, Anis A. Efficacy of systemic treatments for moderate to severe plaque psoriasis: systematic review and meta-analysis. *Dermatology* 2009;219(3):209-18.

[D229] Nixon R, Bansback N, Brennan A. The efficacy of inhibiting tumour necrosis factor alpha and interleukin 1 in patients with rheumatoid arthritis: a meta-analysis and adjusted indirect comparisons. *Rheumatology* 2007;46(7):1140-7.

[D230] Nixon RM, Bansback N, Brennan A. Using mixed treatment comparisons and meta-regression to perform indirect comparisons to estimate the efficacy of biologic treatments in rheumatoid arthritis. *Stat Med* 2007;26(6):1237-54.

[D231] Jandhyala R. Relative potency of incobotulinumtoxinA vs onabotulinumtoxinA a meta-analysis of key evidence. *J Drugs Dermatol* 2012;11(6):731-6.

[D232] Jandhyala R, Fullarton JR, Bennett MI. Efficacy of rapid-onset oral fentanyl formulations vs. oral morphine for cancer-related breakthrough pain: a meta-analysis of comparative trials. *J Pain Symptom Manage* 2013;46(4):573-80.

[D233] Palmieri C, Fullarton JR, Brown J. Comparative efficacy of bisphosphonates in metastatic breast and prostate cancer and multiple myeloma: a mixed-treatment meta-analysis. *Clin Cancer Res* 2013;19(24):6863-72.

[D234] Di Lorenzo G, Casciano R, Malangone E, Buonerba C, Sherman S, Willet J, et al. An adjusted indirect comparison of everolimus and sorafenib therapy in sunitinib-refractory metastatic renal cell carcinoma patients using repeated matched samples. *Expert Opin Pharmacother* 2011;12(10):1491-7.

[D235] Thompson Coon JS, Liu Z, Hoyle M, Rogers G, Green C, Moxham T, et al. Sunitinib and bevacizumab for first-line treatment of metastatic renal cell carcinoma: a systematic review and indirect comparison of clinical effectiveness. *Br J Cancer* 2009;101(2):238-43.

[D236] Bodalia PN, Grosso AM, Sofat R, Macallister RJ, Smeeth L, Dhillon S, et al. Comparative efficacy and tolerability of anti-epileptic drugs for refractory focal epilepsy: systematic review and network meta-analysis reveals the need for long term comparator trials. *Br J Clin Pharmacol* 2013;76(5):649-67.

[D237] Samarasekera EJ, Sawyer L, Wonderling D, Tucker R, Smith CH. Topical therapies for the treatment of plaque psoriasis: systematic review and network meta-analyses. *Br J Dermatol* 2013;168(5):954-67.

[D238] Yuan J, Liu Y, Yang Z, Qin X, Yang K, Mao C. The efficacy and safety of alpha-1 blockers for benign prostatic hyperplasia: an overview of 15 systematic reviews. *Curr Med Res Opin* 2013;29(3):279-87.

[D239] Yuan JQ, Zhang R, Yang Z, Lee J, Liu Y, Tian J, et al. Comparative effectiveness and safety of oral phosphodiesterase type 5 inhibitors for erectile dysfunction: a systematic review and network meta-analysis. *Eur Urol* 2013;63(5):902-12.

[D240] Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, et al. Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. *JAMA* 2003;289(19):2534-44.

[D241] van der Valk R, Webers CA, Lumley T, Hendrikse F, Prins MH, Schouten JS. A network meta-analysis combined direct and indirect comparisons between glaucoma drugs to rank effectiveness in lowering intraocular pressure. *J Clin Epidemiol* 2009;62(12):1279-83.

[D242] Ford JA, Elders A, Shyangdan D, Royle P, Waugh N. The relative clinical effectiveness of ranibizumab and bevacizumab in diabetic macular oedema: an indirect comparison in a systematic review. *BMJ* 2012;345:e5182.

[D243] Ford JA, Jones R, Elders A, Mulatero C, Royle P, Sharma P, et al. Denosumab for treatment of bone metastases secondary to solid tumours: systematic review and network meta-analysis. *Eur J Cancer* 2013;49(2):416-30.

[D244] Dretzke J, Meadows A, Novielli N, Huissoon A, Fry-Smith A, Meads C. Subcutaneous and sublingual immunotherapy for seasonal allergic rhinitis: a systematic review and indirect comparison. *J Allergy Clin Immunol* 2013;131(5):1361-6.

[D245] Virgili G, Novielli N, Menchini F, Murro V, Giacomelli G. Pharmacological treatments for neovascular age-related macular degeneration: can mixed treatment comparison meta-analysis be useful? *Curr Drug Targets* 2011;12(2):212-20.

[D246] Fénix-Caballero S, Alegre-del Rey EJ, Castaño-Lara R, Puigventós-Latorre F, Borrero-Rubio JM, López-Vakkehi JF. Direct and indirect comparison of the efficacy and safety of adalimumab, etanercept, infliximab and golimumab in psoriatic arthritis. *J Clin Pharm Ther* 2013;38(4):286-93.

[D247] Gallego-Galisteo M, Villa-Rubio A, Alegre-del Rey E, Márquez-Fernáandez E, Ramos-Báez JJ. Indirect comparison of biological treatments in refractory rheumatoid arthritis. *J Clin Pharm Ther* 2012;37(3):301-7.

[D248] Germani G, Pleguezuelo M, Gurusamy K, Meyer T, Isgrò G, Burroughs AK. Clinical outcomes of radiofrequency ablation, percutaneous alcohol and acetic acid injection for hepatocelullar carcinoma: a meta-analysis. *J Hepatol* 2010;52(3):380-8.

[D249] Gurusamy KS, Pissanou T, Pikhart H, Vaughan J, Burroughs AK, Davidson BR. Methods to decrease blood loss and transfusion requirements for liver transplantation. *Cochrane Database Syst Rev* 2011;(12):CD009052.

[D250] Sultana A, Ghaneh P, Cunningham D, Starling N, Neoptolemos JP, Smith CT. Gemcitabine based combination chemotherapy in advanced pancreatic cancer-indirect comparison. *BMC Cancer* 2008;8:192.

[D251] Tudur Smith C, Marson AG, Chadwick DW, Williamson PR. Multiple treatment comparisons in epilepsy monotherapy trials. Trials 2007;8:34.

[D252] Caldeira D, Alarcão J, Vaz-Carneiro A, Costa J. Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. *BMJ* 2012;345:e4260.

[D253] Costa J, Fareleira F, Ascenção R, Borges M, Sampaio C, Vaz-Carneiro A. Clinical comparability of the new antiepileptic drugs in refractory partial epilepsy: a systematic review and meta-analysis. *Epilepsia* 2011;52(7):1280-91.

[D254] Del Santo F, Maratea D, Fadda V, Trippoli S, Messori A. Treatments for relapsing-remitting multiple sclerosis: summarising current information by network meta-analysis. *Eur J Clin Pharmacol* 2012;68(4):441-8.

[D255] Zaccara G, Giovannelli F, Maratea D, Fadda V, Verrotti A. Neurological adverse events of new generation sodium blocker antiepileptic drugs. Meta-analysis of randomized, double-blinded studies with eslicarbazepine acetate, lacosamide and oxcarbazepine. *Seizure* 2013;22(7):528-36.

[D256] Dumville JC, Soares MO, O'Meara S, Cullum N. Systematic review and mixed treatment comparison: dressings to heal diabetic foot ulcers. *Diabetologia* 2012;55(7):1902-10.

[D257] Dumville JC, McFarlane E, Edwards P, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev 2013;(3):CD003949.

[D258] Gagne JJ, Bykov K, Choudhry NK, Toomey TJ, Connolly JG, Avorn J. Effect of smoking on comparative efficacy of antiplatelet agents: Systematic review, meta-analysis, and indirect comparison. *BMJ* 2013;347(7927):f5307.

[D259] Schneeweiss S, Gagne JJ, Patrick AR, Choudhry NK, Avorn J. Comparative efficacy and safety of new oral anticoagulants in patients with atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2012;5(4):480-6.

[D260] Sun F, Yu K, Wu S, Zhang Y, Yang Z, Shi L, et al. Cardiovascular safety and glycemic control of glucagon-like peptide-1 receptor agonists for type 2 diabetes mellitus: a pairwise and network meta-analysis. *Diabetes Res Clin Pract* 2012;98(3):386-95.

[D261] Sun F, Yu K, Yang Z, Wu S, Zhang Y, Shi L, et al. Impact of GLP-1 receptor agonists on major gastrointestinal disorders for type 2 diabetes mellitus: a mixed treatment comparison meta-analysis. *Exp Diabetes Res* 2012;2012:230624.

[D262] Levi Marpillat N, Macquin-Mavier I, Tropeano AI, Bachoud-Levi AC, Maison P. Antihypertensive classes, cognitive decline and incidence of dementia: a network meta-analysis. *J Hypertens* 2013;31(6):1073-82.

[D263] Tropeano AI, Saleh N, Hawajri N, Macquin-Mavier I, Maison P. Do all antihypertensive drugs improve carotid intima-media thickness? A network meta-analysis of randomized controlled trials. *Fundam Clin Pharmacol* 2011;25(3):395-404.

[D264] Assiri A, Al-Majzoub O, Kanaan AO, Donovan JL, Silva M. Mixed treatment comparison meta-analysis of aspirin, warfarin, and new anticoagulants for stroke prevention in patients with nonvalvular atrial fibrillation. *Clin Ther* 2013;35(7):967-84.

[D265] Malloy RJ, Kanaan AO, Silva MA, Donovan JL. Evaluation of antiplatelet agents for secondary prevention of stroke using mixed treatment comparison meta-analysis. *Clin Ther* 2013;35(10):1490-500.

[D266] Lee YH, Ji JD, Song GG. Adjusted indirect comparison of celecoxib versus rofecoxib on cardiovascular risk. *Rheumatol Int* 2007;27(5):477-82.

[D267] Lee YH, Woo JH, Rho YH, Choi SJ, Ji JD, Song GG. Meta-analysis of the combination of TNF inhibitors plus MTX compared to MTX monotherapy, and the adjusted indirect comparison of TNF inhibitors in patients suffering from active rheumatoid arthritis. *Rheumatol Int* 2008;28(6):553-9.

[D268] Bolaños R, Francia J. Isoflavones versus hormone therapy for reduction of vertebral fracture risk: indirect comparison. Menopause 2010;17(6):1201-5.

[D269] Bolaños-Diaz R, Zavala-Gonzales JC, Mezones-Holguín E, Francia-Romero J. Soy extracts versus hormone therapy for reduction of menopausal hot flushes: indirect comparison. *Menopause* 2011;18(7):825-9.

[D270] Kabra SK, Lodha R, Pandey RM. Antibiotics for community acquired pneumonia in children. *Cochrane Database Syst Rev* 2006;(3):CD004874.

[D271] Kabra SK, Lodha R, Pandey RM. Antibiotics for community-acquired pneumonia in children. *Cochrane Database Syst Rev* 2010;(3):CD004874.

[D272] Abdullah AK, Khan S. Relative oral corticosteroid-sparing effect of 7 inhaled corticosteroids in chronic asthma: a meta-analysis. *Ann Allergy Asthma Immunol* 2008;101(1):74-81.

[D273] Baldwin D, Woods R, Lawson R, Taylor D. Efficacy of drug treatments for generalised anxiety disorder: systematic review and meta-analysis. *BMJ* 2011;342:d1199.

[D274] Bally M, Dendukuri N, Sinclair A, Ahern SP, Poisson M, Brophy J. A network meta-analysis of antibiotics for treatment of hospitalised patients with suspected or proven meticillin-resistant Staphylococcus aureus infection. *Int J Antimicrob Agents* 2012;40(6):479-95.

[D275] Bangalore S, Kumar S, Kjeldsen SE, Makani H, Grossman E, Wettersley J, et al. Antihypertensive drugs and risk of cancer: network meta-analyses and trial sequential analyses of 324,168 participants from randomised trials. *Lancet Oncol* 2011;12(1):65-82.

[D276] Bansal M, Farrugia A, Balboni S, Martin G. Relative survival benefit and morbidity with fluids in severe sepsis - a network meta-analysis of alternative therapies. *Curr Drug Saf* 2013;8(4):236-45.

[D277] Bash LD, Buono JL, Davies GM, Martin A, Fahrbach K, Phatak H, et al. Systematic review and meta-analysis of the efficacy of cardioversion by vernakalant and comparators in patients with atrial fibrillation. *Cardiovasc Drugs Ther* 2012;26(2):167-79.

[D278] Berner MM, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2006;18(3):229-35.

[D279] Bicket MC, Gupta A, Brown CH 4th, Cohen SP. Epidural injections for spinal pain: a systematic review and meta-analysis evaluating the "control" injections in randomized controlled trials. *Anesthesiology* 2013;119(4):907-31.

[D280] Blanchard P, Hill C, Guihenneuc-Jouyaux C, Baey C, Bourhis J, Pignon JP, et al. Mixed treatment comparison meta-analysis of altered fractionated radiotherapy and chemotherapy in head and neck cancer. *J Clin Epidemiol* 2011;64(9):985-92.

[D281] Boonen S, Lips P, Bouillon R, Bischoff-Ferrari HA, Vanderschueren D, Haentjens P. Need for additional calcium to reduce the risk of hip fracture with vitamin d supplementation: evidence from a comparative metaanalysis of randomized controlled trials. *J Clin Endocrinol Metab* 2007;92(4):1415-23.

[D282] Brigo F, Igwe SC, Nardone R, Tezzon F, Bongiovanni LG, Trinka E. A common reference-based indirect comparison meta-analysis of intravenous valproate versus intravenous phenobarbitone for convulsive status epilepticus. *Epileptic Disord* 2013;15(3):314-23.

[D283] Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev* 2013;(5):CD009329.

[D284] Carter B, Fedorowicz Z. Antiemetic treatment for acute gastroenteritis in children: an updated Cochrane systematic review with meta-analysis and mixed treatment comparison in a Bayesian framework. *BMJ Open* 2012;2(4):e000622.

[D285] Cates CJ, Oleszczuk M, Stovold E, Wieland LS. Safety of regular formoterol or salmeterol in children with asthma: an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2012;10:CD010005.

[D286] Cawston H, Davie A, Paget MA, Sklijarevski V, Happich M. Efficacy of duloxetine versus alternative oral therapies: an indirect comparison of randomised clinical trials in chronic low back pain. *Eur Spine J* 2013;22(9):1996-2009.

[D287] Chapell R, Gould AL, Alexander CM. Baseline differences in A1C explain apparent differences in efficacy of sitagliptin, rosiglitazone and pioglitazone. Diabetes Obes Metab 2009;11(11):1009-16.

[D288] Coleman KA, Xavier VY, Palmer TL, Meaney JV, Randalj LM, Canny LM. An indirect comparison of the efficacy and safety of desvenlafaxine and venlafaxine using placebo as the common comparator. *CNS Spectr* 2012;17(3):131-41.

[D289] Conde-Agudelo A, Romero R, Nicolaides K, Chaiworapongsa T, O'Brien JM, Cetingoz E, et al. Vaginal progesterone vs. cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. *Am J Obstet Gynecol* 2013;208(1):42.e1-42.e18.

[D290] Cooper KL, Fitzgerald P, Dillingham K, Helme K, Akehurst R. Romiplostim and eltrombopag for immune thrombocytopenia: methods for indirect comparison. *Int J Technol Assess Health Care* 2012;28(3):249-58.

[D291] Cota GF, de Sousa MR, Fereguetti TO, Rabello A. Efficacy of anti-leishmania therapy in visceral leishmaniasis among HIV infected patients: a systematic review with indirect comparison. *PLoS Negl Trop Dis* 2013;7(5):e2195.

[D292] Cure S, Diels J, Gavart S, Bianic F, Jones E. Efficacy of telaprevir and boceprevir in treatment-naive and treatment-experienced genotype 1 chronic hepatitis C patients: an indirect comparison using Bayesian network meta-analysis. *Curr Med Res Opin* 2012;28(11):1841-56.

[D293] Danchin N, Marzilli M, Parkhomenko A, Ribeiro JP. Efficacy comparison of trimetazidine with therapeutic alternatives in stable angina pectoris: a network meta-analysis. *Cardiology* 2011;120(2):59-72.

[D294] Datto C, Hellmund R, Siddiqui MK. Efficacy and tolerability of naproxen/esomeprazole magnesium tablets compared with non-specific NSAIDs and COX-2 inhibitors: a systematic review and network analyses. *Open Access Rheumatol* 2013;5:1-19.

[D295] de Menezes GB, Coutinho ES, Fontenelle LF, Vigne P, Figueira I, Versiani M. Second-generation antidepressants in social anxiety disorder: meta-analysis of controlled clinical trials. *Psychopharmacology* 2011;215(1):1-11.

[D296] Delahoy P, Thompson S, Marschner IC. Pregabalin versus gabapentin in partial epilepsy: a meta-analysis of dose-response relationships. *BMC Neurol* 2010;10:104.

[D297] Dong YH, Lin HH, Shau WY, Wu YC, Chang CH, Lai MS. Comparative safety of inhaled medications in patients with chronic obstructive pulmonary disease: systematic review and mixed treatment comparison meta-analysis of randomised controlled trials. *Thorax* 2013;68(1):48-56.

[D298] Elliott WJ, Meyer PM. Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis. Lancet 2007;369(9557):201-7.

[D299] Engelman E, Salengros JC, Barvais L. How much does pharmacologic prophylaxis reduce postoperative vomiting in children? Calculation of prophylaxis effectiveness and expected incidence of vomiting under treatment using Bayesian meta-analysis. *Anesthesiol* 2008;109(6):1023-35.

[D300] Fang Y, Ding Y, Guo Q, Xing J, Long Y, Zong Z. Radioiodine therapy for patients with differentiated thyroid cancer after thyroidectomy: direct comparison and network meta-analyses. *J Endocrinol Invest* 2013;36(10):896-902.

[D301] Fountoulakis KN, Veroniki AA, Siamouli M, Möller HJ. No role for initial severity on the efficacy of antidepressants: results of a multi-meta-analysis. *Ann Gen Psychiatry* 2013;12(1):26.

[D302] Fretheim A, Odgaard-Jensen J, Brørs O, Madsen S, Njølstad I, Norheim OF, et al. Comparative effectiveness of antihypertensive medication for primary prevention of

cardiovascular disease: systematic review and multiple treatments meta-analysis. *BMC Med* 2012;10:33.

[D303] Galvan-Banqueri M, Marin Gil R, Santos Ramos B, Bautista Paloma FJ. Biological treatments for moderate-to-severe psoriasis: indirect comparison. *J Clin Pharm Ther* 2013;38(2):121-30.

[D304] Gao L, Xia L, Zhao FL, Li SC. Clinical efficacy and safety of the newer antiepileptic drugs as adjunctive treatment in adults with refractory partial-onset epilepsy: a meta-analysis of randomized placebo-controlled trials. *Epilepsy Res* 2013;103(1):31-44.

[D305] Ginés J, Sabater E, Martorell C, Grau M, Monroy M, Casado MA. Efficacy of taxanes as adjuvant treatment of breast cancer: a review and meta-analysis of randomised clinical trials. Clin Transl Oncol 2011;13(7):485-98.

[D306] Gómez-Outes A, Terleira-Fernández AI, Suárez-Gea ML, Vargas-Castrillón E. Dabigatran, rivaroxaban, or apixaban versus enoxaparin for thromboprophylaxis after total hip or knee replacement: systematic review, meta-analysis, and indirect treatment comparisons. *BMJ* 2012;344(7863):e3675.

[D307] Goralczyk AD, Cameron S, Amanzada A. Treatment of chronic HCV genotype 1 infection with telaprevir: a Bayesian mixed treatment comparison of fixed-length and response-guided treatment regimens in treatment-naive and -experienced patients. *BMC Gastroenterol* 2013;13(1):148.

[D308] Gupta AK, Paquet M. Network meta-analysis of the outcome 'participant complete clearance' in nonimmunosuppressed participants of eight interventions for actinic keratosis: a follow-up on a Cochrane review. *Br J Dermatol* 2013;169(2):250-9.

[D309] Hoaglin DC, Filonenko A, Glickman ME, Wasiak R, Gidwani R. Use of mixed-treatment-comparison methods in estimating efficacy of treatments for heavy menstrual bleeding. *Eur J Med Res* 2013;18(1):17.

[D310] Hofmeyr GJ, Gülmezoglu AM, Novikova N, Linder V, Ferreira S, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. *Bull World Health Organ* 2009;87(9):666-77.

[D311] Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, et al. Prevention of pain on injection of propofol: systematic review and meta-analysis. *BMJ* 2011;342:d1110.

[D312] Kalil AC, Mindru C, Florescu DF. Effectiveness of valganciclovir 900 mg versus 450 mg for cytomegalovirus prophylaxis in transplantation: direct and indirect treatment comparison meta-analysis. *Clin Infect Dis* 2011;52(3):313-21.

[D313] Karabis A, Lindner L, Mocarski M, Huisman E, Greening A. Comparative efficacy of aclidinium versus glycopyrronium and tiotropium, as maintenance treatment of moderate to severe COPD patients: a systematic review and network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2013;8:405-23.

[D314] Klemp M, Tvete IF, Skomedal T, Gaasemyr J, Natvig B, Aursnes I. A review and Bayesian meta-analysis of clinical efficacy and adverse effects of 4 atypical neuroleptic drugs compared with haloperidol and placebo. *J Clin Psychopharmacol* 2011;31(6):698-704.

[D315] Kotzé A, Scally A, Howell S. Efficacy and safety of different techniques of paravertebral block for analgesia after thoracotomy: a systematic review and metaregression. Br J Anaesth 2009;103(5):626-36.

[D316] Launois R, Avouac B, Berenbaum F, Blin O, Bru I, Fautrel B, et al. Comparison of certolizumab pegol with other anticytokine agents for treatment of rheumatoid arthritis: a multiple-treatment Bayesian metaanalysis. *J Rheumatol* 2011;38(5):835-45.

[D317] Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *BMJ* 2003;326(7404):1427-31.

[D318] Leung HW, Chan AL. Multikinase inhibitors in metastatic renal cell carcinoma: indirect comparison meta-analysis. *Clin Ther* 2011;33(6):708-16.

[D319] Levy AR, Johnston KM, Sambrook J, Donato B, Penrod JR, Corral M, et al. Indirect comparison of the efficacy of cetuximab and cisplatin in squamous cell carcinoma of the head and neck. *Curr Med Res Opin* 2011;27(12):2253-9.

[D320] Liu JL, Dong J, Wang L, Su Y, Yan P, Sun S. Comparative efficacy and acceptability of antidepressants in Parkinson's disease: a network meta-analysis. *Plos One* 2013;8(10):e76651.

[D321] Mantha S, Ansell J. An indirect comparison of dabigatran, rivaroxaban and apixaban for atrial fibrillation. *Thromb Haemost* 2012;108(3):476-84.

[D322] Martyn-St James M, Glanville J, McCool R, Duffy S, Cooper J, Hugel P, et al. The efficacy and safety of retigabine and other adjunctive treatments for refractory partial epilepsy: a systematic review and indirect comparison. *Seizure* 2012;21(9):665-78.

[D323] Maund E, McDaid C, Rice S, Wright K, Jenkins B, Woolacott N. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review. *Br J Anaesth* 2011;106(3):292-7.

[D324] Meader N. A comparison of methadone, buprenorphine and alpha2 adrenergic agonists for opioid detoxification: a mixed treatment comparison meta-analysis. Drug Alcohol Depend 2010;108(1-2):110-4.

[D325] Menzies D, Benedetti A, Paydar A, Martin I, Royce S, Pai M, et al. Effect of duration and intermittency of rifampin on tuberculosis treatment outcomes: a systematic review and meta-analysis. *PLoS Med* 2009;6(9):e1000146.

[D326] Mösges R, Nematian-Samani M, Hellmich M, Shah-Hosseini K. A meta-analysis of the efficacy of quinolone containing otics in comparison to antibiotic-steroid combination drugs in the local treatment of otitis externa. *Curr Med Res Opin* 2011;27(10):2053-60.

[D327] Ollendorf DA, Colby JA, Pearson SD. Comparative effectiveness of anti-vegf agents for diabetic macular edema. *Int J Technol Assess Health Care* 2013;29(4):392-401.

[D328] Otoul C, Arrigo C, van Rijckevorsel K, French JA. Meta-analysis and indirect comparisons of levetiracetam with other second-generation antiepileptic drugs in partial epilepsy. *Clin Neuropharmacol* 2005;28(2):72-8.

[D329] Otten MH, Anink J, Spronk S, van Suijlekom-Smit LW. Efficacy of biological agents in juvenile idiopathic arthritis: a systematic review using indirect comparisons. Ann Rheum Dis 2013;72(11):1806-12.

[D330] Owen A. Antithrombotic treatment for the primary prevention of stroke in patients with non valvular atrial fibrillation: a reappraisal of the evidence and network meta analysis. *Int J Cardiol* 2010;142(3):218-23.

[D331] Packer M, Antonopoulos GV, Berlin JA, Chittams J, Konstam MA, Udelson JE. Comparative effects of carvedilol and metoprolol on left ventricular election fraction in heart failure: results of a meta-analysis. *Am Heart J* 2001;141(6):899-907.

[D332] Piccini JP, Hasselblad V, Peterson ED, Washam JB, Califf RM, Kong DF. Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation. *J Am Coll Cardiol* 2009;54(12):1089-95.

[D333] Pink J, Pirmohamed M, Hughes DA. Comparative effectiveness of dabigatran, rivaroxaban, apixaban, and warfarin in the management of patients with nonvalvular atrial fibrillation. Clin Pharmacol Ther 2013;94(2):269-76.

[D334] Qi WX, Tang LN, He AN, Shen Z, Lin F, Yao Y. Erlotinib and pemetrexed as maintenance therapy for advanced non-small-cell lung cancer: a systematic review and indirect comparison. *Curr Med Res Opin* 2012;28(4):643-50.

[D335] Robenshtok E, Gafter-Gvili A, Goldberg E, Weinberger M, Yeshurun M, Leibovici L, et al. Antifungal prophylaxis in cancer patients after chemotherapy or hematopoietic stem-cell transplantation: systematic review and meta-analysis. *J Clin Oncol* 2007;25(34):5471-89.

[D336] Ronellenfitsch U, Schwarzbach M, Hofheinz R, Kienle P, Kieser M, Slanger TE, et al. Preoperative chemo(radio)therapy versus primary surgery for gastroesophageal adenocarcinoma: systematic review with meta-analysis combining individual patient and aggregate data. *Eur J Cancer* 2013;49(15):3149-58.

[D337] Roush GC, Holford TR, Guddati AK. Chlorthalidone compared with hydrochlorothiazide in reducing cardiovascular events: systematic review and network meta-analyses. *Hypertension* 2012;59(6):1110-7.

[D338] Rudroju N, Bansal D, Talakokkula ST, Gudala K, Hota D, Bhansali A, et al. Comparative efficacy and safety of six antidepressants and anticonvulsants in painful diabetic neuropathy: a network meta-analysis. *Pain Physician* 2013;16(6):E705-14.

[D339] Sauriol L, Laporta M, Edwardes MD, Deslandes M, Ricard N, Suissa S. Meta-analysis comparing newer antipsychotic drugs for the treatment of schizophrenia: evaluating the indirect approach. *Clin Ther* 2001;23(6):942-56.

[D340] Schoels M, Aletaha D, Smolen JS, Wong JB. Comparative effectiveness and safety of biological treatment options after tumour necrosis factor alpha inhibitor failure in rheumatoid arthritis: systematic review and indirect pairwise meta-analysis. *Ann Rheum Dis* 2012;71(8):1303-8.

[D341] Sciarretta S, Palano F, Tocci G, Baldini R, Volpe M. Antihypertensive treatment and development of heart failure in hypertension: a Bayesian network meta-analysis of studies in patients with hypertension and high cardiovascular risk. *Arch Intern Med* 2011;171(5):384-94.

[D342] Shamliyan TA, Choi JY, Ramakrishnan R, Miller JB, Wang SY, Taylor FR, et al. Preventive pharmacologic treatments for episodic migraine in adults. *J Gen Intern Med* 2013;28(9):1225-37.

[D343] Shi KQ, Liu WY, Pan ZZ, Ling XF, Chen SL, Chen YP, et al. Secondary prophylaxis of variceal bleeding for cirrhotic patients: a multiple-treatments meta-analysis. *Eur J Clin Invest* 2013;43(8):844-54.

[D344] Shu T, Chen GH, Rong L, Feng F, Yang B, Chen R, et al. Indirect comparison of anti-TNF-alpha agents for active ankylosing spondylitis: mixed treatment comparison of randomised controlled trials. Clin Exp Rheumatol 2013;31(5):717-22.

[D345] Stegeman BH, de Bastos M, Rosendaal FR, van Hylckama Vlieg A, Helmerhorst FM, Stijnen T, et al. Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis. *BMJ* 2013;347(7925):f5298.

[D346] Stevens JW, Simpson E, Harnan S, Squires H, Meng Y, Thomas S, et al. Systematic review of the efficacy of cilostazol, naftidrofuryl oxalate and pentoxifylline for the treatment of intermittent claudication. *Br J Surg* 2012;99(12):1630-8.

[D347] Szegedi A, Verweij P, van Duijnhoven W, Mackle M, Cazorla P, Fennema H. Meta-analyses of the efficacy of asenapine for acute schizophrenia: comparisons with placebo and other antipsychotics. J Clin Psychiatry 2012;73(12):1533-40.

[D348] Tang DH, Malone DC. A network meta-analysis on the efficacy of serotonin type 3 receptor antagonists used in adults during the first 24 hours for postoperative nausea and vomiting prophylaxis. *Clin Ther* 2012;34(2):282-94.

[D349] Thijs V, Lemmens R, Fieuws S. Network meta-analysis: simultaneous meta-analysis of common antiplatelet regimens after transient ischaemic attack or stroke. *Eur Heart J* 2008;29(9):1086-92.

[D350] Tonelli M, Lloyd A, Clement F, Conly J, Husereau D, Hemmelgarn B, et al. Efficacy of statins for primary prevention in people at low cardiovascular risk: a meta-analysis. *CMAJ* 2011;183(16):E1189-202.

[D351] Trkulja V, Kolundzic R. Rivaroxaban vs dabigatran for thromboprophylaxis after joint-replacement surgery: exploratory indirect comparison based on metaanalysis of pivotal clinical trials. *Croat Med J* 2010;51(2):113-23.

[D352] Turkstra E, Ng SK, Scuffham PA. A mixed treatment comparison of the short-term efficacy of biologic disease modifying anti-rheumatic drugs in established rheumatoid arthritis. *Curr Med Res Opin* 2011;27(10):1885-97.

[D353] Tzellos TG, Toulis KA, Goulis DG, Papazisis G, Zampeli VA, Vakfari A, et al. Gabapentin and pregabalin in the treatment of fibromyalgia: a systematic review and a meta-analysis. *J Clin Pharm Ther* 2010;35(6):639-56.

[D354] Uthman OA, Abdulmalik J. Comparative efficacy and acceptability of pharmacotherapeutic agents for anxiety disorders in children and adolescents: a mixed treatment comparison meta-analysis. Curr Med Res Opin 2010;26(1):53-9.

[D355] Verduyn SC, Biesma B, Schramel FM, van der Scheer FW, Langenfeld MK, de Peuter MA, et al. Estimating quality adjusted progression free survival of first-line treatments for EGFR mutation positive non small cell lung cancer patients in The Netherlands. *Health Qual Life Outcomes* 2012;10:108.

[D356] Whegang Youdom S, Samson A, Basco LK, Thalabard JC. Multiple treatment comparisons in a series of anti-malarial trials with an ordinal primary outcome and repeated treatment evaluations. *Malar J* 2012;11:147.

[D357] Woo G, Tomlinson G, Nishikawa Y, Kowgier M, Sherman M, Wong DK, et al. Tenofovir and entecavir are the most effective antiviral agents for chronic hepatitis B: a systematic review and Bayesian meta-analyses. *Gastroenterology* 2010;139(4):1218-29.

[D358] Yang Q, Wei Y, Chen YX, Zhou SW, Jiang ZM, Xie DR. Indirect comparison showed survival benefit from adjuvant chemoradiotherapy in completely resected gastric cancer with d2 lymphadenectomy. *Gastroenterol Res Pract* 2013;2013:634929.

[D359] Zagmutt FJ, Tarrants ML. Indirect comparisons of adverse events and dropout rates in early Parkinson's disease trials of pramipexole, ropinirole, and rasagiline. Int J Neurosci 2012;122(7):345-53.

[D360] Zeng L, Luo R, Zhang L. Efficacy of high-dose ACTH versus low-dose ACTH in infantile spasms: a meta-analysis with direct and indirect comparison of randomized trials. *J Pediatr Neurol* 2011;9(2):141-9.

[D361] Zou YD, Sheng Z, Niu S, Wang H, Yu J, Xu J. Lenalidomide versus thalidomide based regimens as first-line therapy for patients with multiple myeloma. *Leuk Lymphoma* 2013;54(10):2219-25.

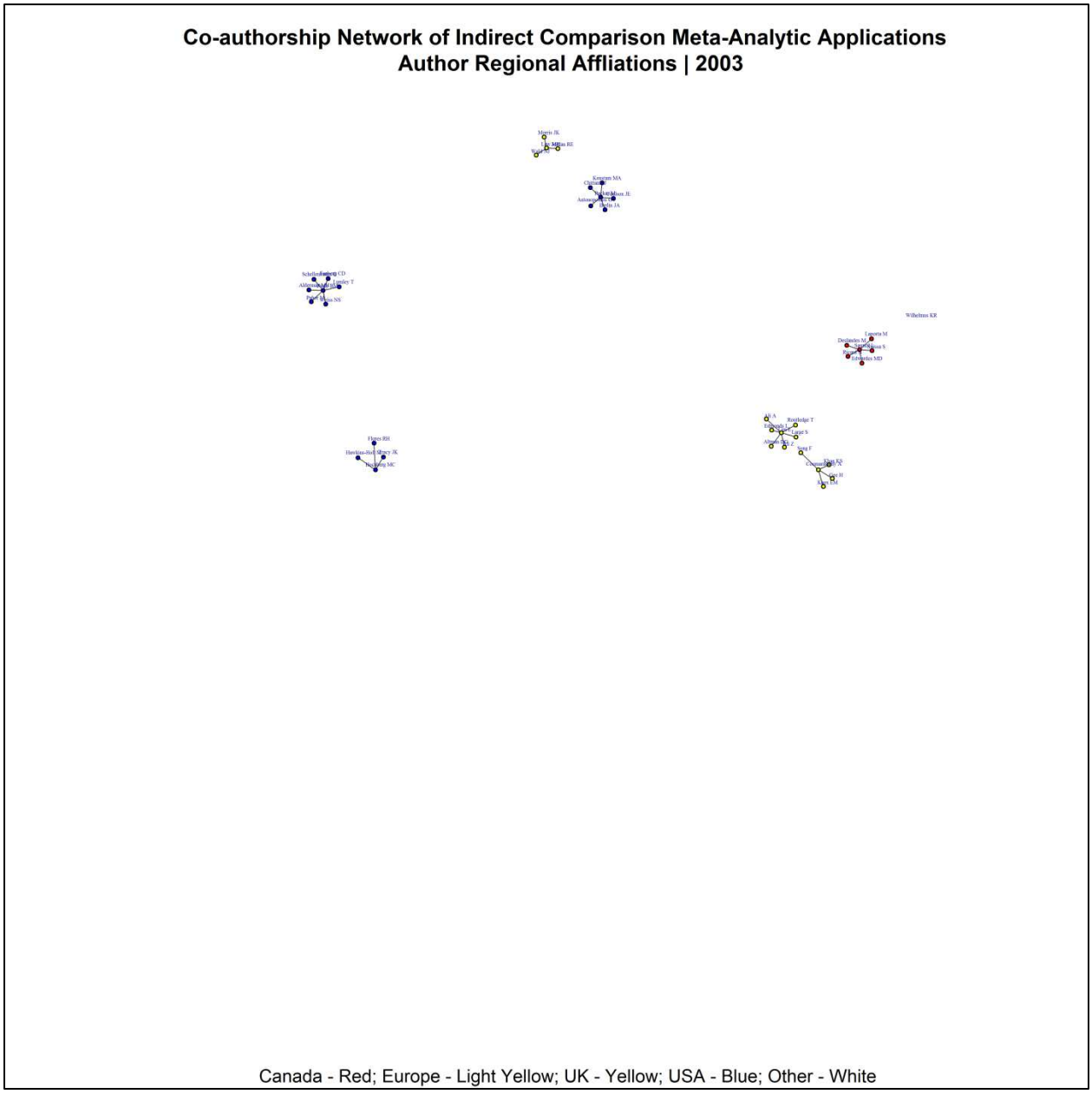
# Appendix E: Co-authorship of indirect comparison meta-analytic methods by country over time

Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000 to 2013. Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), while authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow).

## 2001

## 2002

## 2003



## 2004

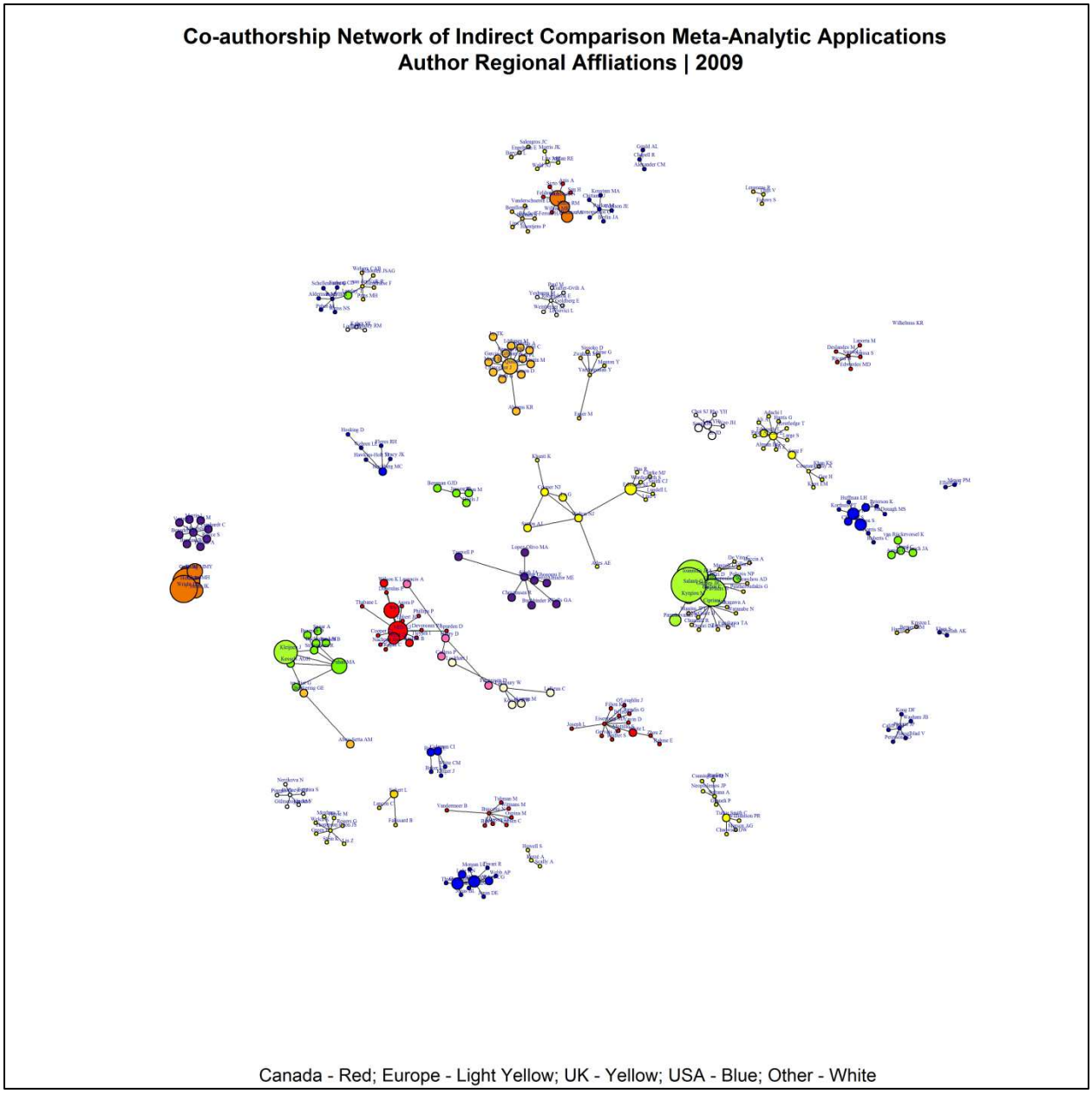
## 2005

## 2006

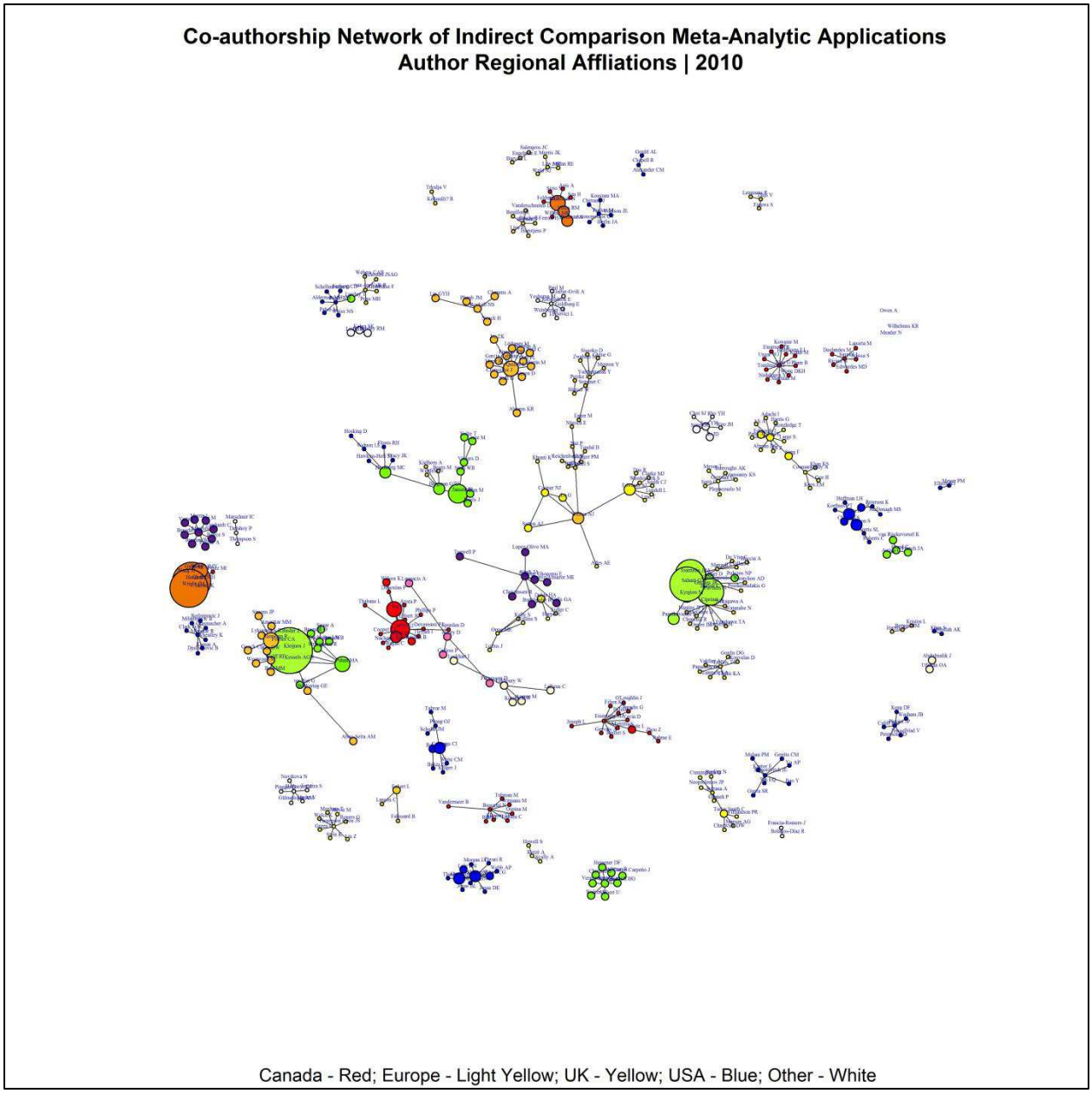
## 2007

## 2008

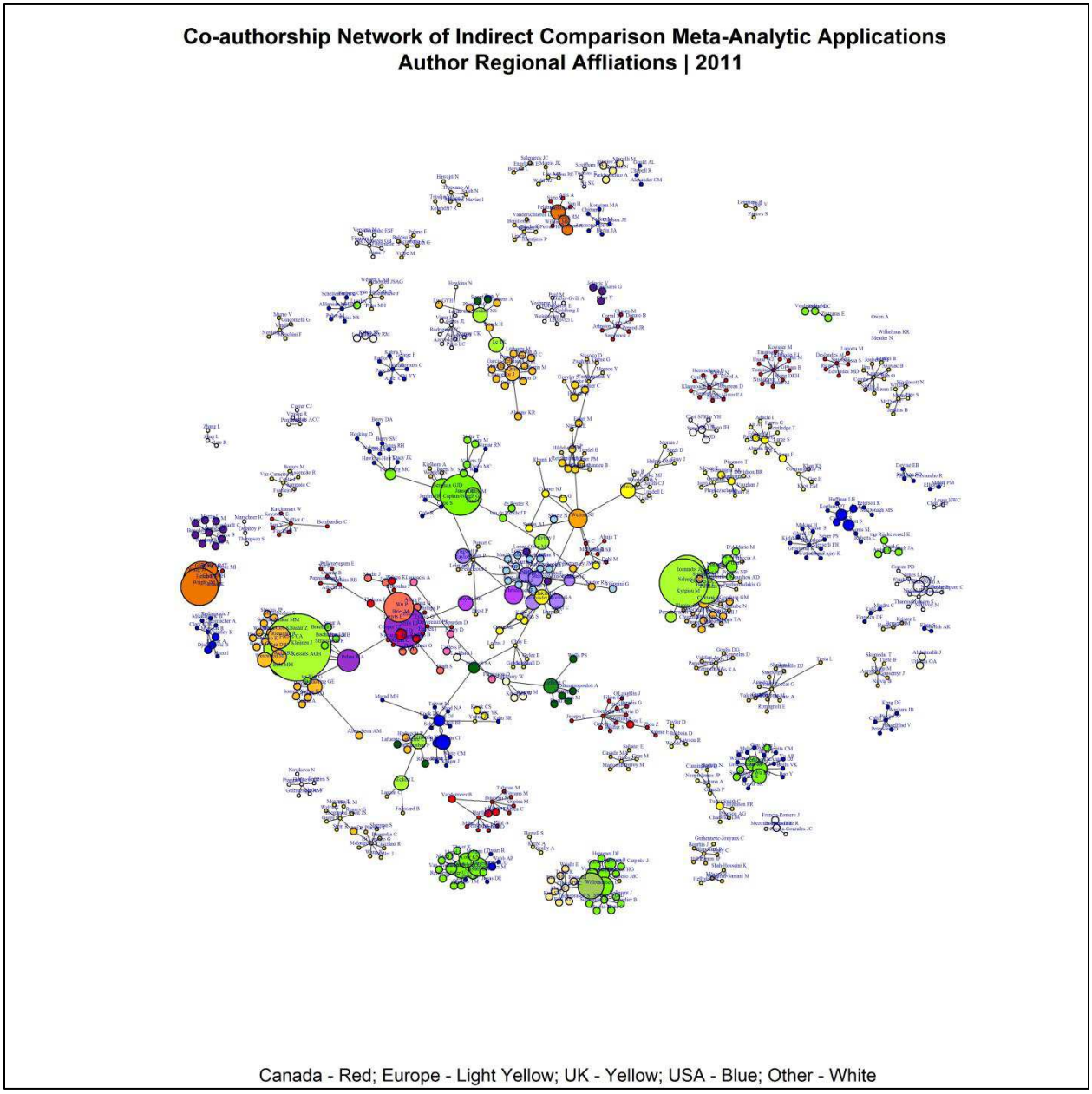
## 2009



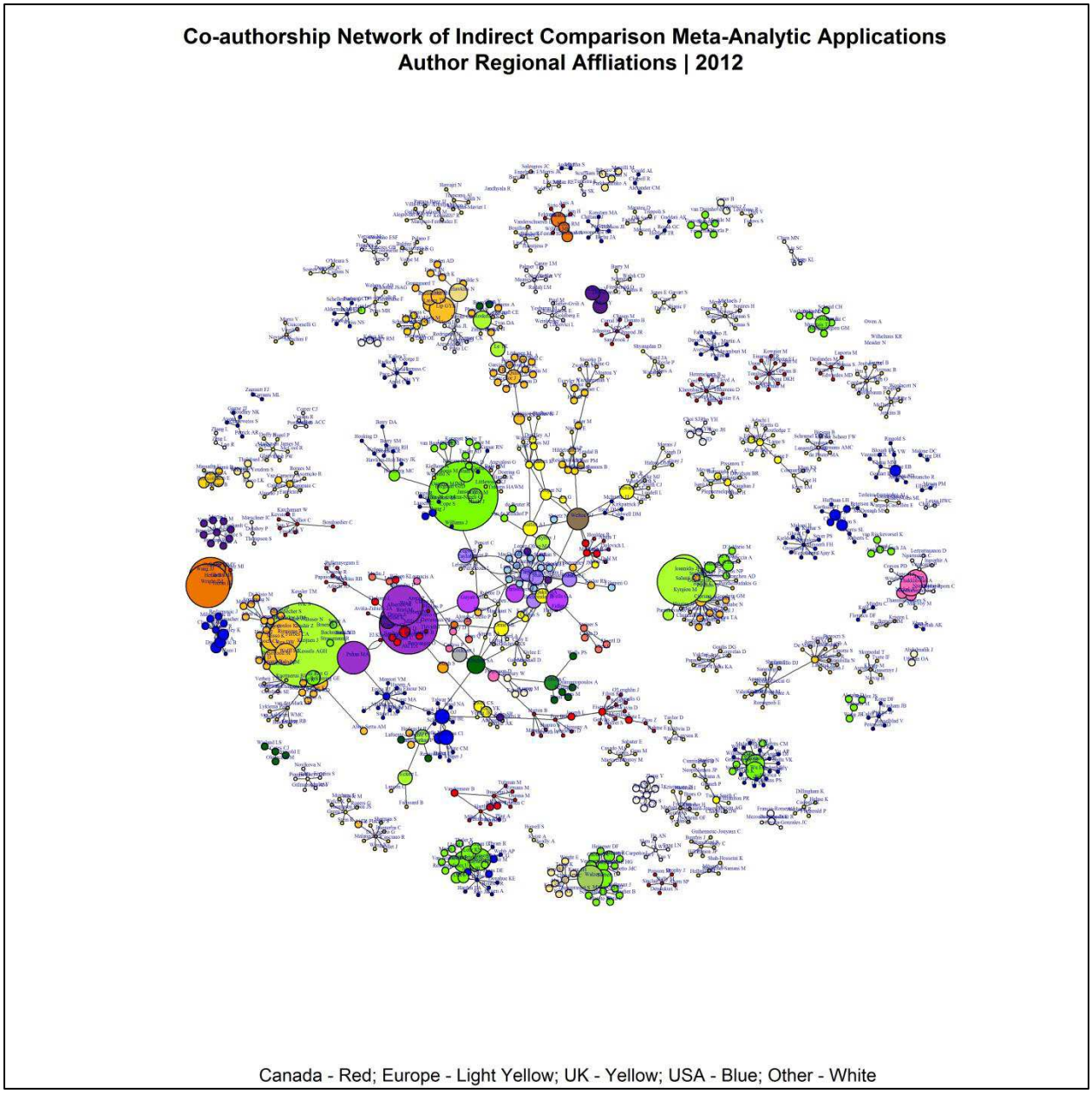
## 2010



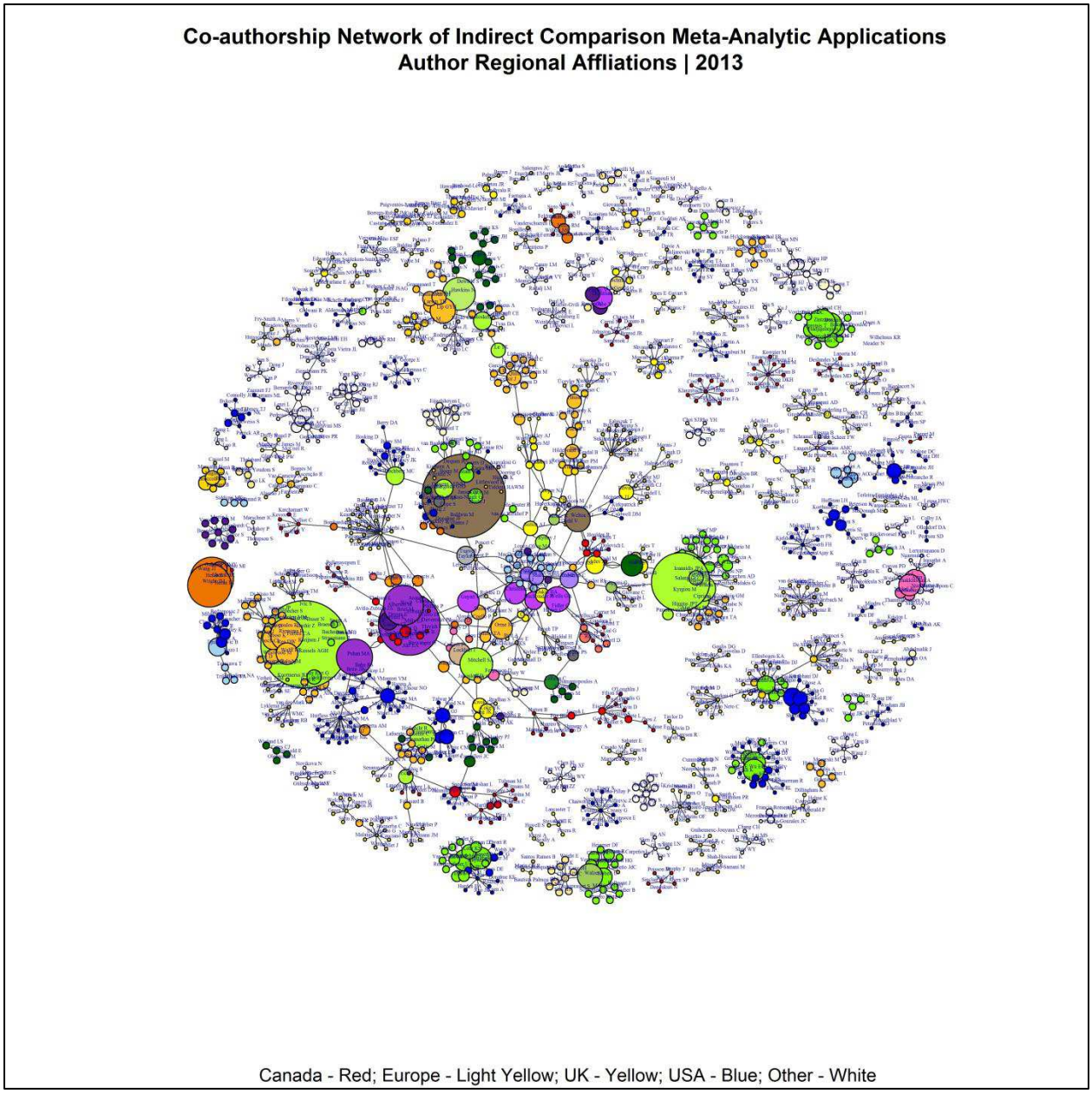
## 2011



## 2012



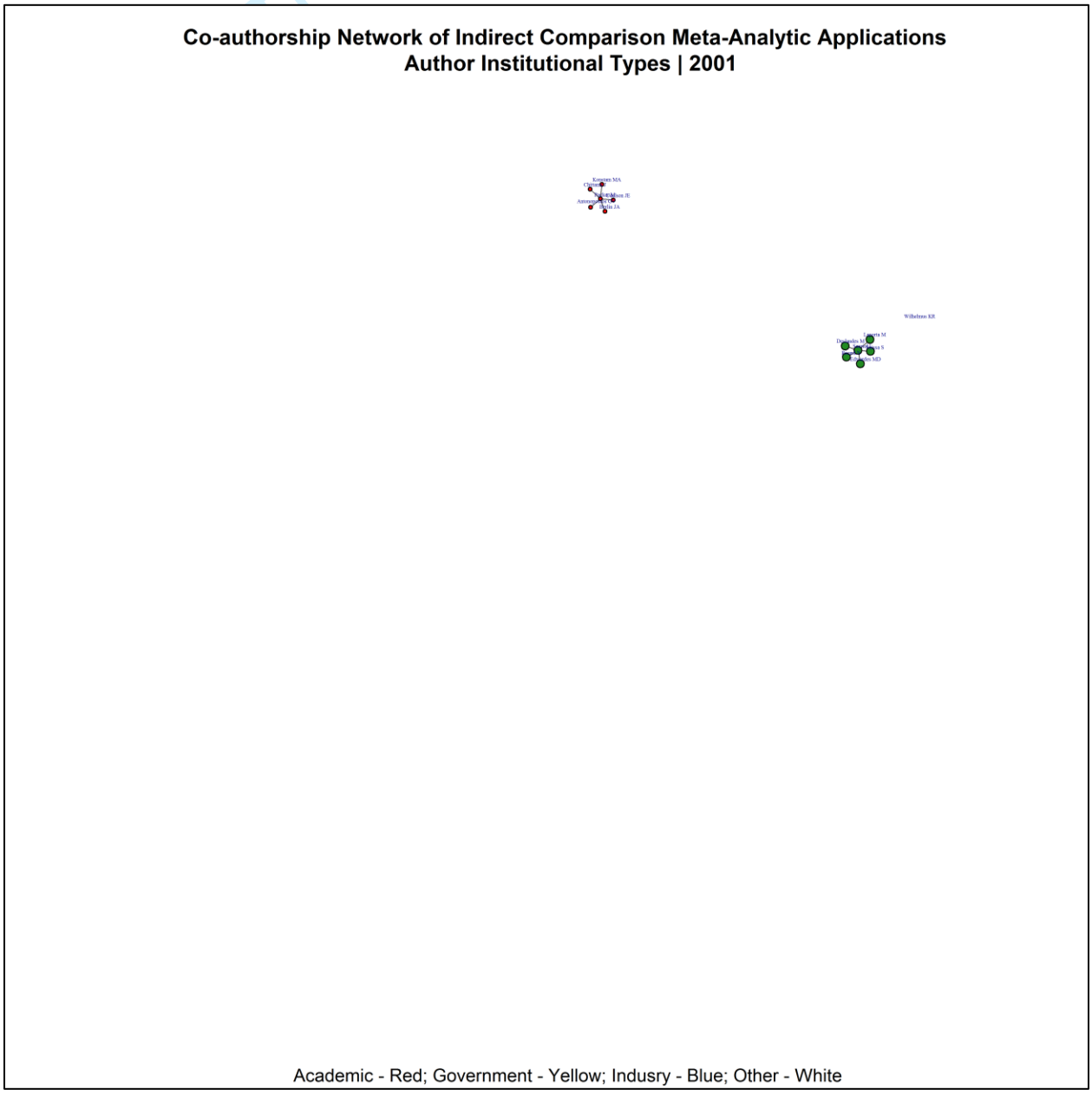
## 2013



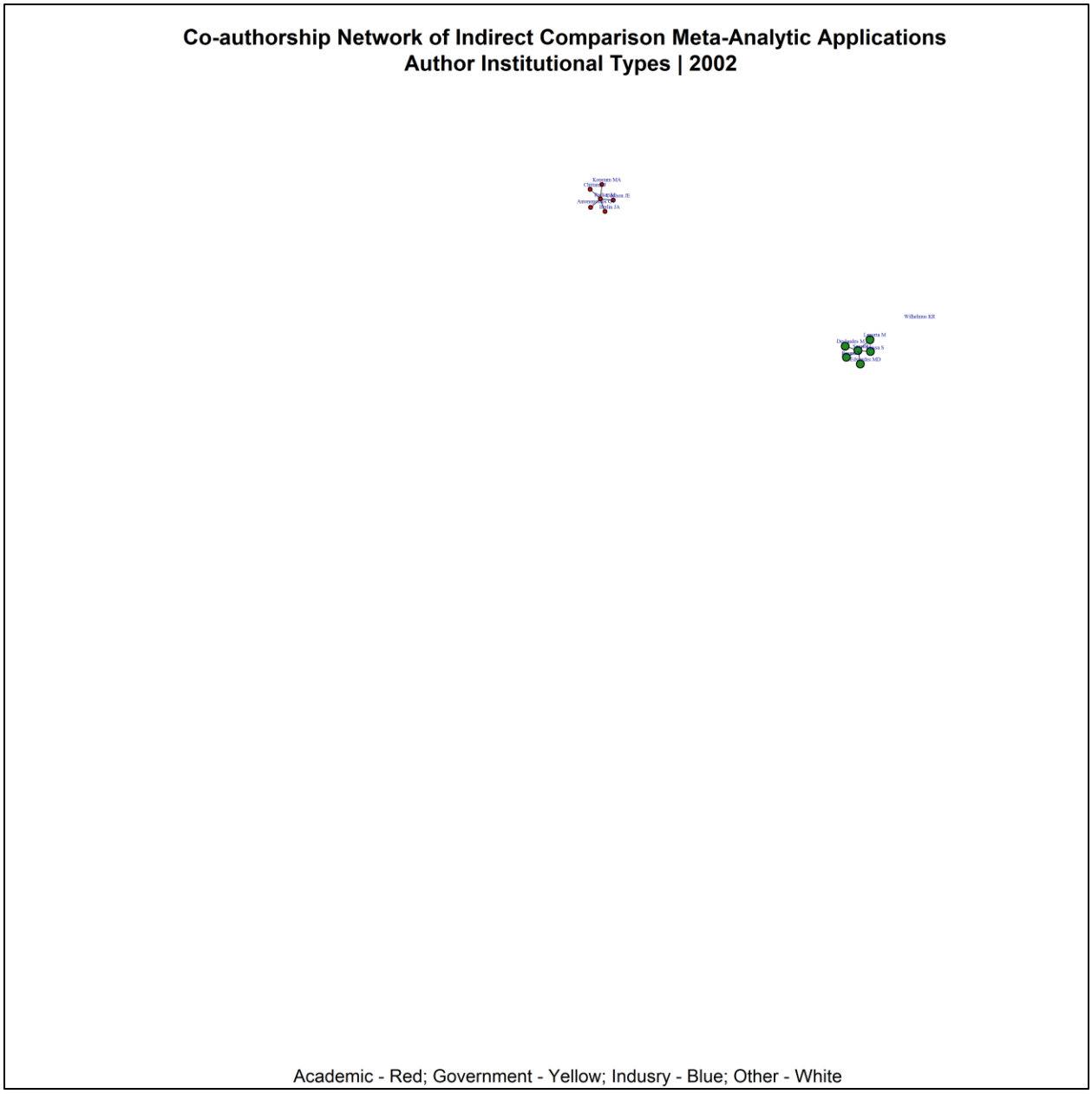
# Appendix F: Co-authorship of indirect comparison meta-analytic methods by affiliation type over time

Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliation types from academia and government were coloured orange (a combination of red and yellow), while authors on papers affiliated with academic, industry, and other were coloured light purple (a combination of red, blue, and white).

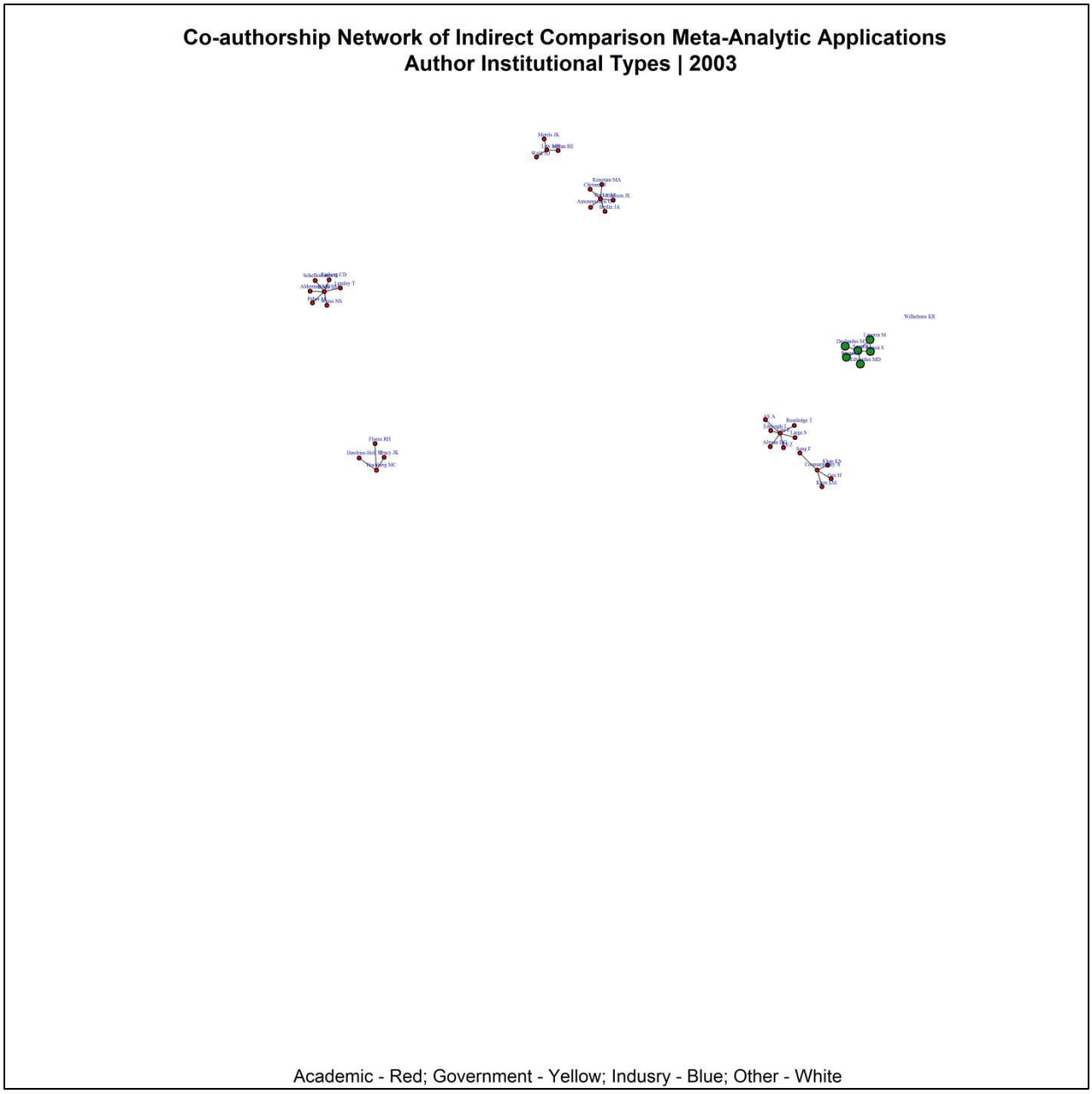
## 2001



## 2002

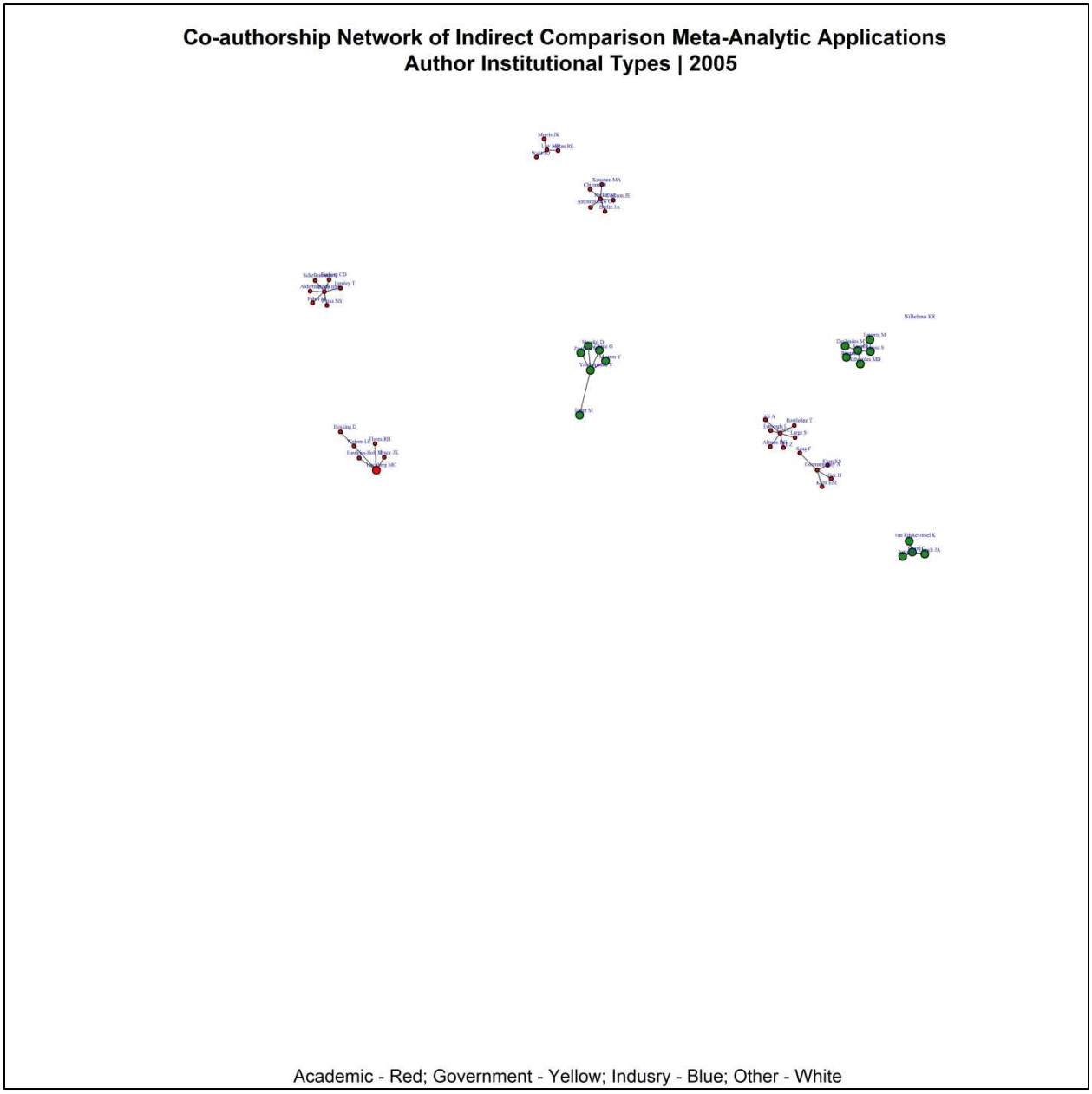


## 2003



## 2004

## 2005

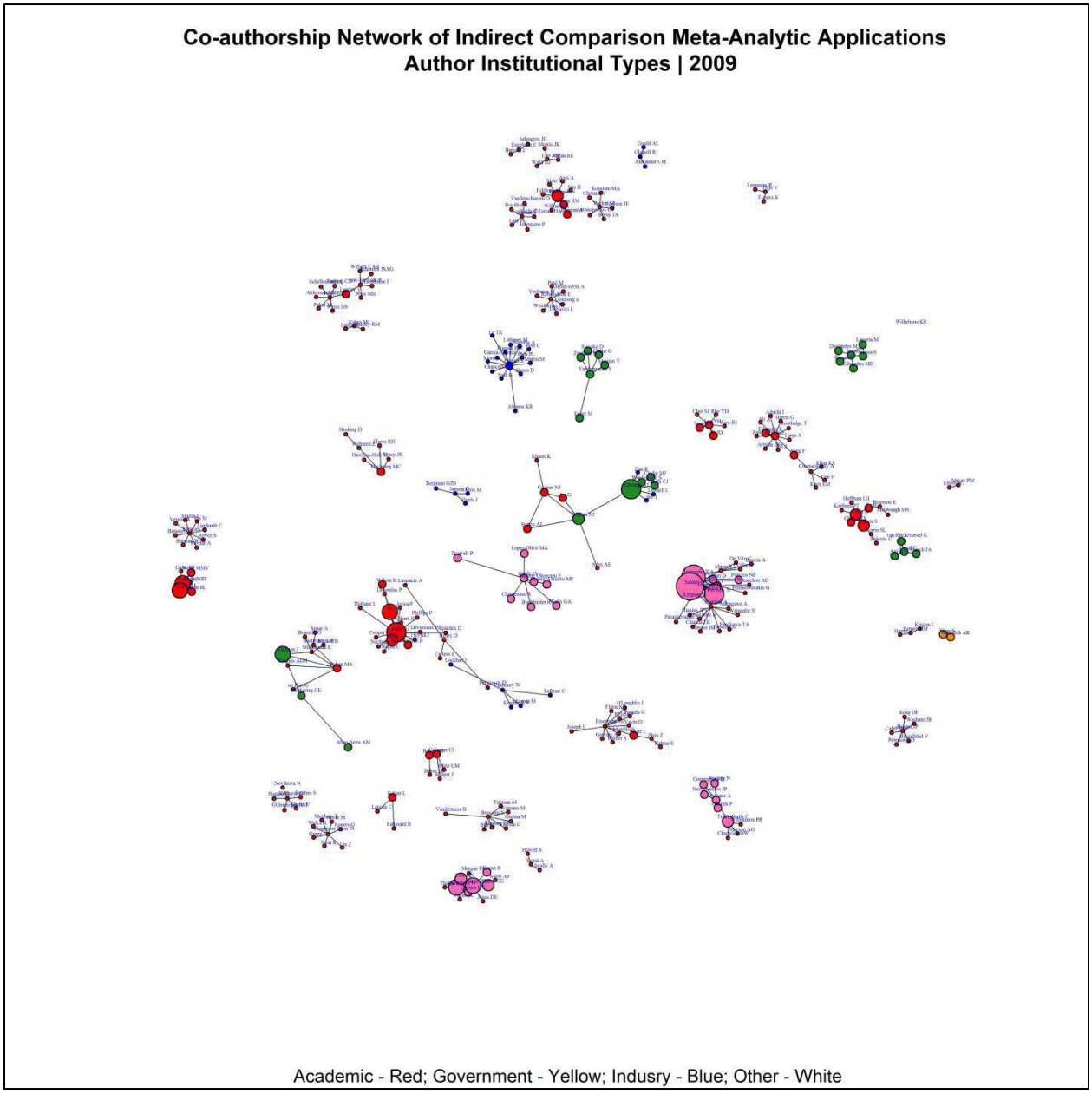


## 2006

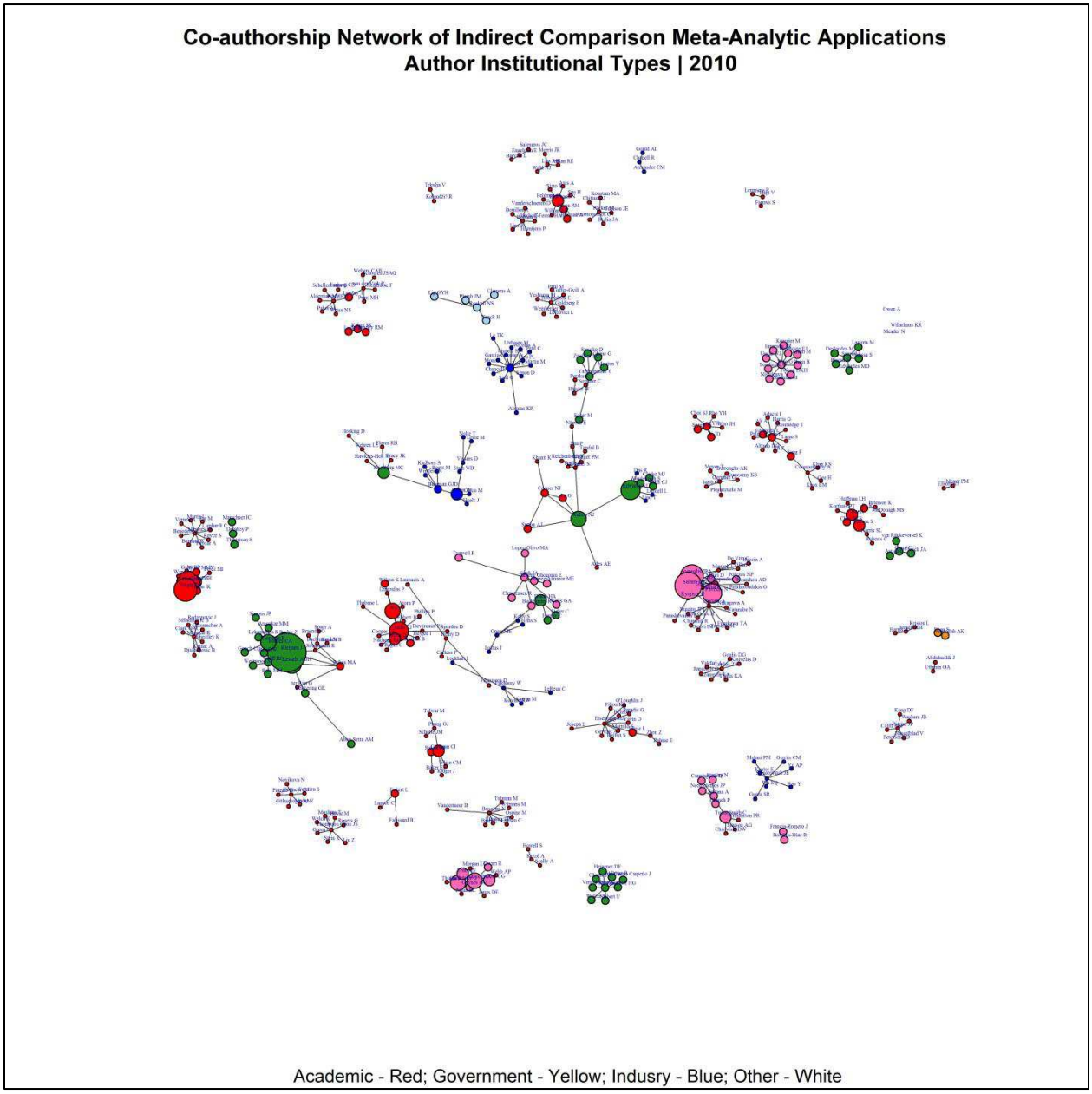
## 2007

## 2008

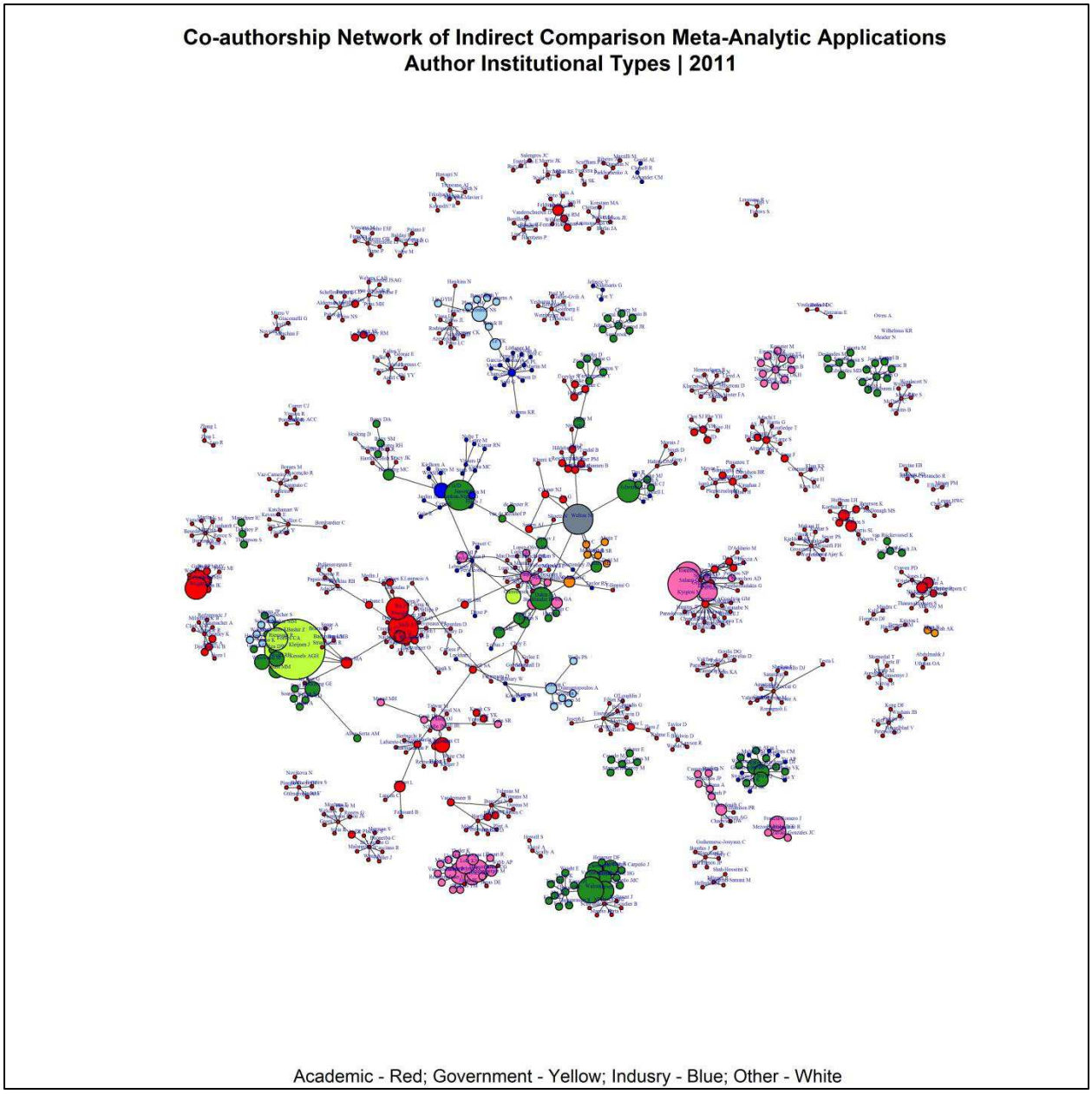
## 2009



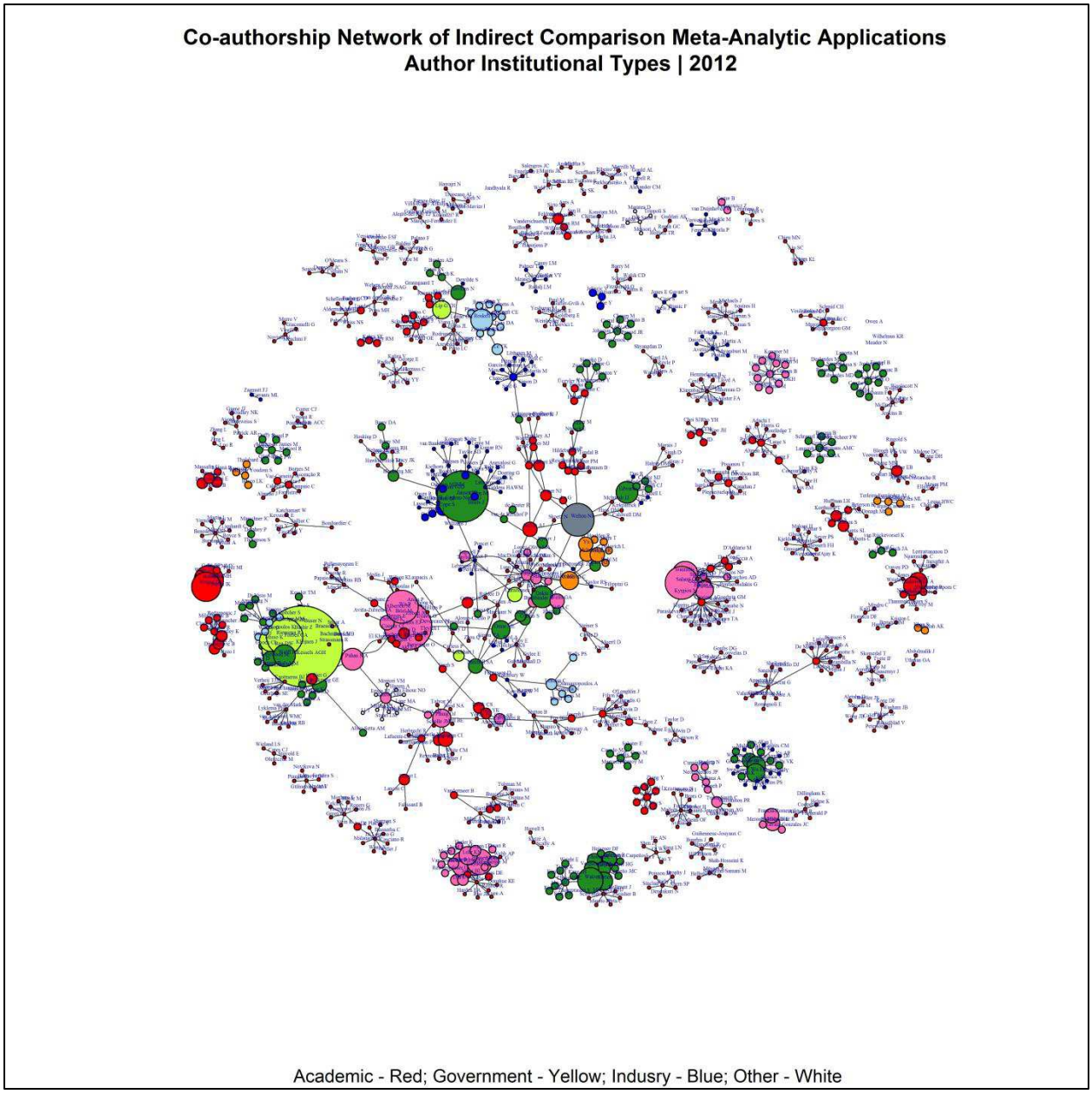
## 2010



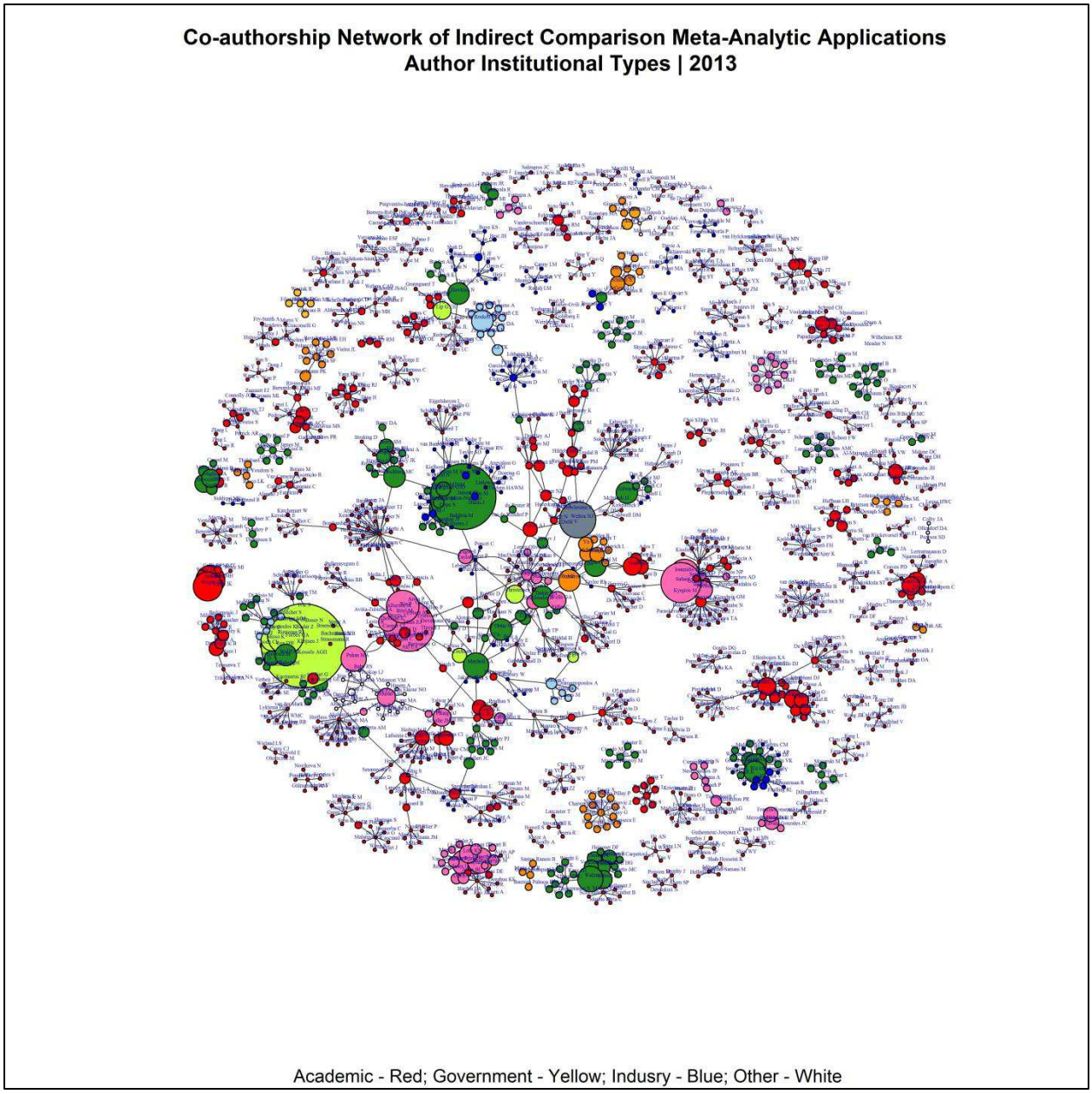
## 2011



## 2012



## 2013



# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-6 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | N/A |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7-8 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 7-8 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 7-8 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 8 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 8 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 8 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | N/A |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | N/A |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | N/A |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | N/A |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 10, 28 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 10-11, 25-27 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | N/A |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | N/A |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | N/A |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | N/A |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 13-16 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 16-18 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 18-19 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 20 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

BMJ Open

# History and Publication Trends in the Diffusion and Early Uptake of Indirect Comparison Meta-Analytic Methods to Study Drugs: Animated Co-Authorship Networks over Time

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-019110.R2 |
| Article Type: | Research |
| Date Submitted by the Author: | 10-May-2018 |
| Complete List of Authors: | Ban, Joann; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Tadrous, Mina; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Lu, Amy; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Cicinelli, Erin; University of Toronto, Leslie Dan Faculty of Pharmacy<br>Cadarette, Suzanne; University of Toronto, Leslie Dan Faculty of Pharmacy |
| Primary Subject Heading: | Research methods |
| Secondary Subject Heading: | Communication |
| Keywords: | Diffusion of innovations, Indirect comparisons, Methodological innovation, Network meta-analysis, Social networks |
| | |

Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.

Supplemental Material 1.mp4
Supplemental Material 2.mp4

# History and Publication Trends in the Diffusion and Early Uptake of Indirect Comparison Meta-Analytic Methods to Study Drugs: Animated Co-Authorship Networks over Time

Joann K. Ban,[1] Mina Tadrous,[1] Amy X. Lu, [1] Erin A. Cicinelli,[1] Suzanne M. Cadarette[1]

[1]Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

**Correspondence to:** Mina Tadrous, Leslie L. Dan Pharmacy Building, University of Toronto, 144 College Street, Toronto, Ontario, M5S 3M2 Canada. Tel: 416-864-6060, E-mail: mina.tadrous@mail.utoronto.ca

**Conflict of Interest:** None related to this work.

**Word Count:** 3,925

**Subject Heading:** Research methods (primary), Communication (secondary)

**Keywords:** Diffusion of Innovations, Indirect Comparisons, Methodological Innovation, Network Meta-Analysis, Social Networks

## ABSTRACT

**Objective:** To characterize the early diffusion of indirect comparison meta-analytic methods to study drugs.

**Design:** Systematic literature synthesis.

**Data sources:** Cochrane Database of Systematic Reviews®, EMBASE®, MEDLINE®, Scopus®, and Web of Science®.

**Study selection:** English language papers that used indirect comparison meta-analytic methods to study the efficacy or safety of three or more interventions, where at least one was a drug.

**Data extraction:** The number of publications and authors were plotted by year and type: methodological contribution, review, or empirical application. Author and methodological details were summarized for empirical applications, and animated co-authorship networks were created to visualize contributors by country and affiliation type (academia, industry, government, or other) over time.

**Results:** We identified 477 papers (74 methodological contributions, 42 reviews, and 361 empirical applications) by 1,689 distinct authors from 1997 to 2013. Prior to 2002, only three applications were published, with contributions from the United States (n=2) and Canada (n=1). The number of applications gradually increased annually with rapid uptake between 2011 and 2013 (n=254, 71%). Early diffusion occurred primarily in Europe with the first application credited to the United Kingdom in 2003. Application spread to other European countries in 2005, and may have been supported by regulatory requirements for drug approval. By the end of 2013, contributions included 49% credited to Europe (22% United Kingdom, 27% other), 37% credited to North America (11% Canada, 26% United States), and 14% from other regions.

**Conclusion:** Indirect comparison meta-analytic methods are an important innovation for health research. Although Canada and the United States were the first to apply these methods, Europe led their diffusion. The increase in uptake of these methods may have been facilitated by acceptance by regulatory agencies, which are calling for more comparative drug effect data to assist in drug accessibility and reimbursement decisions.

**Abstract word count:** 296 (MAX 300 WORDS)

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our paper walks through the development and history of indirect comparison meta-analytic methods and its early diffusion in the study of drugs using co-authorship networks.
- Our animated co-authorship networks are innovative by allowing the visualization of social structures and collaboration trends through authors and their connections with each other over time.
- Mapping contributions based on first and last authors may miss some important contributions by co-authors, yet including second authors had little impact in a prior study.
- We conducted an extensive systematic literature search that identified 477 (361 empirical applications) eligible English language papers that used indirect comparison meta-analytic methods to study drugs through to December 2013, yet some relevant papers such as non-English language papers and grey literature may have been missed.
- We did not consider methodological and reporting quality, since focus was on early uptake by country and institutional affiliation, yet our results set the stage for further research that may consider quality.

## INTRODUCTION

Randomized controlled trials (RCT) are essential for bringing novel pharmaceutical products to market. RCTs for drug approval typically compare new treatment efficacy to placebo and provide safety data for only common adverse effects. However, RCTs are often not powered to identify all important drug efficacy and safety endpoints and thus meta-analytic methods were developed. Meta-analysis is a statistical method that combines the results of two or more studies to evaluate the same intervention in comparison to a control such as placebo, to obtain a more precise estimate of the intervention's effects relative to that control [1-3]. The term *meta-analysis* was first coined by G. V. Glass in 1976, yet use of statistical methods to combine the results of multiple studies dates back to the early part of the 20$^{th}$ century, with early methodological techniques proposed by R. Fisher and W. Cochran in the 1930s [1, 2].

When completed using high quality RCTs, meta-analyses are regarded as providing the highest level of evidence [4]. However, traditional pairwise meta-analysis is limited by only being able to combine and estimate the benefits or harms of two treatments if they have been compared directly. In addition, meta-analysis cannot compare more than two treatments at a time [3, 5]. This presents a challenge to policy-makers, clinicians, and patients who often need to select the most optimal treatment from several competing options [6]. Indirect comparisons have been made informally using point estimates and 95% confidence intervals of treatments [7]. However, this informal approach does not provide a precise estimate of the relative difference between two treatments because the relative effects are not measured.

In 1997, the *adjusted indirect comparison* method was proposed by H. C. Bucher, as an innovative meta-analytic approach that utilizes indirect evidence to estimate the relative benefits and risks between two treatments [8]. Unlike traditional pairwise meta-analysis, adjusted indirect

comparisons estimate the relative effects of two treatments that have not been compared directly by leveraging results from each treatment that has been compared to a common comparator, such as a placebo [6, 8, 9]. However, the adjusted indirect comparison method ignores direct evidence, even when available. In 2002, *network meta-analysis* was proposed as an extension of the adjusted indirect comparison method that combines direct and indirect comparative data across several sets of pairwise treatment comparisons [5, 10]. The combination of direct and indirect data yields more precise effect estimates [6]. A similar method, coined *mixed treatment comparison*, was proposed in 2004 [11], and the term *multiple treatment meta-analysis* was also introduced to describe concepts of combining both direct and indirect evidence in 2005 [5], **Table 1**.

Indirect comparison meta-analytic methods have become valuable tools in clinical and policy decision making, and have thus, been rapidly adopted since their introduction [7, 12-14]. However, application of these methodological innovations varies widely [6, 12, 15]. Rogers' Diffusion of Innovations Model defines *diffusion* as the process by which an innovation is communicated across individuals within a social system, particularly during the initial stages of its use [16, 17]. Our study sought to characterize the early diffusion of indirect comparison meta-analytic methods used to study drugs [16]. We interpreted diffusion and uptake relative to the social system, by creating co-authorship networks to examine the speed of uptake (number of publications) and spread of these methods (collaboration between authors, authors' countries, and across institutions) over time.

## MATERIALS AND METHODS

We recently examined the diffusion of two confounder summary score methods and illustrate the importance of innovation attributes (**relative advantage, compatibility, simplicity, trialability,** and **observability**) and seminal author engagement on the uptake of methodological innovations using Rogers' Diffusion of Innovations Model [16]. In addition to innovation attributes, Rogers' Model identifies key aspects of the social system that may impact the rate of adoption [17]. In particular, a methodological innovation will have a quicker rate of adoption if members within the social system (e.g., researchers, clinicians, and policymakers) share similar system norms. For example, regulatory agencies make decisions for drug approval and formulary coverage. Regulatory agencies are therefore well-positioned to influence the uptake of methodological innovations that support the drug approval process. If novel methods become a requirement for drug approval, pharmaceutical companies, which share a vested interest in the drug approval process, may willingly adopt the methodological innovation in question. We examined the diffusion and early uptake of indirect comparison meta-analytic methods used to study drugs, and interpreted contributions by country and affiliation type using Rogers' Diffusion of Innovations Model.

### Systematic Search

We completed a systematic literature search to identify all papers that utilized indirect comparison meta-analytic methods to study drug effects in humans. We searched the Cochrane Database of Systematic Reviews®, EMBASE®, and MEDLINE® from their dates of inception to 31 December 2013 using keywords based on a recent search (**Appendix A Table A**) [18]. We then used SCOPUS® and Web of Science® to perform a citation search to identify papers that

referenced key seminal papers [8, 10], major methodological contributions [19-21], and reviews [7, 13-15, 22, 23] on indirect comparison meta-analytic methods [18].

All English language papers that used indirect meta-analytic methods to compare the clinical efficacy or safety of three or more interventions among humans were eligible if at least one intervention was a drug. We excluded abstracts, letters, commentaries, cost-effectiveness studies, overviews of systematic reviews, protocols, and papers with no identifiable authors. Papers that used informal indirect comparisons (e.g., simply compared point estimates with 95% confidence intervals) or did not clearly describe the techniques used to perform the indirect comparison in the title, abstract, introduction, or methods sections were also excluded. Two authors (JKB and MT) independently searched and screened all titles and abstracts for eligibility. Discrepancies following full text review were resolved by a third author (SMC).

The number of papers and cumulative authors were plotted by calendar year and type: methodological contribution, review paper, or empirical application; and important social system events (e.g., publication of seminal papers) were added to the graph. We then focused exclusively on empirical applications. A proportional Venn diagram was used to illustrate the yield of each database search strategy that contributed to the identification of eligible empirical applications. We abstracted: author(s), journal, year of publication, area of study, primary outcomes (efficacy, safety, or both), first and last author institutional affiliations, terminology used to describe methods, and presence and details of network diagrams. If no primary outcome was explicitly stated, all outcomes were considered primary. When multiple diagrams were present, the total number of unique comparators across all network diagrams was taken. Two authors (JKB and EAC) abstracted all the data, and another (MT) verified the data.

## Co-Authorship Network of Empirical Applications

An Excel macro™ was used to generate a co-authorship matrix from author names downloaded into Microsoft Excel 2010 from Endnote X5 (Thomson Reuters, 2011). Names of authors presented in multiple forms were collapsed into the most common presentation or, in the event of a tie, the one with more initials. Publication (authors and order) and paper characteristics (country and institutional type ascribed) were imported into R®, version 3.3.1 (R Foundation for Statistical Computing, 2016), leveraging RStudio®, version 0.99.887 (RStudio, Inc., 2009), to generate directed co-authorship networks, and identify components. Co-authorship networks depict authors as "nodes" with "ties" between nodes denoting co-authorship. Directed co-authorship networks clarify network structure by sending "ties" depicted as arrows, from first authors to co-authors. A component is a group of authors connected directly as co-authors on the same paper, or indirectly through a mutual co-author on separate papers. A disconnected co-authorship network is based on the total number of components. The more components found in a co-authorship network, the more disconnected authors are from each other as a result of isolated publishing. Institutional affiliations and corresponding countries of the first and last authors of each empirical application were used to ascribe credit to each application and the network [16]. Institutions were categorized by country and type (academia, government, industry, or other). Node size was created proportional to the number of publications by that author. Node colour was created, first based on country affiliation attributed to each paper, and second based on institutional type. The networks were animated by calendar year of publication to visualize growth in application and contributions over time.

## Patient and Public Involvement

No patients or the public were involved in the development and design of this research.

# RESULTS

## Systematic Search

We identified 477 eligible papers: 74 methodological contributions (**Appendix B**), 42 review papers (**Appendix C**), and 361 empirical applications (**Appendix D**), **Figure 1**; published by 1,691 distinct authors between 1997 and 2013. A steady increase in the number of eligible papers was seen over time, and proportionally more were published in recent years, **Figure 2**. Focusing exclusively on the 361 empirical applications, the keyword search strategy identified most applications (n=314, 87%; 30% unique). EMBASE® identified the most (n=282, 78%; 6% unique), followed by MEDLINE® (n=239, 66%; 3% unique), and relatively few were identified by the Cochrane Database of Systematic Reviews® (n=20, 6%; <1% unique), **Appendix A Figure A**. The citation search identified an additional 47 (13%) papers outside keyword searches, **Appendix A Figure B**.

The indirect comparison meta-analytic applications were published in 188 different journals. The most common areas of study were cardiovascular disorders (22%), cancers (12%), musculoskeletal disorders (12%), infectious diseases (10%), and psychiatry (9%), **Table 2**. Sixty-nine percent of primary outcomes assessed therapeutic efficacy, 25% assessed efficacy and drug safety, and 6% assessed drug safety alone. Of the 361 empirical applications, only 161 (45%) published network diagrams illustrating the direct or indirect comparisons. The median number of interventions compared was 7 (interquartile range of 5-10, min=3, max=145). The most common terminology used was network meta-analysis (38%), followed by mixed treatment comparison (26%), Bucher's method (24%), and adjusted indirect comparison (21%). The sum of these percentages is greater than 100% due to an overlap in the terminology used. More

specifically, 18% (n=65) of all eligible empirical applications used two or more terms to describe the methods used.

## Co-Authorship Network of Empirical Applications

**Figure 3 (A: country, B: affiliation)** summarizes the final co-authorship networks, and **Appendix E-F** maps the growth of each network by country affiliation and institution type over time. The largest component included 143 (40%) papers and 567 (37%) authors, including innovators Guyatt GH, Lu G, and Ades AE, **Appendix D1-143**. Of the remaining 128 components, ninety (70%) included only a single paper (25% of all applications made up single-paper components), demonstrating a relatively disconnected network.

Early application of these methods started in 2000, with three papers published by 2002 [24-26]; and each referencing the innovator paper [8]. Authors were from Canada (red) and the United States (blue), and published in isolation of each other, **Appendix E**. In 2003, five papers were published in isolation of each other, with two credited to the United States (blue), and three credited to the United Kingdom (yellow). The majority referenced innovator Bucher [8], yet one paper referenced innovator Lumley [10]. By 2004, an increase in collaboration between authors from different countries was noted, with the first multi-paper component (France) published in 2004, and the first single-paper component with institutional affiliations from two countries (United States and Belgium) published in 2005. By 2006, another 13 papers were published: 11 papers referenced innovator Bucher with institutional affiliations credited to many countries worldwide (Belgium, Canada, France, Germany, India, United States), and two papers referenced two innovator papers [10, 11], with one paper credited to the United States, the United Kingdom, and Greece, and the other credited to the United Kingdom. From 2007 to 2013, we noted an increase in the number of applications published over time, with fastest uptake noted

in 2011, and an increase in authors publishing from a broad range of countries depicted by the increase in colours observed in the animated networks (**Appendix E-F** and **Supplemental Files 1-2**). In particular, a rapid increase in collaboration between authors was noted in 2009, as demonstrated by the merging of smaller components into larger components. Europe led the diffusion with node colours of yellow (United Kingdom), light yellow (all other Europe), and combinations of yellow with other primary colours comprising the majority of nodes in the co-authorship network.

Overall, institutional credit was given to 358 unique institutions around the world: 77% of contributions came from academic institutions, 18% from industry, 1% from government, and 4% from other institutions, **Table 3**. Europe led the diffusion with 49% of credited papers (22% United Kingdom, 27% other); 37% were credited to North America (26% United States, 11% Canada), and 14% to other regions.

## DISCUSSION

Indirect comparison meta-analytic methods are an important methodological innovation that has become valuable in providing comparative drug effect data in the absence of head-to-head trials. In this paper, we found that uptake was concentrated primarily in Europe (49%) with further contributions from North America (37%). Despite initial development from Canada (1997) and the United States (2002) [8, 10], our results are not surprising given that refined methods were published by core innovators from the Universities of Bristol and Washington [10, 11]. Early use of indirect comparison meta-analytic applications predominated from the United Kingdom, and may have been the result of an increase in demand by the United Kingdom government for more comparative effectiveness research to assist with clinical practice guideline development and to guide drug funding decisions. Indeed, the need for clinical practice guideline development was one of the major reasons for the establishment of the National Institute for Health and Clinical Excellence (NICE) in 1999 [27], which has since become a world leader in providing guidance on the clinical- and cost-effectiveness of new and established health technologies (including drugs). NICE decisions are made by independent committees of researchers, clinicians, industry and lay representatives; and have included innovator Ades, and early adopters from the NICE Guidelines Technical Support Unit, University of Bristol [5, 20, 28-30].

The steady increase in the use of indirect comparison meta-analytic methods, and effective diffusion to Europe and North America, may also be partially explained by consideration of the five key innovation attributes described in Rogers' Diffusion of Innovations Model (**relative advantage, compatibility, simplicity, trialability,** and **observability**) [16]. The Multi-Parameter Evidence Synthesis (MPES) Research Group (from which the NICE Guidelines Technical Support Unit is based) has offered introductory short-courses and workshops to

facilitate understanding and application of these methods to health economists, statisticians, and policy-makers worldwide in collaboration with other academic institutions in the United Kingdom (Universities of Sheffield and York) since 2002 (**observability, simplicity, trialability**) [30]. Active workshops demonstrating the use of this methodological innovation likely provided a vehicle for peer observation to occur, so that the results and benefits of using this innovation were visible to potential adopters (**observability**). The provision of sample datasets and statistical code, as well as the integration of these methods into established software and software packages, may have also eased the use of these methods (**simplicity**), and allowed potential adopters the chance to try using these methods with direct guidance from the innovators and early adopters themselves (**trialability**). In addition, the MPES Research Group published tutorials and case-studies highlighting the advantages of using pairwise, indirect comparison, and network meta-analyses for evidence synthesis (**advantage**), and highlighting the validity of these methods to inform clinical and policy decision-making (**compatibility**) [28, 31-34]. We noted rapid uptake since 2011, coinciding with the publication of guidelines and reviews on these methods by health technology assessment and reimbursement agencies (e.g., Canadian Agency for Drugs and Technologies in Health, Hauté Autorité de Santé, Institute for Quality and Efficiency in Health Care, Pharmaceutical Benefits Advisory Committee, and Scottish Medicines Consortium) from many countries around the world [19, 35-41].

Given the economic pressure on payers to better allocate healthcare resources, many regulatory agencies have been calling for the use of comparative effectiveness research to assist in drug accessibility and reimbursement decisions [40, 41]. In addition, applications focused on drug efficacy tie into payer demands for more cost-effectiveness analyses of newly marketed drugs in comparison with competing or existing therapies. For example, the Canadian Agency

for Drugs and Technologies in Health (CADTH) has published guidance documents to facilitate best practices in the use of indirect comparison meta-analytic methods to assess clinical and economic value of drugs and other health technologies in Canada, including how to best incorporate these methods to inform clinical parameters in these types of evaluations [19, 42]. Consequently, many pharmaceutical companies and contract research organizations have started to apply these methods. For example, the International Society for Pharmaceutical Outcomes Research Indirect Comparisons Good Research Practice Task Force adopted methods and statistical code from the MPES Research Group to publish a two-part report to guide researchers, clinicians, and policy-makers on good research practices for indirect comparisons; given its value and increasing acceptance by regulatory agencies [6, 15]. Co-authors mainly comprised of research experts from pharmaceutical companies and contract research organization (including J. P. Jansen who collaborated with innovator A. E. Ades and co-authors from the MPES Research Group), which may have helped disseminate use of these methods into industry. In addition, publication of this report may partially explain rapid and large uptake from 2011 since co-authors from the two-part report were from multiple countries (Belgium, Canada, the Netherlands, the United Kingdom, the United States). We believe that this observation may have been a response to requests by these agencies, as we noted collaboration with core innovators from academia, and an increase in the number of industry-sponsored applications published from 2009.

Our findings demonstrated rapid increase in the use of indirect comparison meta-analytic methods in recent years, with contributions increasing worldwide. With 70% (n=90) of the co-authorship network comprised of single paper components; and 81% (n=1,121) of authors having published only a single paper; use of indirect comparison meta-analytic methods has indeed

spread to many distinct research groups. However, uptake of these methods has been diffuse and highly disconnected when compared to the diffusion and early uptake of other methodological innovations [16], since many authors are publishing in isolation of each other (i.e., smaller, single paper components). In a prior study that examined the diffusion and early uptake of two confounder summary scores (the disease risk score and high-dimensional propensity score), only 19% and 11% of all eligible applications made up single paper components in their respective co-authorship networks in comparison with 25% of all indirect comparison meta-analytic applications [16]. Rapid and widespread use by academics, and more recently, government and industry, suggests that use of these methods has become diffuse and are no longer in the early stages of adoption, but rather, mainstream and accepted methods. As we also noted a lack of standardization in the terminology used to describe the indirect comparison meta-analytic methods used, we encourage use of the term, *network meta-analysis*, as it is clearer than mixed treatment or multiple treatments meta-analysis, which may be assumed to indicate the concomitant administration of two or more drug therapies (e.g., adjuvant therapy).

Our results are subject to some limitations. First, our analysis limited the co-authorship of empirical applications to English language papers identified in select bibliographic databases: the Cochrane Database of Systematic Reviews®, EMBASE®, MEDLINE®, Scopus®, and Web of Science®. The limitation of our search to these databases may have resulted in missed articles that were published in other languages, or identifiable in other bibliographic databases, such as Google Scholar®, JSTOR®, Pubmed®, and RevMan5®. Articles that did not clearly describe the techniques used to perform these methods were also excluded, since we could not assume that these methods were used. While we acknowledge that this may have resulted in the exclusion of some applications, we included articles that clearly described these methods in the

title, abstract, introduction, or methods sections to allow for as much inclusion as possible. Consequently, we believe that our systematic search is both comprehensive and robust, as this is the largest and only search completed to date that examines the diffusion of indirect comparison meta-analytic methods in the study of drugs. However, it is worth noting that the term *matching-adjusted indirect comparison*, an extension of the adjusted indirect comparison which was introduced in 2010 and uses individual patient data from single-comparator-RCTs to adjust for differences in patient characteristics across studies was not considered in our analysis [43]. However, 6 eligible papers were published using this term, and we expect to see an increase in the future.

Secondly, our study only ascribed country and institutional credit to the first and last author of each paper. Although the first (principal) and last (often senior) authors traditionally contribute the most, and thus receive the most credit, for papers in the biomedical sciences, other co-authors in the authorship order may also help drive use of novel methods. Consequently, mapping contributions based on first and last authors may have resulted in missed contributions by other co-authors. Nonetheless, inclusion of the second authors in a previous study that examined the diffusion of two confounder summary scores found little impact on country and institutional credit [16].

Finally, our work did not examine the quality of eligible empirical articles, or explore the correlation and impact of early diffusion on the quality of indirect comparison meta-analytic methods. Given the large number of authors who published in isolation of each other, it is possible that the degree of interconnectedness between authors in the network may have influenced the quality of eligible applications, as inconsistencies in methodological and reporting quality of indirect comparison meta-analytic methods have been documented [18]. Similar to

traditional pairwise meta-analysis; limitations related to the quality of the search conducted, quality and heterogeneity of studies included, and publication bias; can all influence the quality of the study. Uniquely, indirect comparison meta-analytic methods have additional limitations that should be accounted for, such as issues with transitivity and inconsistency of networks, as well as the presentation of results [44]. A recent systematic review of network meta-analyses in clinical research demonstrated improvement in methodological and reporting quality over time [45]. However, we acknowledge that this is an important area of future research that should be explored.

In conclusion, prior research identified challenges with integrating new statistical methods into practice [46, 47]. We recently identified the importance of considering the five innovation attributes from Rogers' Diffusion of Innovations Model to facilitate knowledge translation of new methods for rapid integration [16]. In this paper, we used indirect comparison meta-analytic methods to examine the impact of social systems on the diffusion of novel methods. We demonstrated rapid adoption by effective consideration of innovation attributes by innovators, and rapid adoption due to collaboration between innovators from the United Kingdom and a large number of early adopters from many countries around the world. Although speculative, and while there are likely multiple reasons for the relatively rapid adoption of these methods, we believe that adoption by government agencies may have contributed to more rapid uptake, and is worth noting; though further research should be explored. We believe that the social system can play a major role in facilitating the adoption of innovative methods, here through regulation, and by the increase in demand by government for more comparative effectiveness research. As many health technology assessment and regulatory agencies have started to call for more evidence synthesis methods to assist in drug accessibility and

reimbursement decisions [41], use of indirect comparison meta-analytic methods has become more widely accepted, and will likely continue to be a key tool for policy decision making. We encourage authors of novel methods to consider the five innovation attributes when integrating new methods into practice (**relative advantage, compatibility, simplicity, trialability,** and **observability**), with emphasis on early collaboration with potential adopters, such as government regulatory bodies.

## ACKNOWLEDGEMENTS

No specific funding was received to support this work. Joann K. Ban was supported in part by a Canadian Institute of Health Research (CIHR) Program in Drug Safety and Effectiveness Cross-Disciplinary Training. Mina Tadrous was supported in part by a CIHR Frederick Banting and Charles Best Canada Graduate Scholarship (GSD-11342). Erin A. Cicinelli was supported in part by a CIHR Health Professional Student Research Award.

This research was presented at the Canadian Association for Health Services and Policy Research (CAHSPR) Annual Conference in Toronto, ON, Canada, May 2016, and at the International Conference on Pharmacoepidemiology and Therapeutic Risk Management (ICPE) in Dublin, Ireland, August 2016. Participation at CAHSPR was supported by a CAHSPR Student Travel Bursary, and participation at ICPE was supported by an ICPE Travel Scholarship, the Leslie Dan Faculty of Pharmacy Student Experience Fund, and a University of Toronto School of Graduate Studies Conference Grant.

Authors thank Dave Dubins, PhD for initial work in creating Excel macros for co-authorship matrix generation; and Gina Matesic, MLIS for helping with search strategies.

## DATA SHARING STATEMENT

Data sharing: technical appendix and supplemental material available at [/doi].

## CONTRIBUTORSHIP STATEMENT

JB, MT, and SC were responsible for the conception and design of this study. JB, EC, and MT collected the data, and verified the results with SC. Data analysis was performed by JB and AL. JB led drafting of the manuscript in consultation with MT and SC. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

## REFERENCES

[1] Friedman HP, Goldberg JD. Meta-analysis: an introduction and point of view. *Hepatology*. 1996;23:917-28.
[2] O'Rourke K. An historical perspective on meta-analysis: dealing quantitatively with varying study results. *J R Soc Med*. 2007;100:579-82.
[3] Jansen JP, Naci H. Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect modifiers. *BMC Med*. 2013;11:159.
[4] Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg*. 2011;128:305-10.
[5] Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ*. 2005;331:897-900.
[6] Jansen JP, Fleurence R, Devine B, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. *Value Health*. 2011;14:417-28.
[7] Edwards SJ, Clarke MJ, Wordsworth S, et al. Indirect comparisons of treatments based on systematic reviews of randomised controlled trials. *Int J Clin Pract*. 2009;63:841-54.
[8] Bucher HC, Guyatt GH, Griffith LE, et al. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol*. 1997;50:683-91.
[9] Song F, Altman DG, Glenny AM, et al. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ*. 2003;326:472.
[10] Lumley T. Network meta-analysis for indirect treatment comparisons. *Stat Med*. 2002;21:2313-24.
[11] Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med*. 2004;23:3105-24.
[12] Lee AW. Review of mixed treatment comparisons in published systematic reviews shows marked increase since 2009. *J Clin Epidemiol*. 2014;67:138-43.
[13] Song F, Loke YK, Walsh T, et al. Methodological problems in the use of indirect comparisons for evaluating healthcare interventions: survey of published systematic reviews. *BMJ*. 2009;338:b1147.
[14] Donegan S, Williamson P, Gamble C, et al. Indirect comparisons: a review of reporting and methodological quality. *PLoS One*. 2010;5:e11054.
[15] Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. *Value Health*. 2011;14:429-37.
[16] Cadarette SM, Ban JK, Consiglio GP, et al. Diffusion of Innovations model helps interpret the comparative uptake of two methodological innovations: co-authorship network analysis and recommendations for integration of novel methods in practice. *J Clin Epidemiol*. 2017;84:150-160.
[17] Rogers EM. Diffusion of Innovations. Fifth ed. Toronto: Free Press; 2003.
[18] Bafeta A, Trinquart L, Seror R, et al. Analysis of the systematic reviews process in reports of network meta-analyses: methodological systematic review. *BMJ*. 2013;347:f3675.
[19] Wells GA, Sultan SA, Chen L, et al. Indirect Evidence: Indirect Treatment Comparisons in Meta-Analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.

[20] Lu G, Ades AE, Sutton AJ, et al. Meta-analysis of mixed treatment comparisons at multiple follow-up times. *Stat Med*. 2007;26:3681-99.
[21] Salanti G, Higgins JP, Ades AE, et al. Evaluation of networks of randomized trials. *Stat Methods Med Res*. 2008;17:279-301.
[22] Glenny AM, Altman DG, Song F, et al. Indirect comparisons of competing interventions. *Health Technol Assess*. 2005;9:1-134, iii-iv.
[23] Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol*. 2011;64:163-71.
[24] Wilhelmus KR. The treatment of herpes simplex virus epithelial keratitis. *Trans Am Ophthalmol Soc*. 2000;98:505-32.
[25] Packer M, Antonopoulos GV, Berlin JA, et al. Comparative effects of carvedilol and metoprolol on left ventricular ejection fraction in heart failure: results of a meta-analysis. *Am Heart J*. 2001;141:899-907.
[26] Sauriol L, Laporta M, Edwardes MD, et al. Meta-analysis comparing newer antipsychotic drugs for the treatment of schizophrenia: evaluating the indirect approach. *Clin Ther*. 2001;23:942-56.
[27] Chalkidou K. Comparative effectiveness review within the U.K.'s National Institute for Health and Clinical Excellence. Issue Brief (Commonw Fund). 2009;59:1-11.
[28] Caldwell DM, Welton NJ, Ades AE. Mixed treatment comparison analysis provides internally coherent treatment effect estimates based on overviews of reviews and can reveal inconsistency. *J Clin Epidemiol*. 2010;63:875-82.
[29] Dias S, Welton NJ, Caldwell DM, et al. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med*. 2010;29:932-44.
[30] University of Bristol. Multi-parameter Evidence Synthesis Research. Multi-parameter Evidence Synthesis Research Group | School of Social and Community Medicine | University of Bristol. 2017. http://www.bristol.ac.uk/social-community-medicine/centres/cresyda/mpes/ (accessed 23 Jul 2017).
[31] Dias S, Sutton AJ, Ades AE, et al. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making*. 2013;33:607-17.
[32] Sutton A, Ades AE, Cooper N, et al. Use of indirect and mixed treatment comparisons for technology assessment. *Pharmacoeconomics*. 2008;26:753-67.
[33] Dias S, Sutton AJ, Welton NJ, et al. Evidence synthesis for decision making 3: heterogeneity--subgroups, meta-regression, bias, and bias-adjustment. *Med Decis Making*. 2013;33:618-40.
[34] Dias S, Welton NJ, Sutton AJ, et al. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making*. 2013;33:641-56.
[35] Haute Autorité de Santé. Indirect Comparisons: Methods and Validity. Saint-Denis: Haute Autorité de Santé; 2009.
[36] Institute for Quality and Efficiency in Health Care. General Methods (Version 4.1). Cologne: Institute for Quality and Efficiency in Health Care; 2013.
[37] Indirect Comparisons Working Group. Report of the Indirect Comparisons Working Group to the Pharmaceutical Benefits Advisory Committee: assessing indirect comparisons. Canberra: Australian Government Department of Health and Ageing; 2013.

[38] Pharmaceutical Benefits Advisory Committee. Guidelines for Preparing Submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Australian Government Department of Health and Ageing; 2008.
[39] National Institute for Health and Care Excellence. Guide to the Methods of Technology Appraisal 2013, Process and Method Guides. National Institute for Healh and Care Excellence; 2013.
[40] Lebioda A, Gasche D, Dippel FW, et al. Relevance of indirect comparisons in the German early benefit assessment and in comparison to HTA processes in England, France and Scotland. *Health Econ Rev*. 2014;4:31.
[41] Laws A, Kendall R, Hawkins N. A comparison of national guidelines for network meta-analysis. *Value Health*. 2014;17:642-54.
[42] Use of Network Meta-Analysis to Inform Clinical Parameters in Economic Evaluation. Ottawa: Canadian Agency for Drugs and Technologies in Health.
[43] Signorovitch JE, Wu EQ, Yu AP, et al. Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept. *Pharmacoeconomics*. 2010;28:935-45.
[44] Cipriani A, Higgins JP, Geddes JR, et al. Conceptual and technical challenges in network meta-analysis. *Annals Intern Med*. 2013 ;159 :130-7.
[45] Petropoulou M, Nikolakopoulou A, Veroniki AA, et al. Bibliographic study showed improving statistical methodology of network meta-analyses published between 1999 and 2015. *J Clin Epidemiol*. 2017;82:20-28.
[46] Altman DG, Goodman SN. Transfer of technology from statistical journals to the biomedical literature. Past trends and future predictions. *JAMA*. 1994;272:129-32.
[47] Pullenayegum EM, Platt RW, Barwick M, et al. Knowledge translation in biostatistics: a survey of current practices, preferences, and barriers to the dissemination and uptake of new statistical methods. *Stat Med*. 2016;35:805-18.

# In-Text Figures and Tables

## Tables

**Table 1:** Timeline of Meta-analytic Methodological Innovations

| Innovation | Year | Innovators | Institution | Country | Description |
|---|---|---|---|---|---|
| Traditional Pairwise Meta-Analysis [1] | 1904 | Pearson K | University College London | UK | Combines direct evidence from multiple RCTs comparing the same intervention and comparator (e.g., placebo) to strengthen the intervention's effect estimate relative to that comparator. |
| | 1935 | Fisher R | Rothamsted Experimental Station | UK | |
| | 1937 | Cochran W | Rothamsted Experimental Station | UK | |
| | 1976 | Glass GV | University of Colorado | USA | |
| Adjusted Indirect Comparison [8] | 1997 | Bucher HC<br>Guyatt GH<br>Griffith LE<br>Walter SD | McMaster University | Canada | Combines odds ratios from multiple RCTs comparing one of two interventions of interest to a common comparator (e.g. placebo) to estimate the effects of two interventions that have not been compared directly. |
| Network Meta-Analysis* [10] | 2002 | Lumley T | University of Washington | USA | Combines direct and indirect data from multiple RCTs to compare several sets of pairwise treatment comparisons. |
| Mixed Treatment Comparison* [11] | 2004 | Lu G<br>Ades AE | University of Bristol | UK | |

RCT: randomized controlled trials, UK: United Kingdom, USA: United States of America

* To our knowledge, Caldwell et al. (2005) introduced the term *multiple treatments meta-analysis* to describe the concept of combining direct and indirect evidence to compare multiple treatments connected by a network of RCTs, as seen in both methods [5].

**Table 2:** Characteristics of empirical indirect comparison meta-analytic applications in the study of drugs, n=361

| Characteristics | N | % |
|---|---|---|
| **Area of Study** | | |
| Blood Disorders | 1 | 0.3 |
| Cancers | 45 | 12.5 |
| Cardiovascular Disorders | 79 | 21.9 |
| Dermatology/Skin Disorders | 11 | 3.0 |
| Endocrine/Metabolic Disorders | 18 | 5.0 |
| Gastrointestinal Disorders | 8 | 2.2 |
| Genitourinary Disorders | 4 | 1.1 |
| Infectious Diseases | 36 | 10.0 |
| Musculoskeletal Disorders | 45 | 12.5 |
| Neurologic Disorders | 21 | 5.8 |
| Ophthalmic Disorders | 6 | 1.7 |
| Pain | 20 | 5.5 |
| Pregnancy | 4 | 1.1 |
| Psychiatric Disorders | 31 | 8.6 |
| Renal Disorders | 2 | 0.6 |
| Respiratory Disorders | 16 | 4.4 |
| Sexual Health | 6 | 1.7 |
| Surgery | 8 | 2.2 |
| **Primary Outcome** | | |
| Efficacy Only | 249 | 69.0 |
| Safety Only | 23 | 6.4 |
| Both Efficacy and Safety | 89 | 24.6 |
| **Terminology** | | |
| Adjusted Indirect Comparison | 75 | 20.8 |
| Bucher's Method | 88 | 24.4 |
| Indirect Comparison | 45 | 12.5 |
| Matching-Adjusted Indirect Comparison | 6 | 1.7 |
| Mixed Treatment Comparison | 95 | 26.3 |
| Multiple Treatments Meta-Analysis | 29 | 8.0 |
| Network Meta-Analysis | 137 | 38.0 |
| **Network Diagram(s)** | 161 | 44.6 |
| Interventions* | | |
| 3 | 7 | 4.3 |
| 4 | 16 | 9.9 |
| 5 | 23 | 14.3 |
| 6 | 24 | 14.9 |

| | | |
|---|---|---|
| 7 | 18 | 11.2 |
| 8 | 17 | 10.6 |
| 9 | 14 | 8.7 |
| 10-19 | 30 | 18.6 |
| 20+ | 12 | 7.4 |

* Based on the total number of interventions studied, indicated in the network diagram(s) published, n=161.

**Table 3:** Institutional affiliations by country (n=35) and institution type (n=7) for the entire indirect comparison meta-analytic applications network

| Institution | First and Last Author Credit (%) |
|---|---|
| **Country** | |
| Australia | 2.0 |
| Belgium | 1.7 |
| Brazil | 2.4 |
| Canada | 11.3 |
| China | 3.0 |
| France | 3.0 |
| Germany | 3.6 |
| Greece | 1.9 |
| India | 1.0 |
| Italy | 4.7 |
| Netherlands | 3.8 |
| Spain | 1.8 |
| Switzerland | 2.5 |
| Taiwan | 1.7 |
| United Kingdom | 22.1 |
| United States of America | 26.0 |
| Other* | 7.4 |
| **Type** | |
| **Academic** | **77.4** |
| School | 56.4 |
| Hospital | 21.0 |
| **Government** | **1.5** |
| **Industry** | **17.5** |
| Contract Research Organization | 11.3 |
| Pharmaceutical Company | 6.2 |
| **Other** | **3.6** |
| Independent Research Groups | 1.1 |
| Non-profit Organizations | 2.4 |
| Trade Associations | 0.1 |

* Institutional affiliations from other countries with <1% first and last author credit each (Austria, Bahrain, Cameroon, Croatia, Denmark, Hong Kong, Ireland, Israel, Japan, New Zealand, Nigeria, Norway, Peru, Poland, Portugal, Saudi Arabia, South Africa, South Korea, and Thailand).

## Figure Captions

**Figure 1:** Flow diagram of systematic search results.

**Figure 2:** Number of publications on indirect comparison meta-analytic methods by year of publication, n=477. Methodological contributions (checkered bar), review papers (horizontal stripes), and empirical applications (solid). Cumulative number of unique authors represented by the solid grey line, n=1689. [†]Innovators by seminal publication: Bucher et al. 1997 (Canada) [8]; Lumley (USA) 2002 [10]; Lu and Ades 2004 (UK) [11]. Early adopters: [§]government-sponsored academic groups and health technology and reimbursement assessment agencies (National Institute for Health and Clinical Excellence Guidelines Technical Support Unit 2002 (UK) [30]; Pharmaceutical Benefits Advisory Committee 2005 (Australia) [37, 38]; Canadian Agency for Drugs and Technologies in Health 2009 (Canada) [19]; Haute Autorité de Santé 2009 (France) [35]; Institute for Quality and Efficiency in Health Care 2013 (Germany) [36]); [#]independent research organizations: Indirect Treatment Comparisons Good Research Practices Task Force 2011 (Canada, The Netherlands, USA, UK) [6, 15].

**Figure 3:** Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. The lines represent the relationships (co-authorship) between authors, with arrows directed from first author to co-authors of each paper. Node size is proportional to the number of published articles.

**A.** Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), while authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow).

**B.** Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliation types from academia and government were coloured orange (a combination of red and yellow), while authors on papers affiliated with academic, industry, and other were coloured light purple (a combination of red, blue, and white).

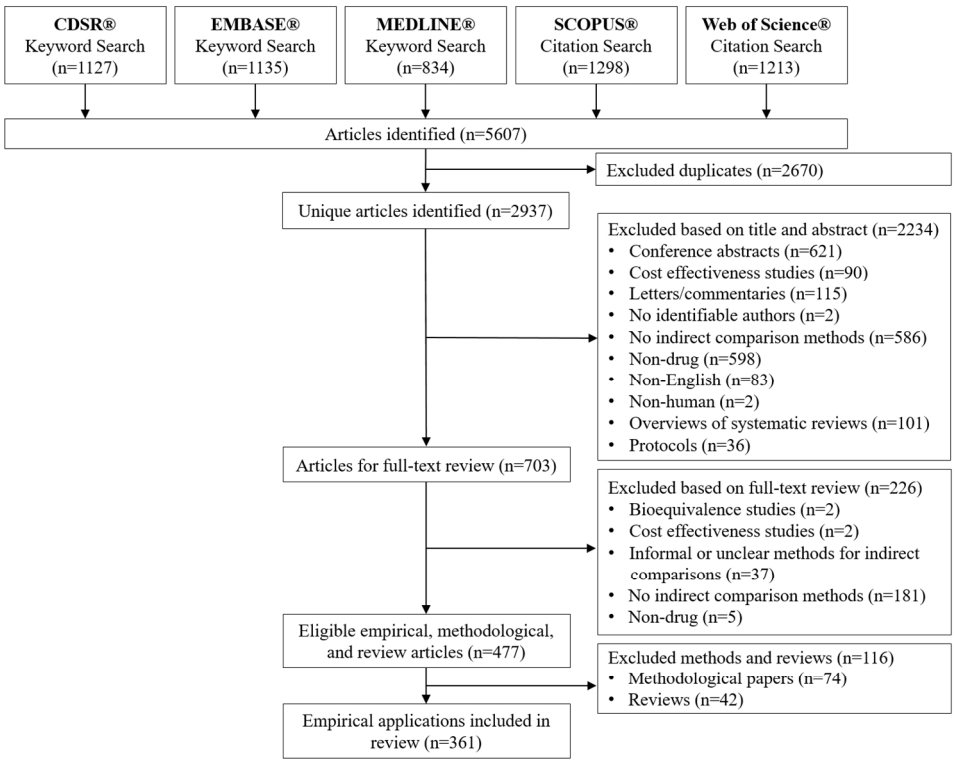



Figure 1: Flow diagram of systematic search results.

135x106mm (300 x 300 DPI)

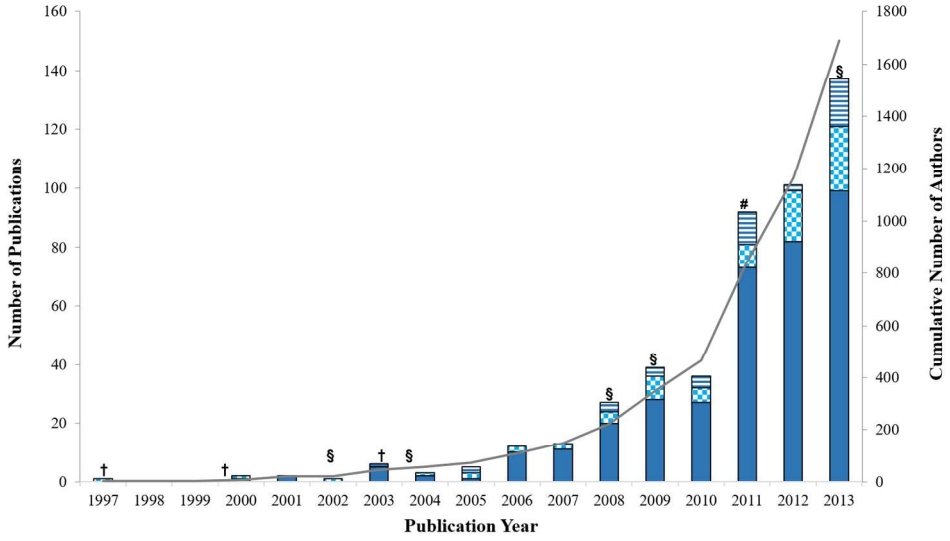
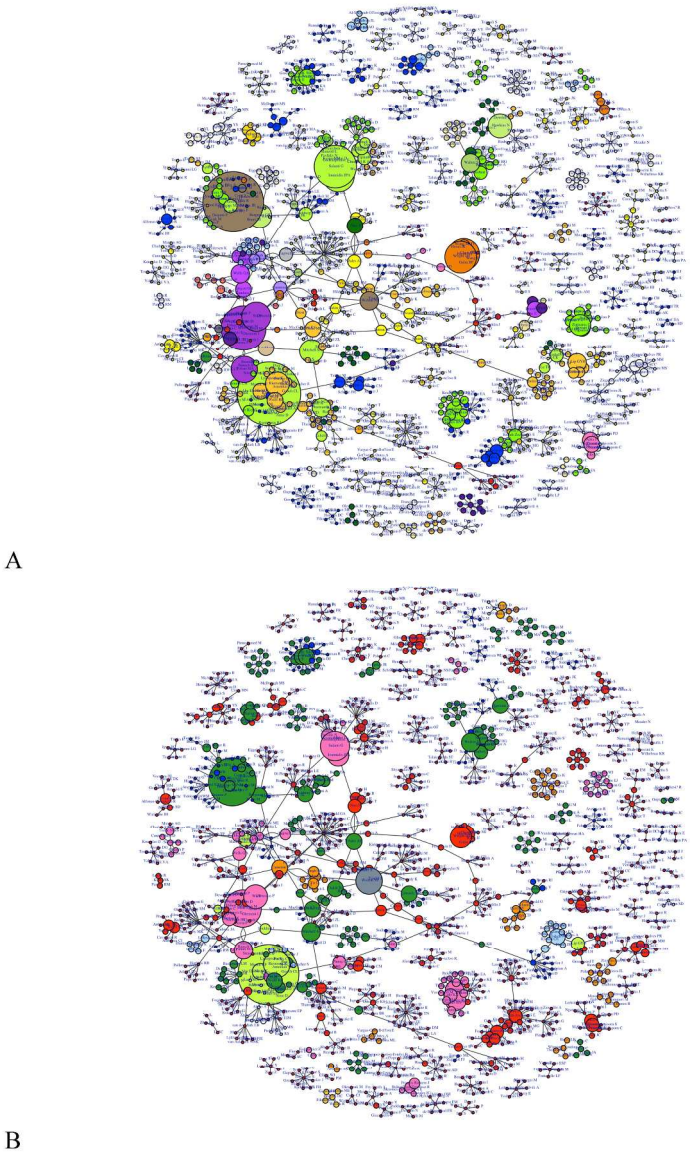



Figure 2: Number of publications on indirect comparison meta-analytic methods by year of publication, n=477. Methodological contributions (checkered bar), review papers (horizontal stripes), and empirical applications (solid). Cumulative number of unique authors represented by the solid grey line, n=1689. †Innovators by seminal publication: Bucher et al. 1997 (Canada) [8]; Lumley (USA) 2002 [10]; Lu and Ades 2004 (UK) [11]. Early adopters: §government-sponsored academic groups and health technology and reimbursement assessment agencies (National Institute for Health and Clinical Excellence Guidelines Technical Support Unit 2002 (UK) [30]; Pharmaceutical Benefits Advisory Committee 2005 (Australia) [37, 38]; Canadian Agency for Drugs and Technologies in Health 2009 (Canada) [19]; Haute Autorité de Santé 2009 (France) [35]; Institute for Quality and Efficiency in Health Care 2013 (Germany) [36]); #independent research organizations: Indirect Treatment Comparisons Good Research Practices Task Force 2011 (Canada, The Netherlands, USA, UK) [6, 15].

144x79mm (300 x 300 DPI)



A

B

Figure 3: Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. The lines represent the relationships (co-authorship) between authors, with arrows directed from first author to co-authors of each paper. Node size is proportional to the number of published articles.

A. Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), while authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow).

B. Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white. For example, authors on papers with affiliation

types from academia and government were coloured orange (a combination of red and yellow), while authors on papers affiliated with academic, industry, and other were coloured light purple (a combination of red, blue, and white).

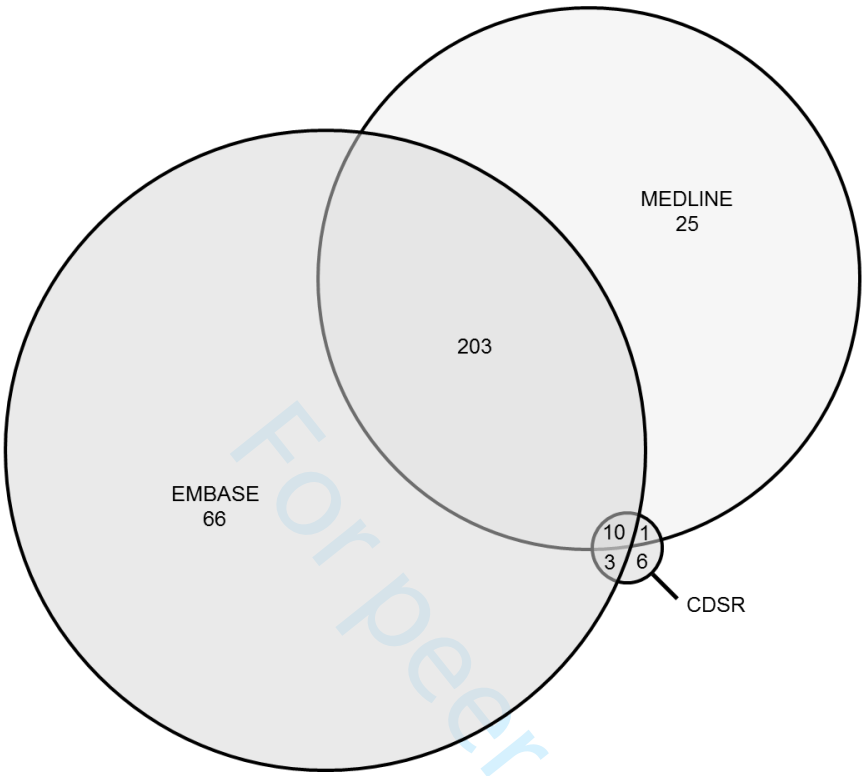
274x370mm (300 x 300 DPI)

# Appendix A: Systematic Literature Search

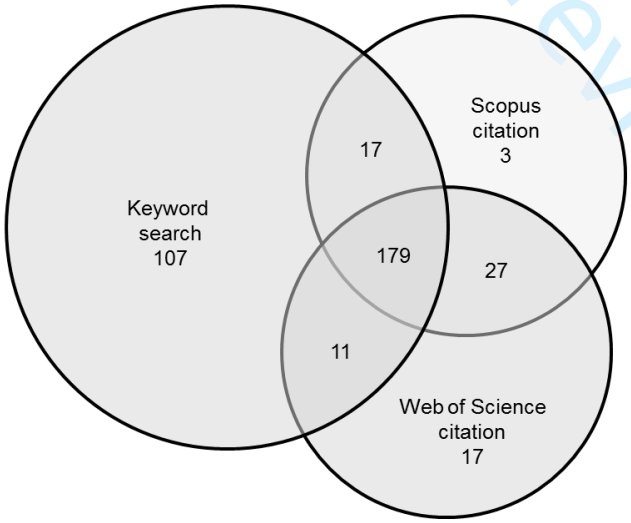
**Appendix Table A:** Systematic Literature Keyword and Citation Search Strategy

| KEYWORD SEARCH | | | | |
|---|---|---|---|---|
| **Databases** | | Cochrane Database of Systematic Reviews® | OVID® (without revisions) | |
| | | | MEDLINE® | EMBASE® |
| **Limits** | | - Date of inception to 31 December 2013 | - Date of inception (1946) to 31 December 2013<br>- English language<br>- Humans<br>- Publication types: meta-analysis, systematic reviews | - Date of inception (1974) to 31 December 2013<br>- English language<br>- Humans<br>- Publication types: meta-analysis, systematic reviews |
| **Keyword Search** | | #1 OR #2 OR #3 OR #4 | | |
| **Indirect Comparisons** | **#1** | "network meta-analysis" OR "network meta-regression" OR "multiple treatment meta-analysis" OR "multiple treatments meta-analysis" OR "mixed treatment comparison" OR "mixed treatment comparisons" | | |
| | **#2** | "mixed treatment" OR "mixed treatments" OR "multiple treatment" OR "multiple treatments" OR "treatment network" OR "treatment networks" OR "multiple comparison" OR "multiple comparisons" | | |
| | **#3** | "indirect comparison" OR "indirect comparisons" | | |
| **Overview of Reviews** | **#4** | "overview of reviews" OR "umbrella review" OR "overview of systematic reviews" OR "overview of meta-analyses" OR "multiple systematic reviews" OR "multiple meta-analyses" OR "overview of Cochrane reviews" OR "multiple Cochrane reviews" OR "overview of Cochrane" | | |

| CITATION SEARCH | | |
|---|---|---|
| **Databases** | | SCOPUS® \| Web of Science® |
| **Limits** | | - Date of inception to 31 December 2013<br>- English language |
| **Citation Search** | | Articles citing the following 11 articles below |
| | **#1** | Bucher HC, Guyatt GH, Griffith LE, Walter SD. J Clin Epidemiol 1997;50(6):683-91. |
| | **#2** | Lumley T. Stat Med 2002;21(16):2313-24. |
| | **#3** | Donegan S, Williamson P, Gamble C, Tudur-Smith C. PLoS One 2010;5(11):e11054. |
| | **#4** | Song F, Loke YK, Walsh T, Glenny AM, Eastwood AJ, Altman DG. BMJ 2009;338:b1147. |
| | **#5** | Wells GA, Sultan SA, Chen L, Khan M, Coyle D. Indirect Evidence: Indirect Treatment Comparisons in Meta-analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2009. |
| | **#6** | Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R, et al. Health Technol Assess 2005;9(26):1-134, iii-iv. |
| | **#7** | Hoaglin DC, Hawkins N, Jansen JP, Scott DA, Itzler R, Cappelleri JC, et al. Value Health 2011;14(4):429-37. |
| | **#8** | Edwards SJ, Clarke MJ, Wordsworth S, Borrill J. Int J Clin Pract 2009;63:841-54. |
| | **#9** | Lu G, Ades AE, Sutton AJ, Cooper NJ, Briggs AH, Caldwell DM. Stat Med 2007;26(20):3681-99. |
| | **#10** | Salanti G, Higgins JP, Ades AE, Ioannidis JPStat Methods Med Res 2008;17(3):279-301. |
| | **#11** | Salanti G, Ades AE, Ioannidis JP. J Clin Epidemiol 64(2):163-71. |




**A**




**B**

**Appendix A Figure A and B:** Proportional Venn diagrams of systematic search yields for indirect comparison meta-analytic empirical applications depicting unique and overlap applications identified by each search strategy, N=361. Circle size is proportional to the number of papers identified from each search strategy.

**A.** Empirical applications identified by each keyword search, n=314 (EMBASE keyword, n=282; MEDLINE keyword, n=239; and Cochrane Database of Systematic Reviews (CDSR) keyword, n=20).

**B.** Empirical applications identified by each keyword and citation search, n=361 (keyword (EMBASE, MEDLINE, CDSR), n=314; Web of Science citation, n=234; Scopus citation, n=226).

# Appendix B: List of references of identified methodological contributions of indirect comparison meta-analytic methods

[B1] Achana FA, Cooper NJ, Dias S, Lu G, Rice SJ, Kendrick D, et al. Extending methods for investigating the relationship between treatment effect and baseline risk from pairwise meta-analysis to network meta-analysis. *Stat Med* 2013; 32(5):752-71.

[B2] Ades AE, Mavranezouli I, Dias S, Welton NJ, Whittington C, Kendall T. Network meta-analysis with competing risk outcomes. *Value Health* 2010;13(8):976-83.

[B3] Ballesteros, J. Orphan comparisons and indirect meta-analysis: a case study on antidepressant efficacy in dysthymia comparing tricyclic antidepressants, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors by using general linear models. *J Clin Psychpharmacol* 2005;25(2):127-31.

[B4] Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol* 1997;50(6):683-91.

[B5] Caldwell DM, Welton NJ, Ades AE. Mixed treatment comparison analysis provides internally coherent treatment effect estimates based on overviews of reviews and can reveal inconsistency. *J Clin Epidemiol* 2010;63(8):875-82.

[B6] Chaimani A, Vasiliadis HS, Pandis N, Schmid CH, Welton NJ, Salanti G. Effects of study precision and risk of bias in networks of interventions: a network meta-epidemiological study. *Int J Epidemiol* 2013;42(4):1120-131.

[B7] Chaimani A, Higgins JP, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One* 2013;8(10):e76654.

[B8] Chootrakool H, Shi JQ, Yue R. Meta-analysis and sensitivity analysis for multi-arm trials with selection bias. *Stat Med* 2011;30(11):1183-98.

[B9] Chung H, Lumley T. Graphical exploration of network meta-analysis data: the use of multidimensional scaling. *Clin Trials* 2008;5(4):301-7.

[B10] Cooper NJ, Sutton AJ, Morris D, Ades AE, Welton NJ. Addressing between-study heterogeneity and inconsistency in mixed treatment comparisons: application to stroke prevention treatments in individuals with non-rheumatic atrial fibrillation. *Stat Med* 2009;28(14):1861-81.

[B11] Cooper NJ, Peters J, Lai MC, Juni P, Wandel S, Palmer S, et al. How valuable are multiple treatment comparison methods in evidence-based health-care evaluation? *Value Health* 2011;14(2):371-80.

[B12] Cope S, Jansen JP. Quantitative summaries of treatment effect estimates obtained with network meta-analysis of survival curves to inform decision-making. *BMC Med Res Methodol* 2013;13:147.

[B13] Del Giovane C, Vacchi L, Mavridis D, Filippini G, Salanti G. Network meta-analysis models to account for variability in treatment definitions: application to dose effects. *Stat Med* 2013;32(1):25-39.

[B14] Dias S, Welton NJ, Caldwell DM, Ades AE. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med* 2010;29:932-44.

[B15] Dias S, Welton NJ, Marinho VCC, Salanti G, Higgins JPT, Ades AE. Estimation and adjustment of bias in randomized evidence by using mixed treatment comparison meta-analysis. *J R Statist Soc A* 2010;173(3):613-29.

[B16] Ding Y, Fu H. Bayesian indirect and mixed treatment comparisons across longitudinal time points. *Stat Med* 2013;32(15):2613-28.

[B17] Donegan S, Williamson P, D'Alessandro U, Tudur Smith C. Assessing the consistency assumption by exploring treatment by covariate interactions in mixed treatment comparison meta-analysis: individual patient-level covariates versus aggregate trial-level covariates. *Stat Med* 2012;31(29):3840-57.

[B18] Donegan S, Williamson P, D'Alessandro U, Garner P, Smith CT. Combining individual patient data and aggregate data in mixed treatment comparison meta-analysis: individual patient data may be beneficial if only for a subset of trials. *Stat Med* 2013;32(6):914-30.

[B19] Druyts E, Thorlund K, Humphreys S, Lion M, Cooper CL, Mills EJ. Interpreting discordant indirect and multiple treatment comparison meta-analyses: an evaluation of direct acting antivirals for chronic hepatitis C infection. *Clin Epidemiol* 2013;5(1):173-183.

[B20] Eckermann S, Coory M, Willan AR. Indirect comparison: relative risk fallacies and odds solution. *J Clin Epidemiol* 2009;62:1031-6.

[B21] Fu H, Price KL, Nilsson ME, Ruberg SJ. Identifying potential adverse events dose-response relationships via Bayesian indirect and mixed treatment comparison models. *J Biopharm Stat* 2013;23(1):26-42.

[B22] Griffin S, Bojke L, Main C, Palmer S. Incorporating direct and indirect evidence using bayesian methods: an applied case study in ovarian cancer. *Value Health* 2006;9(2):123-31.

[B23] Gross JL, Rogers J, Polhamus D, Gillespie W, Friedrich C, Gong Y, et al. A novel model-based meta-analysis to indirectly estimate the comparative efficacy of two medications: an example using DPP-4 inhibitors, sitagliptin and linagliptin, in treatment of type 2 diabetes mellitus. *BMJ Open* 2013;3(3):e001844.

[B24] Gwaza L, Gordon J, Welink J, Potthast H, Hansson H, Stahl M, et al. Statistical approaches to indirectly compare bioequivalence between generics: a comparison of methodologies employing artemether/lumefantrine 20/120 mg tablets as prequalified by WHO. *Eur J Clin Pharmacol* 2012;68(12):1611-8.

[B25] Hawkins N, Scott DA, Woods B. How far do you go? Efficient searching for indirect evidence. *Med Decis Making* 2009;29(3):273-81.

[B26] Hawkins N, Scott DA, Woods BS, Thatcher N. No study left behind: a network meta-analysis in non-small-cell lung cancer demonstrating the importance of considering all relevant data. *Value Health* 2009;12(6):996-1003.

[B27] Hong H, Carlin BP, Shamliyan TA, Wyman JF, Ramakrishnan R, Sainfort F, et al. Comparing Bayesian and frequentist approaches for multiple outcome mixed treatment comparisons. *Med Decis Making* 2013;33(5):702-14.

[B28] Jansen JP, Cope S. Meta-regression models to address heterogeneity and inconsistency in network meta-analysis of survival outcomes. *BMC Med Res Method* 2012;12:152.

[B29] Jansen JP, Schmid CH, Salanti G. Directed acyclic graphs can help understand bias in indirect and mixed treatment comparisons. *J Clin Epidemiol* 2012;65(7):798-807.

[B30] Jansen JP. Network meta-analysis of survival data with fractional polynomials. *BMC Med Res Methodol* 2011;11:61.

[B31] König J, Krahn U, Binder H. Visualizing the flow of evidence in network meta-analysis and characterizing mixed treatment comparisons. *Stat Med* 2013;32(30): 5414-29.

[B32] Krahn U, Binder H, König J. A graphical tool for locating inconsistency in network meta-analyses. *BMC Med Res Methodol* 2013;13(1):35.

[B33] Lee C, Hunsche E, Balshaw R, Kong SX, Scnitzer TJ. Need for common internal controls when assessing the relative efficacy of pharmacologic agents using a meta-analytic approach: Case study of cyclooxygenase 2-selective inhibitors for the treatment of osteoarthritis. *Arthritis Rheum* 2005;53(4):510-8.

[B34] Lu G, Ades A. Modeling between-trial variance structure in mixed treatment comparisons. *Biostatistics* 2009;10(4):792-805.

[B35] Lu G, Ades AE. Assessing evidence inconsistency in mixed treatment comparisons. *JASA* 2006;101(474):447-459.

[B36] Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med* 2004;23(20):3105-24.

[B37] Lu G, Ades AE, Sutton AJ, Cooper NJ, Briggs AH, Caldwell DM. Meta-analysis of mixed treatment comparisons at multiple follow-up times. *Stat Med* 2007;26(20):3681-99.

[B38] Lumley T. Network meta-analysis for indirect treatment comparisons. *Stat Med* 2002;21(16):2313-24.

[B39] Lunn D, Barrett J, Sweeting M, Thompson S. Fully Bayesian hierarchical modelling in two stages, with application to meta-analysis. *J R Stat Soc C Appl Stat* 2013;62(4):551-72.

[B40] Madan J, Stevenson MD, Cooper KL, Ades AE, Whyte S, Akehurst R. Consistency between direct and indirect trial evidence: is direct evidence always more reliable? *Value Health* 2011;14(6):953-60.

[B41] Mavridis D, Sutton A, Cipriani A, Salanti G. A fully Bayesian application of the Copas selection model for publication bias extended to network meta-analysis. *Stat Med* 2013;32(1):51-66.

[B42] Mills EJ, Ghement I, O'Regan C, Thorlund K. Estimating the power of indirect comparisons: a simulation study. *PLoS One* 2011;6(1):e16237.

[B43] Mills EJ, Kanters S, Thorlund K, Chaimani A, Veroniki AA, Ioannidis JP. The effects of excluding treatments from network meta-analyses: survey. *BMJ* 2013;347:f5195.

[B44] Mills, E.J., K. Thorlund, and J.P.A. Ioannidis, Calculating additive treatment effects from multiple randomized trials provides useful estimates of combination therapies. *J Clin Epidemiol* 2012;65(12):1282-8.

[B45] Norton EC, Miller MM, Wang JJ, Coyne K, Kleinman LC. Rank reversal in indirect comparisons. *Value Health* 2012;15(8):1137-40.

[B46] O'Regan C, Ghement I, Eyawo O, Guyatt GH, Mills EJ. Incorporating multiple interventions in meta-analysis: an evaluation of the mixed treatment comparison with the adjusted indirect comparison. *Trials* 2009;10:86.

[B47] Piepho HP, Williams ER, Madden LV. The use of two-way linear mixed models in multitreatment meta-analysis. *Biometrics* 2012;68(4):1269-77.

[B48] Price MJ, Welton NJ, Ades AE. Parameterization of treatment effects for meta-analysis in multi-state Markov models. *Stat Med* 2011;30(2):140-51.

[B49] Salanti G, Dias S, Welton NJ, Ades AE, Golfinopoulos V, Kyrgiou M, et al. Evaluating novel agent effects in multiple-treatments meta-regression. *Stat Med* 2010;29(23):2369-83.

[B50] Salanti G, Higgins JP, Ades AE, Ioannidis JP. Evaluation of networks of randomized trials. *Stat Methods Med Res* 2008;17(3):279-301.

[B51] Salanti G, Kavvoura FK, Ioannidis JP. Exploring the geometry of treatment networks. *Ann Intern Med* 2008;148(7):544-53.

[B52] Salanti G, Marinho V, Higgins JP. A case study of multiple-treatments meta-analysis demonstrates that covariates should be considered. *J Clin Epidemiol* 2009;62(8):857-64.

[B53] Saramago P, Sutton AJ, Cooper NJ, Manca A. Mixed treatment comparisons using aggregate and individual participant level data. *Stat Med* 2012;31(28):3516-36.

[B54] Schmidli H, Wandel S, Neuenschwander B. The network meta-analytic-predictive approach to non-inferiority trials. *Stat Methods Med Res* 2013;22(2):219-40.

[B55] Schmitz S, Adams R, Walsh C. The use of continuous data versus binary data in MTC models: a case study in rheumatoid arthritis. *BMC Med Res Methodol* 2012;12:167.

[B56] Signorovitch JE, Sikirica V, Erder MH, Xie J, Lu M, Hodgkins PS, et al. Matching-adjusted indirect comparisons: a new tool for timely comparative effectiveness research. *Value Health* 2012;15(6):940-7.

[B57] Song F, Glenny AM, Altman DG, Indirect comparison in evaluating relative efficacy illustrated by antimicrobial prophylaxis in colorectal surgery. *Control Clin Trials* 2000;21(5):488-97.

[B58] Song F, Xiong T, Parekh-Bhurke S, Loke YK, Sutton AJ, Eastwood AJ, et al. Inconsistency between direct and indirect comparisons of competing interventions: meta-epidemiological study. *BMJ* 2011;343:d4909.

[B59] Song F, Clark A, Bachmann MO, Maas J. Simulation evaluation of statistical properties of methods for indirect and mixed treatment comparisons. *BMC Med Res Methodol* 2012;12:138.

[B60] Song F, Harvey I, Lilford R. Adjusted indirect comparison may be less biased than direct comparison for evaluating new pharmaceutical interventions. *J Clin Epidemiol* 2008;61(5):455-63.

[B61] Spineli LM, Higgins JP, Cipriani A, Leucht S, Salanti G. Evaluating the impact of imputations for missing participant outcome data in a network meta-analysis. *Clin Trials* 2013;10(3):378-88.

[B62] Thorlund K, Mills E. Stability of additive treatment effects in multiple treatment comparison meta-analysis: a simulation study. *Clin Epidemiol* 2012;4(1):75-85.

[B63] Thorlund K, Mills EJ. Sample size and power considerations in network meta-analysis. *Syst Rev* 2012;1(1):41.

[B64] Thorlund K, Thabane L, Mills EJ. Modelling heterogeneity variances in multiple treatment comparison meta-analysis - are informative priors the better solution? *BMC Med Res Methodol* 2013;13:2.

[B65] Trinquart L, Abbé A, Ravaud P. Impact of reporting bias in network meta-analysis of antidepressant placebo-controlled trials. *PLoS One* 2012;7(4):e35219.

[B66] Trinquart L, Chatellier G, Ravaud P. Adjustment for reporting bias in network meta-analysis of antidepressant trials. *BMC Med Res Methodol* 2012;12:150.

[B67] van Valkenhoef G, Tervonen T, de Brock B, Hillege H. Algorithmic parameterization of mixed treatment comparisons. *Stat Comput* 2012;22(5):1099-111.

[B68] van Valkenhoef G, Tervonen T, Zhao J, de Brock B, Hillege HL, Postmus D. Multicriteria benefit-risk assessment using network meta-analysis. *J Clin Epidemiol* 2012;65(4):394-403.

[B69] Vandermeer BW, Buscemi N, Liang Y, Witmans M. Comparison of meta-analytic results of indirect, direct, and combined comparisons of drugs for chronic insomnia in adults: a case study. *Med Care* 2007;45(10):S166-72.

[B70] Veroniki AA, Vasiliadis HS, Higgins JP, Salanti G. Evaluation of inconsistency in networks of interventions. *Int J Epidemiol* 2013;42(1):332-45.

[B71] Wei YH, Higgins JP. Bayesian multivariate meta-analysis with multiple outcomes. *Stat Med* 2013;32(17):2911-34.

[B72] Wells GA, Sultan SA, Chen L, Khan M, Coyle D. Indirect Evidence: Indirect Treatment Comparisons in Meta-analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2009.

[B73] White IR. Multivariate random-effects meta-regression: updates to mvmeta. *Stata J* 2011;11(2):255-70.

[B74] Xiong T, Parekh-Bhurke S, Loke YK, Abdelhamid A, Sutton AJ, Eastwood AJ, et al. Overall similarity and consistency assessment scores are not sufficiently accurate for predicting discrepancy between direct and indirect comparison estimates. *J Clin Epidemiol* 2013;66(2):184-91.

# Appendix C: List of references of identified reviews of indirect comparison meta-analytic methods

[C1] Ades AE, Madan J, Welton NJ. Indirect and mixed treatment comparisons in arthritis research. *Rheumatology* 2011;50 Suppl 4:iv5-9.

[C2] Bafeta A, Trinquart L, Seror R, Ravaud P. Analysis of the systematic reviews process in reports of network meta-analyses: methodological systematic review. *BMJ* 2013;347:f3675.

[C3] Buti J, Glenny AM, Worthington HV, Nieri M, Baccini M. Network meta-analysis of randomised controlled trials: direct and indirect treatment comparisons. *Eur J Oral Implantol* 2011;4(1):55-62.

[C4] Caldwell DM, Ades AE, Higgins JP. Simultaneous comparison of multiple treatments: combining direct and indirect evidence. *BMJ* 2005;331:897-900.

[C5] Caro JJ, Ishak KJ. No head-to-head trial? Simulate the missing arms. *Pharmacoeconomics* 2010;28(10):957-67.

[C6] Carpiuc KT, Rosti G, Castagnetti F, Treur M, Stephens J. Indirect comparisons of second-generation tyrosine kinase inhibitors in CML: case study using baseline population characteristics. *Onco Targets Ther* 2010;3:205-10.

[C7] Cepeda MS, Fife D, Lobanov V, Sutton A. Can soccer predictions boost the use of indirect comparison to assess the safety of drugs? *Open Drug Saf J* 2011;2(1):25-8.

[C8] Chu J, Sloan CE, Freedberg KA, Yazdanpanah Y, Losina E. Drug efficacy by direct and adjusted indirect comparison to placebo: an illustration by Mycobacterium avium complex prophylaxis in HIV. *AIDS Res Ther* 2011;8:14.

[C9] Cipriani A, Higgins JP, Geddes JR, Salanti G. Conceptual and technical challenges in network meta-analysis. *Ann Intern Med* 2013;159(2):130-7.

[C10] Cipriani A, Barbui C, Rizzo C, Salanti G. What is a multiple treatments meta-analysis? *Epidemiol Psychiatr Sci* 2012;21(2):151-3.

[C11] Cooper NJ, Spiegelhalter D, Bujkiewicz S, Dequen P, Sutton AJ. Use of implicit and explicit bayesian methods in health technology assessment. *Int J Technol Assess Health Care* 2013;29(3):336-42.

[C12] Dias S, Sutton AJ, Ades AE, Welton NJ. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making* 2013;33(5):607-17.

[C13] Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. *Med Decis Making* 2013;33(5):641-56.

[C14] Dias S, Welton NJ, Sutton AJ, Ades AE. Evidence synthesis for decision making 5: the baseline natural history model. *Med Decis Making* 2013;33(5):657-70.

[C15] Donegan S, Williamson P, Gamble C, Tudur-Smith C. Indirect comparisons: a review of reporting and methodological quality. *PLoS One* 2010;5(11):e11054.

[C16] Edwards SJ, Clarke MJ, Wordsworth S, Borrill J. Indirect comparisons of treatments based on systematic reviews of randomised controlled trials. *Int J Clin Pract* 2009;63:841-54.

[C17] Gartlehner G, Moore CG. Direct versus indirect comparisons: a summary of the evidence. *Int J Technol Assess Health Care* 2008;24:170-7.

[C18] Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R, et al. Indirect comparisons of competing interventions. *Health Technol Assess* 2005;9(26):1-134, iii-iv.

[C19] Harenberg J, Weiss C. Clinical trials with new oral anticoagulants. Additive value of indirect comparisons also named network meta-analyses. *Hamostaseologie* 2013;33(1):62-70.

[C20] Hoaglin DC, Hawkins N, Jansen JP, Scott DA, Itzler R, Cappelleri JC, et al. Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. *Value Health* 2011;14(4):429-37.

[C21] Ioannidis JP. Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. *CMAJ* 2009;181(8):488-93.

[C22] Jansen JP, Naci H. Is network meta-analysis as valid as standard pairwise meta-analysis? It all depends on the distribution of effect modifiers. *BMC Med* 2013;11(1):159.

[C23] Jansen JP, Crawford B, Bergman G, Stam W. Bayesian meta-analysis of multiple treatment comparisons: an introduction to mixed treatment comparisons. *Value Health* 2008;11(5):956-64.

[C24] Jansen JP, Fleurence R, Devine B, Itzler R, Barrett A, Hawkins N, et al. Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 1. *Value Health* 2011;14(4):417-28.

[C25] Jones B, Roger J, Lane PW, Lawton A, Fletcher C, Cappelleri JC, et al. Statistical approaches for conducting network meta-analysis in drug development. *Pharm Stat* 2011;10(6): 523-31.

[C26] Mavridis D, Salanti G. A practical introduction to multivariate meta-analysis. *Stat Methods Med Res* 2013;22(2):133-58.

[C27] Mills EJ, Ioannidis JP, Thorlund K, Schünemann HJ, Puhan MA, Guyatt GH. How to use an article reporting a multiple treatment comparison meta-analysis. *JAMA* 2012;308(12):1246-53.

[C28] Mills EJ, Bansback N, Ghement I, Thorlund K, Kelly S, Puhan MA, et al. Multiple treatment comparison meta-analyses: a step forward into complexity. *Clin Epidemiol* 2011;3(1):193-202.

[C29] Mills EJ, Thorlund K, Ioannidis JP. Demystifying trial networks and network meta-analysis. *BMJ* 2013;346:f2914.

[C30] Naci H, O'Connor AB. Assessing comparative effectiveness of new drugs before approval using prospective network meta-analyses. *J Clin Epidemiol* 2013;66(8):812-6.

[C31] Naci H, Fleurence R. Using indirect evidence to determine the comparative effectiveness of prescription drugs: do benefits outweigh risks? *Health Outcomes Res Med* 2011;2(4):e241-9.

[C32] Salanti G, Ades AE, Ioannidis JP. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol* 64(2):163-71.

[C33] Schacht A, Dyachkova Y, Walton RJ. Critical evaluation of mixed treatment comparison meta-analyses using examples assessing antidepressants and opioid detoxification treatments. Int *J Methods Psychiatr Res* 2013;22(2):166-74.

[C34] Senn S, Gavini F, Magrez D, Scheen A. Issues in performing a network meta-analysis. *Stat Methods Med Res* 2013;22(2):169-89.

[C35] Snapinn S, Jiang Q. Indirect comparisons in the comparative efficacy and non-inferiority settings. *Pharm Stat* 2011;10(5):420-6.

[C36] Sobieraj DM, Cappelleri JC, Baker WL, Phung OJ, White CM, Coleman CI. Methods used to conduct and report Bayesian mixed treatment comparisons published in the medical literature: a systematic review. *BMJ Open* 2013;3(7):e003111.

[C37] Song F, Loke YK, Walsh T, Glenny AM, Eastwood AJ, Altman DG. Methodological problems in the use of indirect comparisons for evaluating healthcare interventions: survey of published systematic reviews. *BMJ* 2009;338:b1147.

[C38] Song F, Altman DG, Glenny AM, Deeks JJ. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *BMJ* 2003;326(7387):472-5.

[C39] Sutton A, Ades AE, Cooper N, Abrams K. Use of indirect and mixed treatment comparisons for technology assessment. *Pharmacoeconomics* 2008;26(9):753-67.

[C40] Tan SH, Bujkiewicz S, Sutton A, Dequen P, Cooper N. Presentational approaches used in the UK for reporting evidence synthesis using indirect and mixed treatment comparisons. *J Health Serv Res Policy* 2013;18(4):224-32.

[C41] Thorlund K, Druyts E, Aviña-Zubieta JA, Wu P, Milles EJ. Why the findings of published multiple treatment comparison meta-analyses of biologic treatments for rheumatoid arthritis are

different: an overview of recurrent methodological shortcomings. *Ann Rheum Dis* 2013;72(9): 1524-35.

[C42] Woods BS, Hawkins N, Scott DA. Network meta-analysis on the log-hazard scale, combining count and hazard ratio statistics accounting for multi-arm trials: a tutorial. *BMC Med Res Methodol* 2010;10:54.

# Appendix D: List of references of identified empirical applications of indirect comparison meta-analytic methods

Component 1: D1-143
Component 2: D144-152
Component 3: D153-160
Component 4: D161-166
Component 5: D167-171
Component 6: D172-176
Component 7: D177-181
Component 8: D182-186
Component 9: D187-191
Component 10: D192-196
Component 11: D197-200
Component 12: D201-204
Component 13: D205-208
Component 14: D209-212
Component 15: D213-216
Component 16: D217-220
Component 17: D221-224
Component 18: D225-227
Component 19: D228-230
Component 20: D231-233
Component 21: D234-235
Component 22: D236-237
Component 23: D238-239
Component 24: D240-241
Component 25: D242-243
Component 26: D244-245
Component 27: D246-247
Component 28: D248-249
Component 29: D250-251
Component 30: D252-253
Component 31: D254-255
Component 32: D256-257
Component 33: D258-259
Component 34: D260-261
Component 35: D262-263
Component 36: D264-265
Component 37: D266-267
Component 38: D268-269
Component 39: D270-271
Component 40: D272
Component 41: D273
Component 42: D274

Component 43: D275
Component 44: D276
Component 45: D277
Component 46: D278
Component 47: D279
Component 48: D280
Component 49: D281
Component 50: D282
Component 51: D283
Component 52: D284
Component 53: D285
Component 54: D286
Component 55: D287
Component 56: D288
Component 57: D289
Component 58: D290
Component 59: D291
Component 60: D292
Component 61: D293
Component 62: D294
Component 63: D295
Component 64: D296
Component 65: D297
Component 66: D298
Component 67: D299
Component 68: D300
Component 69: D301
Component 70: D302
Component 71: D303
Component 72: D304
Component 73: D305
Component 74: D306
Component 75: D307
Component 76: D308
Component 77: D309
Component 78: D310
Component 79: D311
Component 80: D312
Component 81: D313
Component 82: D314
Component 83: D315
Component 84: D316
Component 85: D317
Component 86: D318
Component 87: D319
Component 88: D320

Component 89: D321
Component 90: D322
Component 91: D323
Component 92: D324
Component 93: D325
Component 94: D326
Component 95: D327
Component 96: D328
Component 97: D329
Component 98: D330
Component 99: D331
Component 100: D332
Component 101: D333
Component 102: D334
Component 103: D335
Component 104: D336
Component 105: D337
Component 106: D338
Component 107: D339
Component 108: D340
Component 109: D341
Component 110: D342
Component 111: D343
Component 112: D344
Component 113: D345
Component 114: D346
Component 115: D347
Component 116: D348
Component 117: D349
Component 118: D350
Component 119: D351
Component 120: D352
Component 121: D353
Component 122: D354
Component 123: D355
Component 124: D356
Component 125: D357
Component 126: D358
Component 127: D359
Component 128: D360
Component 129: D361

[D1] Akbar A, Abu Dayyeh BK, Baron TH, Wang Z, Altayar O, Murad MH. Rectal nonsteroidal anti-inflammatory drugs are superior to pancreatic duct stents in preventing pancreatitis after endoscopic retrograde cholangiopancreatography: a network meta-analysis. *Clin Gastroenterol Hepatol* 2013;11(7):778-83.

[D2] Akshintala VS, Hutfless SM, Colantuoni E, Kim KJ, Khashab MA, Li T, et al. Systematic review with network meta-analysis: pharmacological prophylaxis against post-ERCP pancreatitis. *Aliment Pharmacol Ther* 2013;38(11-12):1325-37.

[D3] Alberton M, Wu P, Druyts E, Briel M, Mills EJ. Adverse events associated with individual statin treatments for cardiovascular disease: an indirect comparison meta-analysis. *QJM* 2012;105(2):145-57.

[D4] Alonso-Coello P, Zhou Q, Guyatt G. Home-monitoring of oral anticoagulation vs. dabigatran. An indirect comparison. *Thromb Haemost* 2012;108(4):647-53.

[D5] Baker WL, Baker EL, Coleman CI. Pharmacologic treatments for chronic obstructive pulmonary disease: a mixed-treatment comparison meta-analysis. *Pharmacotherapy* 2009;29(8): 891-905.

[D6] Baker WL, Phung OJ. Systematic review and adjusted indirect comparison meta-analysis of oral anticoagulants in atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2012;5(5):711-9.

[D7] Bekkering GE, Abou-Setta AM, Kleijnen J. The application of quantitative methods for identifying and exploring the presence of bias in systematic reviews: PDE-5 inhibitors for erectile dysfunction. *Int J Impot Res* 2008;20(3):264-77.

[D8] Bekkering GE, Soares-Weiser K, Reid K, Kessels AG, Dahan A, Treede RD, et al. Can morphine still be considered to be the standard for treating chronic pain? A systematic review including pair-wise and network meta-analyses. *Curr Med Res Opin* 2011;27(7):1477-91.

[D9] Bergman GJ, Hochberg MC, Boers M, Wintfeld N, Kielhorn A, Jansen JP. Indirect comparison of tocilizumab and other biologic agents in patients with rheumatoid arthritis and inadequate response to disease-modifying antirheumatic drugs. *Semin Arthritis Rheum* 2010;39(6):425-41.

[D10] Berry SM, Broglio KR, Berry DA. Addressing the incremental benefit of histamine dihydrochloride when added to interleukin-2 in treating acute myeloid leukemia: a Bayesian meta-analysis. *Cancer Invest* 2011;29(4):293-9.

[D11] Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet* 2013;382(9894):769-79.

[D12] Bottomley JM, Taylor RS, Ryttov J. The effectiveness of two-compound formulation calcipotriol and betamethasone dipropionate gel in the treatment of moderately severe scalp psoriasis: a systematic review of direct and indirect evidence. *Curr Med Res Opin* 2011;27(1):251-68.

[D13] Buscemi N, Vandermeer B, Friesen C, Bialy L, Tubman M, Ospina M, et al. The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs. *J Gen Intern Med* 2007;22(9):1335-50.

[D14] Buser N, Ivic S, Kessler TM, Kessels AG, Bachmann LM. Efficacy and adverse events of antimuscarinics for treating overactive bladder: network meta-analyses. *Eur Urol* 2012;62(6):1040-60.

[D15] Castellucci LA, Cameron C, Le Gal G, Rodger MA, Coyle D, Wells PS, et al. Efficacy and safety outcomes of oral anticoagulants and antiplatelet drugs in the secondary prevention of venous thromboembolism: systematic review and network meta-analysis. *BMJ* 2013;347:f5133.

[D16] Choy E, Marshall D, Gabriel ZL, Mitchell SA, Gylee E, Dakin HA. A systematic review and mixed treatment comparison of the efficacy of pharmacological treatments for fibromyalgia. *Semin Arthritis Rheum* 2011;41(3):335-45.e6.

[D17] Cipriani A, Furukawa TA, Salanti G, Geddes JR, Higgins JP, Churchill R, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* 2009;373(9665):746-58.

[D18] Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, et al. Comparative efficacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. *Lancet* 2011;378(9799):1306-15.

[D19] Cohen A, Drost P, Marchant N, Mitchell S, Orme M, Rublee D, et al. The efficacy and safety of pharmacological prophylaxis of venous thromboembolism following elective knee or hip replacement: systematic review and network meta-analysis. *Clin Appl Thromb Hemost* 2012;18(6):611-27.

[D20] Coleman CI, Baker WL, Kluger J, White CM. Antihypertensive medication and their impact on cancer incidence: a mixed treatment comparison meta-analysis of randomized controlled trials. *J Hypertens* 2008;26(4):622-9.

[D21] Cooper CL, Druyts E, Thorlund K, Nachega JB, El Khoury AC, O'Regan C, et al. Boceprevir and telaprevir for the treatment of chronic hepatitis C genotype 1 infection: an indirect comparison meta-analysis. *Ther Clin Risk Manag* 2012;8:105-30.

[D22] Cooper C, Lester R, Thorlund K, Druyts E, El Khoury AC, Yaya S, et al. Direct-acting antiviral therapies for hepatitis c genotype 1 infection: a multiple treatment comparison meta-analysis. *QJM* 2013;106(2):153-63.

[D23] Cooper NJ, Sutton AJ, Lu G, Khunti K. Mixed comparison of stroke prevention treatments in individuals with nonrheumatic atrial fibrillation. Arch Intern Med 2006;166(12):1269-75.

[D24] Cope S, Cupkun-Niggli G, Gale R, Jardim JR, Jansen JP. Comparative efficacy of indacaterol 150 mug and 300 mug versus fixed-dose combinations of formoterol + budesonide or salmeterol + fluticasone for the treatment of chronic obstructive pulmonary disease - a network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2011;6(1):329-44.

[D25] Cope S, Zhang J, Williams J, Jansen JP. Efficacy of once-daily indacaterol 75 μg relative to alternative bronchodilators in COPD: a study level and a patient level network meta-analysis. BMC Pulm Med 2012;12:29.

[D26] Cope S, Kraemer M, Zhang J, Capkun-Niggli G, Jansen JP. Efficacy of indacaterol 75 mug versus fixed-dose combinations of formoterol-budesonide or salmeterol-fluticasone for COPD: a network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2012;7:415-20.

[D27] Cope S, Capkun-Ziggli G, Gale R, Lassen C, Owen R, Ouwens MJ, et al. Efficacy of once-daily indacaterol relative to alternative bronchodilators in COPD: a patient-level mixed treatment comparison. *Value Health* 2012;15(3):524-33.

[D28] Cope S, Donohue JF, Jansen JP, Kraemer M, Capkun-Niggli G, Baldwin M, et al. Comparative efficacy of long-acting bronchodilators for COPD: a network meta-analysis. *Respir Res* 2013;14:100.

[D29] Cope S, Ouwens MJ, Jansen JP, Schmid P. Progression-free survival with fulvestrant 500 mg and alternative endocrine therapies as second-line treatment for advanced breast cancer: a network meta-analysis with parametric survival models. *Value Health* 2013;16(2):403-17.

[D30] Dakin H, Fidler C, Harper H. Mixed treatment comparison meta-analysis evaluating the relative efficacy of nucleos(t)ides for treatment of nucleos(t)ide-naive patients with chronic hepatitis B. *Value Health* 2010;13(8):934-45.

[D31] Dakin HA, Welton NJ, Ades AE, Collins S, Orme M, Kelly S. Mixed treatment comparison of repeated measurements of a continuous endpoint: an example using topical treatments for primary open-angle glaucoma and ocular hypertension. *Stat Med* 2011;30(20):2511-35.

[D32] Dequen P, Lorigan P, Jansen JP, van Baardewijk M, Ouwens MJ, Kotapati S. Systematic review and network meta-analysis of overall survival comparing 3 mg/kg ipilimumab with alternative therapies in the management of pretreated patients with unresectable stage III or IV melanoma. *Oncologist* 2012;17(11):1376-85.

[D33] Dunkley AJ, Charles K, Gray LJ, Camosso-Stefinovic J, Davies MJ, Khunti K. Effectiveness of interventions for reducing diabetes and cardiovascular disease risk in people with metabolic syndrome: systematic review and mixed treatment comparison meta-analysis. *Diabetes Obes Metab* 2012;14(7):616-25.

[D34] Eckert L, Falissard B. Using meta-regression in performing indirect-comparisons: Comparing escitalopram with venlafaxine XR. *Curr Med Res Opin* 2006;22(11):2313-21.

[D35] Eckert L, Lançon C. Duloxetine compared with fluoxetine and venlafaxine: use of meta-regression analysis for indirect comparisons. *BMC Psychiatry* 2006;6:30.

[D36] Edwards SJ, Lind T, Lundell L, Das R. Systematic review: standard- and double-dose proton pump inhibitors for the healing of severe erosive oesophagitis - a mixed treatment comparison of randomized controlled trials. *Aliment Pharmacol Ther* 2009;30(6):547-56.

[D37] Edwards SJ, Smith CJ. Tolerability of atypical antipsychotics in the treatment of adults with schizophrenia or bipolar disorder: a mixed treatment comparison of randomized controlled trials. *Clin Ther* 2009;31:1345-59.

[D38] Edwards SJ, Clarke MJ, Wordsworth S, Welton NJ. Carbapenems versus other beta-lactams in the treatment of hospitalised patients with infection: a mixed treatment comparison. *Curr Med Res Opin* 2009;25(1):251-61.

[D39] Eisenberg MJ, Fillion KB, Yavin D, Bélisle P, Mottillo S, Joseph L, et al. Pharmacotherapies for smoking cessation: a meta-analysis of randomized controlled trials. *CMAJ* 2008;179(2):135-44.

[D40] Fakhoury W, Lockhart I, Kotchie RW, Aagren M, LeReun C. Indirect comparison of once daily insulin detemir and glargine in reducing weight gain and hypoglycaemic episodes when administered in addition to conventional oral anti-diabetic therapy in patients with type-2 diabetes. *Pharmacology* 2008;82(2):156-63.

[D41] Filippini G, Del Giovane C, Vacchi L, D'Amico R, Di Pietrantonj C, Beecher D, et al. Immunomodulators and immunosuppressants for multiple sclerosis: a network meta-analysis. *Cochrane Database of Syst Rev* 2013;6;CD008933.

[D42] Fox BD, Kahn SR, Langleben D, Eisenberg MJ, Shimony A. Efficacy and safety of novel oral anticoagulants for treatment of acute venous thromboembolism: direct and adjusted indirect meta-analysis of randomised controlled trials. *BMJ* 2012;345:e7498.

[D43] Freemantle N, Lafuente-Lafuente C, Mitchell S, Eckert L, Reynolds M. Mixed treatment comparison of dronedarone, amiodarone, sotalol, flecainide, and propafenone, for the management of atrial fibrillation. *Europace* 2011;13(3):329-45.

[D44] Freemantle N, Tharmanathan P, Herbrecht R. Systematic review and mixed treatment comparison of randomized evidence for empirical, pre-emptive and directed treatment strategies for invasive mould disease. *J Antimicrob Chemother* 2011;66 Suppl 1:i25-35.

[D45] Freemantle N, Cooper C, Diez-Perez A, Gitlin M, Radcliffe H, Shepherd S, et al. Results of indirect and mixed treatment comparison of fracture efficacy for osteoporosis treatments: a meta-analysis. *Osteoporos Int* 2013;24(1):209-17.

[D46] Golfinopoulos V, Salanti G, Pavlidis N, Ioannidis JP. Survival and disease-progression benefits with treatment regimens for advanced colorectal cancer: a meta-analysis. *Lancet Oncol* 2007;8(10):898-911.

[D47] Golfinopoulos V, Pentheroudakis G, Salanti G, Nearchou AD, Ioannidis JP, Pavlidis N. Comparative survival with diverse chemotherapy regimens for cancer of unknown primary site: multiple-treatments meta-analysis. *Cancer Treat Rev* 2009;35(7):570-3.

[D48] Gray LJ, Cooper N, Dunkley A, Warren FC, Ara R, Abrams K, et al. A systematic review and mixed treatment comparison of pharmacological interventions for the treatment of obesity. *Obes Rev* 2012;13(6):483-98.

[D49] Guyot P, Taylor P, Christensen R, Pericleous L, Poncet C, Lebmeier M, et al. Abatacept with methotrexate versus other biologic agents in treatment of patients with active rheumatoid arthritis despite methotrexate: a network meta-analysis. *Arthritis Res Ther* 2011;13(6):R204.

[D50] Haas DM, Caldwell DM, Kirkpatrick P McIntosh JJ, Welton NJ. Tocolytic therapy for preterm delivery: systematic review and network meta-analysis. *BMJ* 2012;345:e6226.

[D51] Halpin DM, Gray J, Edwards SJ, Morais J, Singh D. Budesonide/formoterol vs. salmeterol/fluticasone in COPD: a systematic review and adjusted indirect comparison of pneumonia in randomised controlled trials. *Int J Clin Pract* 2011;65(7):764-74.

[D52] Harenberg J, Marx S, Diener HC, Lip GY, Marder VJ, Wehling M, et al. Comparison of efficacy and safety of dabigatran, rivaroxaban and apixaban in patients with atrial fibrillation using network meta-analysis. *Int Angiol* 2012;31(4):330-9.

[D53] Harenberg J, Marx S, Dahl OE, Marder VJ, Schulze A, Wehling M, et al. Interpretation of endpoints in a network meta-analysis of new oral anticoagulants following total hip or total knee replacement surgery. *Thromb Haemost* 2012;108(5):903-12.

[D54] Hartling L, Fernandes RM, Bialy L, Milne A, Johnson D, Plint A, et al. Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis. *BMJ* 2011;342:d1714.

[D55] Häuser W, Petzke F, Sommer C. Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. *J Pain* 2010;11(6):505-21.

[D56] Häuser W, Petzke F, Üçeyler N, Sommer C. Comparative efficacy and acceptability of amitriptyline, duloxetine and milnacipran in fibromyalgia syndrome: a systematic review with meta-analysis. *Rheumatology* 2011;50(3):532-43.

[D57] Henry D, Carless P, Fergusson D, Laupacis A. The safety of aprotinin and lysine-derived antifibrinolytic drugs in cardiac surgery: a meta-analysis. *CMAJ* 2009;180(2):183-93.

[D58] Hochberg MC, Tracy JK, Hawkins-Holt M, Flores RH. Comparison of the efficacy of the tumour necrosis factor α blocking agents adalimumab, etanercept, and infliximab when added to methotrexate in patients with active rheumatoid arthritis. *Ann Rheum Dis* 2003;62 Supply 2:13-6.

[D59] Hochberg MC, Berry S, Broglio K, Rosenblatt L, Nadkarni A, Trivedi D, et al. Mixed treatment comparison of efficacy and tolerability of biologic agents in patients with rheumatoid arthritis. *Curr Med Res Opin* 2013;29(10):1213-22.

[D60] Hopkins RB, Goeree R, Pullenayegum E, Adachi JD, Papaioannou A, Xie F, et al. The relative efficacy of nine osteoporosis medications for reducing the rate of fractures in post-menopausal women. *BMC Musculoskelet Disord* 2011;12:209.

[D61] Howell N, Senanayake E, Freemantle N, Pagano D. Putting the record straight on aprotinin as safe and effective: results from a mixed treatment meta-analysis of trials of aprotinin. *J Thorac Cardiovasc Surg* 2013;145(1):234-40.

[D62] Hutton B, Joseph L, Fergusson D, Mazer CD, Shapiro S, Tinmouth A. Risks of harms using antifibrinolytics in cardiac surgery: systematic review and network meta-analysis of randomised and observational studies. BMJ 2012;345:e5798.

[D63] Jansen JP, Bergman GJ, Huels J, Olson M. Prevention of vertebral fractures in osteoporosis: mixed treatment comparison of bisphosphonate therapies. *Curr Med Res Opin* 2009;25(8):1861-8.

[D64] Jansen JP, Bergman GJ, Huels J, Olson M. The efficacy of bisphosphonates in the prevention of vertebral, hip, and nonvertebral-nonhip fractures in osteoporosis: a network meta-analysis. *Semin Arthritis Rheum* 2011;40(4):275-84.e1-2.

[D65] Kinnaird T, Medic G, Casella G, Schiele F, Kaul U, Radke PW, et al. Relative efficacy of bivalirudin versus heparin monotherapy in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: a network meta-analysis. *J Blood Med* 2013;4:129-40.

[D66] Knottnerus BJ, Grigoryan L, Geerlings SE, Moll van Charante EP, Verheij TJ, Kessels AG, et al. Comparative effectiveness of antibiotics for uncomplicated urinary tract infections: network meta-analysis of randomized trials. *Fam Pract* 2012;29(6):659-70.

[D67] Krogh TP, Bartels EM, Ellingsen T, Stengaard-Pedersen K, Buchbinder R, Fredberg U, et al. Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network meta-analysis of randomized controlled trials. *Am J Sports Med* 2013;41(6):1435-46.

[D68] Kwok CS, Yeong JK, Loke YK. Meta-analysis: risk of fractures with acid-suppressing medication. *Bone* 2011;48(4):768-76.

[D69] Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, Loke YK. Risk of Clostridium difficile infection with acid suppressing drugs and antibiotics: meta-analysis. *Am J Gastroenterol* 2012;107(7):1011-9.

[D70] Kwok CS, Pradhan S, Yeong JK, Loke YK. Relative effects of two different enoxaparin regimens as comparators against newer oral anticoagulants: meta-analysis and adjusted indirect comparison. *Chest* 2013;144(2):593-600.

[D71] Kyrgiou M, Salanti G, Pavlidis N, Paraskevaidis E, Ioannidis JP. Survival benefits with diverse chemotherapy regimens for ovarian cancer: meta-analysis of multiple treatments. *J Natl Cancer Inst* 2006;98(22):1655-63.

[D72] Lanas A, Wu P, Medin J, Mills EJ. Low doses of acetylsalicylic acid increase risk of gastrointestinal bleeding in a meta-Analysis. *Clin Gastroenterol Hepatol* 2011;9(9):762-82.e6.

[D73] Lang SH, Manning N, Armstrong N, Misso K, Allen A, Di Nisio M, et al. Treatment with tirofiban for acute coronary syndrome (ACS): a systematic review and network analysis. *Curr Med Res Opin* 2012;28(3):351-70.

[D74] Larkin J, Paine A, Tumur I, Cappelleri JC, Healey PJ Sr, Foley G, et al. Second-line treatments for the management of advanced renal cell carcinoma: systematic review and meta-analysis. *Expert Opin Pharmacother* 2013;14(1):27-39.

[D75] Lereun C, Wells P, Diamantopoulos A, Rasul F, Lees M, Sengupta N. An indirect comparison, via enoxaparin, of rivaroxaban with dabigatran in the prevention of venous thromboembolism after hip or knee replacement. J Med Econ 2011;14(2):238-44.

[D76] Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, Richter F, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet* 2013;382(9896):951-62.

[D77] Lip GYH, Larsen TB, Skjøth F, Rasmussen LH. Indirect comparisons of new oral anticoagulant drugs for efficacy and safety when used for stroke prevention in atrial fibrillation. *J Am Coll Cardiol* 2012;60(8):738-46.

[D78] Littlewood KJ, Higashi K, Jansen JPO, Capkun-Niggli G, Balp MM, Doering G, et al. A network meta-analysis of the efficacy of inhaled antibiotics for chronic Pseudomonas infections in cystic fibrosis. *J Cyst Fibros* 2012;11(5):419-26.

[D79] Loke YK, Kwok CS. Dabigatran and rivaroxaban for prevention of venous thromboembolism - systematic review and adjusted indirect comparison. *J Clin Pharm Ther* 2011;36(1):111-24.

[D80] Manzoli L, Salanti G, De Vito C, Boccia A, Ioannidis JP, Villari P. Immunogenicity and adverse events of avian influenza A H5N1 vaccine in healthy adults: multiple-treatments meta-analysis. *Lancet Infect Dis* 2009;9(8):482-92.

[D81] Manzoli L, De Vito C, Salanti G, D'Addario M, Villari P, Ioannidis JP. Meta-analysis of the immunogenicity and tolerability of pandemic influenza A 2009 (H1N1) vaccines. PLoS One 2011;6(9):e24384.

[D82] Mauri D, Polyzos NP, Salanti G, Pavlidis N, Ioannidis JP. Multiple-treatments meta-analysis of chemotherapy and targeted therapies in advanced breast cancer. *J Natl Cancer Inst* 2008;100(24):1780-91.

[D83] McIntosh B, Cameron C, Singh SR, Yu C, Ahuja T, Welton NJ, et al. Second-line therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed-treatment comparison meta-analysis. *Open Med* 2011;5(1):35-48.

[D84] McIntosh B, Cameron C, Singh SR, Yu C, Dolovich L, Houlden R. Choice of therapy in patients with type 2 diabetes inadequately controlled with metformin and a sulphonylurea: a systematic review and mixed-treatment comparison meta-analysis. *Open Med* 2012;6(2):e62-74.

[D85] Meissner K, Fässler M, Rücker G, Kleijnen J, Hróbjartsson A, Schneider A, et al. Differential effectiveness of placebo treatments: a systematic review of migraine prophylaxis. *JAMA Intern Med* 2013;173(21):1941-51.

[D86] Mills EJ, Rachlis B, Wu P, Devereaux PJ, Arora P, Perri D. Primary prevention of cardiovascular mortality and events with statin treatments: a network meta-analysis involving more than 65,000 patients. *J Am Coll Cardiol* 2008;52(22):1769-81.

[D87] Mills EJ, Perri D, Cooper C, Nachega JB, Wu P, Tleyjeh I, et al. Antifungal treatment for invasive Candida infections: a mixed treatment comparison meta-analysis. *Ann Clin Microbiol Antimicrob* 2009;8:23.

[D88] Mills EJ, Rachlis B, O'Regan C, Thabane L, Perri D. Metastatic renal cell cancer treatments: an indirect comparison meta-analysis. *BMC Cancer* 2009;9:34.

[D89] Mills EJ, Wu P, Spurden D, Ebbert JO, Wilson K. Efficacy of pharmacotherapies for short-term smoking abstinance: a systematic review and meta-analysis. Harm Reduct J 2009;6:25.

[D90] Mills EJ, Druyts E, Ghement I, Puhan MA. Pharmacotherapies for chronic obstructive pulmonary disease: a multiple treatment comparison meta-analysis. *Clin Epidemiol* 2011;3(1):107-29.

[D91] Mills EJ, Wu P, Chong G, Ghement I, Singh S, Akl EA, et al. Efficacy and safety of statin treatment for cardiovascular disease: a network meta-analysis of 170,255 patients from 76 randomized trials. *QJM* 2011;104(2):109-24.

[D92] Mills EJ, Wu P, Lockhart I, Thorlund K, Phuan M, Ebbert JO. Comparisons of high-dose and combination nicotine replacement therapy, varenicline, and bupropion for smoking cessation: a systematic review and multiple treatment meta-analysis. *Ann Med* 2012;44(6):588-97.

[D93] Mitchell SA, Simon TA, Raza S, Jakouloff D, Orme ME, Lockhart I, et al. The efficacy and safety of oral anticoagulants in warfarin-suitable patients with nonvalvular atrial fibrillation: systematic review and meta-analysis. *Clin Appl Thromb Hemost* 2013;19(6):619-31.

[D94] Murad MH, Drake MT, Mullan RJ, Mauck KF, Stuart LM, Lane MA, et al. Clinical review. Comparative effectiveness of drug treatments to prevent fragility fractures: a systematic review and network meta-analysis. *J Clin Endocrinol Metab* 2012;97(6):1871-80.

[D95] Naci H, Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ* 2013;347:f5577.

[D96] Naci H, Brugts JJ, Ades T. Comparative tolerability and harms of individual statins: a study-level network meta-analysis of 246 955 participants from 135 randomized, controlled trials. *Circ Cardiovasc Qual Outcomes* 2013;6(4):390-9.

[D97] Naci H, Brugts JJ, Fleurence R, Tsoi B, Toor H, Ades AE. Comparative benefits of statins in the primary and secondary prevention of major coronary events and all-cause mortality: a network meta-analysis of placebo-controlled and active-comparator trials. *Eur J Prev Cardiol* 2013;20(4):641-57.

[D98] Naci H, Brugts JJ, Fleurence R, Ades AE. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. *Eur J Prev Cardiol* 2013;20(4):658-70.

[D99] Naci H, Brugts JJ, Fleurence R, Ades AE. Comparative effects of statins on major cerebrovascular events: a multiple-treatments meta-analysis of placebo-controlled and active-comparator trials. *QJM* 2013;106(4):299-306.

[D100] Naudet F, Millet B, Charlier P, Reymann JM, Maria AS, Falissard B. Which placebo to cure depression? A thought-provoking network meta-analysis. *BMC Med* 2013;11(1):230.

[D101] Navarese EP, Buffon A, Andreotti F, Kozinski M, Welton N, Fabiszak T, et al. Meta-analysis of impact of different types and doses of statins on new-onset diabetes mellitus. *Am J Cardiol* 2013;111(8):1123-30.

[D102] Nüesch E, Häuser W, Bernardy K, Barth J, Jüni P. Comparative efficacy of pharmacological and non-pharmacological interventions in fibromyalgia syndrome: network meta-analysis. *Ann Rheum Dis* 2013;72(6):955-62.

[D103] Orme M, Collins S, Dakin H, Kelly S, Loftus J. Mixed treatment comparison and meta-regression of the efficacy and safety of prostaglandin analogues and comparators for primary open-angle glaucoma and ocular hypertension. *Curr Med Res Opin* 2010;26(3):511-28.

[D104] Orme ME, Macgilchrist KS, Mitchell S, Spurden D, Bird A. Systematic review and network meta-analysis of combination and monotherapy treatments in disease-modifying antirheumatic drug-experienced patients with rheumatoid arthritis: analysis of American college of Rheumatology criteria scores 20, 50, and 70. *Biologics* 2012;6:429-64.

[D105] Phung OJ, Scholle JM, Talwar M, Coleman CI. Effect of noninsulin antidiabetic drugs added to metformin therapy on glycemic control, weight gain, and hypoglycemia in type 2 diabetes. *JAMA* 2010;303(14):1410-8.

[D106] Phung OJ, Kahn SR, Cook DJ, Murad MH. Dosing frequency of unfractionated heparin thromboprophylaxis: a meta-analysis. *Chest* 2011;140(2):374-81.

[D107] Phung OJ, Sood NA, Sill BE, Coleman CI. Oral anti-diabetic drugs for the prevention of Type 2 diabetes. *Diabet Med* 2011;28(8):948-64.

[D108] Puhan MA, Bachmann LM, Kleijnen J, Ter Riet G, Kessels AG. Inhaled drugs to reduce exacerbations in patients with chronic obstructive pulmonary disease: a network meta-analysis. *BMC Med* 2009;7:2.

[D109] Quilici S, Abrams KR, Nicolas A, Martin M, Petit C, Lleu PL, et al. Meta-analysis of the efficacy and tolerability of pramipexole versus ropinirole in the treatment of restless legs syndrome. *Sleep Med* 2008;9(7):715-26.

[D110] Quilici S, Chancellor J, Löthgren M, Simon D, Said G, Le TK, et al. Meta-analysis of duloxetine vs. pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain. *BMC Neurol* 2009;9:6.

[D111] Rashiq S, Vandermeer B, Abou-Setta AM, Beaupre LA, Jones CA, Dryden DM. Efficacy of supplemental peripheral nerve blockade for hip fracture surgery: multiple treatment comparison. *Can J Anesth* 2013;60(3):230-43.

[D112] Rasmussen LH, Larsen TB, Graungaard T, Skjøth F, Lip GY. Primary and secondary prevention with new oral anticoagulant drugs for stroke prevention in atrial fibrillation: indirect comparison analysis. *BMJ* 2012;345:e7097.

[D113] Riemsma R, Simons JP, Bashir Z, Gooch CL, Kleijnen J. Systematic Review of topotecan (Hycamtin) in relapsed small cell lung cancer. *BMC Cancer* 2010;10:436.

[D114] Riemsma R, Forbes CA, Kessels A, Lykopoulos K, Amonkar MM, Rea DW, et al. Systematic review of aromatase inhibitors in the first-line treatment for hormone sensitive advanced or metastatic breast cancer. *Breast Cancer Res Treat* 2010;123(1):9-24.

[D115] Riemsma R, Forbes C, Harker J, Worthy G, Misso K, Schäfer M, et al. Systematic review of tapentadol in chronic severe pain. *Curr Med Res Opin* 2011;27(10):1907-30.

[D116] Riemsma R, Forbes CA, Amonkar MM, Lykopoulos K, Diaz JR, Kleijnen J, et al. Systematic review of lapatinib in combination with letrozole compared with other first-line treatments for hormone receptor positive(HR+) and HER2+ advanced or metastatic breast cancer(MBC). *Curr Med Res Opin* 2012;28(8):1263-79.

[D117] Roskell NS, Lip GY, Noack H, Clemens A, Plumb JM. Treatments for stroke prevention in atrial fibrillation: a network meta-analysis and indirect comparisons versus dabigatran etexilate. *Thromb Haemost* 2010;104(6):1106-15.

[D118] Roskell NS, Beard SM, Zhao Y, Le TK. A meta-analysis of pain response in the treatment of fibromyalgia. *Pain Pract* 2011;11(6):516-27.

[D119] Roskell NS, Zimovetz EA, Rycroft CE, Eckert BJ, Tyas DA. Annualized relapse rate of first-line treatments for multiple sclerosis: a meta-analysis, including indirect comparisons versus fingolimod. *Curr Med Res Opin* 2012;28(5):767-80.

[D120] Salliot C, Finckh A, Katchamart W, Lu Y, Sun Y, Bombardier C, et al. Indirect comparisons of the efficacy of biological antirheumatic agents in rheumatoid arthritis in patients with an inadequate response to conventional disease-modifying antirheumatic drugs or to an anti-tumour necrosis factor agent: a meta-analysis. *Ann Rheum Dis* 2011;70(2):266-71.

[D121] Singh JA, Christensen R, Wells GA, Suarez-Almazor ME, Buchbinder R, Lopez-Olivo MA, et al. A network meta-analysis of randomized controlled trials of biologics for rheumatoid arthritis: a Cochrane overview. *CMAJ* 2009;181(11):787-96.

[D122] Singh JA, Wells GA, Christensen R, Tanjong Ghogomu E, Maxwell L, Macdonald JK, et al. Adverse effects of biologics: a network meta-analysis and Cochrane overview. *Cochrane Database Syst Rev* 2011;(2):CD008794.

[D123] Skoetz N, Trelle S, Rancea M, Haverkamp H, Diehl V, Engert A, et al. Effect of initial treatment strategy on survival of patients with advanced-stage Hodgkin's lymphoma: a systematic review and network meta-analysis. *Lancet Oncol* 2013;14(10):943-52.

[D124] Snedecor SJ, Sudharshan L, Cappelleri JC, Sadosky A, Desai R, Jalundhwala YJ, et al. Systematic review and comparison of pharmacologic therapies for neuropathic pain associated with spinal cord injury. *J Pain Res* 2013;6:539-47.

[D125] Stam WB, Jansen J, Taylor S. Efficacy of etoricoxib, celecoxib, lumiracoxib, non-selective NSAIDs, and acetaminophen in osteoarthritis: a mixed treatment comparison. *Open Rheumatol J* 2012;6(1):6-20.

[D126] Steiner S, Moertl D, Chen L, Coyle D, Wells GA. Network meta-analysis of prasugrel, ticagrelor, high- and standard-dose clopidogrel in patients scheduled for percutaneous coronary interventions. *Thromb Haemost* 2012;108(2):318-27.

[D127] Strassmann R, Bausch B, Spaar A, Kleijnen J, Braendli O, Puhan MA. Smoking cessation interventions in COPD: a network meta-analysis of randomised trials. *Eur Respir J* 2009;34(3):634-40.

[D128] Sundaresh V, Brito JP, Wang Z, Prokop LJ, Stan MN, Murad MH, et al. Comparative effectiveness of therapies for graves' hyperthyroidism: a systematic review and network meta-Analysis. *J Clin Endocrinol Metab* 2013;98(9):3671-7.

[D129] Thorlund K, Druyts E, Aviña-Zubieta JA, Mills EJ. Anti-tumor necrosis factor (TNF) drugs for the treatment of psoriatic arthritis: an indirect comparison meta-analysis. *Biologics* 2012;6:417-27.

[D130] Trelle S, Reichenbach S, Wandel S, Hildebrand P, Tschannen B, Villiger PM, et al. Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. *BMJ* 2011;342:c7086.

[D131] van de Kerkhof P, de Peuter R, Ryttov J, Jansen JP. Mixed treatment comparison of a two-compound formulation (TCF) product containing calcipotriol and betamethasone dipropionate with other topical treatments in psoriasis vulgaris. *Curr Med Res Opin* 2011;27(1): 225-38.

[D132] van der Mark LB, Lyklema PH, Geskus RB, Mohrs J, Bindels PJ, van Aalderen WM, et al. A systematic review with attempted network meta-analysis of asthma therapy recommended for five to eighteen year olds in GINA steps three and four. *BMC Pulm Med* 2012;12:63.

[D133] Vieira MC, Kumar RN, Jansen JP. Comparative effectiveness of efavirenz, protease inhibitors, and raltegravir-based regimens as first-line treatment for HIV-infected adults: a mixed treatment comparison. *HIV Clin Trials* 2011;12(4):175-89.

[D134] Vissers D, Stam W, Nolte T, Lenre M, Jansen J. Efficacy of intranasal fentanyl spray versus other opioids for breakthrough pain in cancer. *Curr Med Res Opin* 2010;26(5):1037-45.

[D135] Wandel S, Jüni P, Tendal B, Nüesch E, Villiger PM, Welton NJ, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ* 2010;341:c4675.

[D136] Wehren LE, Hosking D, Hochberg MC. Putting evidence-based medicine into clinical practice: comparing anti-resorptive agents for the treatment of osteoporosis. *Curr Med Res Opin* 2004;20(4):525-31.

[D137] Welton NJ, Cooper NJ, Ades AE, Lu G, Sutton AJ. Mixed treatment comparison with multiple outcomes reported inconsistently across trials: evaluation of antivirals for treatment of influenza A and B. *Stat Med* 2008;27(27):5620-39.

[D138] Wolff RF, Bala MM, Westwood M, Kessels AG, Kleijnen J. 5% lidocaine medicated plaster in painful diabetic peripheral neuropathy (DPN): a systematic review. *Swiss Med Wkly* 2010;140(21-22):297-306.

[D139] Wolff RF, Bala MM, Westwood M, Kessels AG, Kleijnen J. 5% lidocaine-medicated plaster vs other relevant interventions and placebo for post-herpetic neuralgia (PHN): a systematic review. *Acta Neurol Scand* 2011;123(5):295-309.

[D140] Wolff RF, Aune D, Truyers C, Hernandez AV, Misso K, Riemsma R, et al. Systematic review of efficacy and safety of buprenorphine versus fentanyl or morphine in patients with chronic moderate to severe pain. *Curr Med Res Opin* 2012;28(5):833-45.

[D141] Wu P, Wilson K, Dimoulas P, Mills EJ. Effectiveness of smoking cessation therapies: a systematic review and meta-analysis. *BMC Public Health* 2006;6:300.

[D142] Yazdanpanah Y, Sissoko D, Egger M, Mouton Y, Zwahlen M, Chêne G. Clinical efficacy of antiretroviral combination therapy based on protease inhibitors or non-nucleoside analogue reverse transcriptase inhibitors: indirect comparison of controlled trials. *BMJ* 2004;328(7434):249.

[D143] Zhou Z, Rahme E, Pilote L. Are statins created equal? Evidence from randomized trials of pravastatin, simvastatin, and atorvastatin for cardiovascular disease prevention. *Am Heart J* 2006;151(2):273-81.

[D144] Biondi-Zoccai G, Lotrionte M, Agostoni P, Abbate A, Romagnoli E, Sangiorgi G, et al. Adjusted indirect comparison meta-analysis of prasugrel versus ticagrelor for patients with acute coronary syndromes. *Int J Cardiol* 2011;150(3):325-31.

[D145] Biondi-Zoccai G, Malavasi V, D'Ascenzo F, Abbate A, Agostoni P, Lotrionte M, et al. Comparative effectiveness of novel oral anticoagulants for atrial fibrillation: evidence from pair-wise and warfarin-controlled network meta-analyses. *HSR Proc Intensive Care Cardiovasc Anesth* 2013;5(1):40-54.

[D146] Chatterjee S, Biondi-Zoccai G, Abbate A, D'Ascenzo F, Castagno D, Van Tassell B, et al. Benefits of beta blockers in patients with heart failure and reduced ejection fraction: network meta-analysis. *BMJ* 2013;346:f55.

[D147] Chatterjee S, Sardar P, Biondi-Zoccai G, Kumbhani DJ. New oral anticoagulants and the risk of intracranial hemorrhage: traditional and Bayesian meta-analysis and mixed treatment comparison of randomized trials of new oral anticoagulants in atrial fibrillation. *JAMA Neurol* 2013;70(12):1486-90.

[D148] Chatterjee S, Ghose A, Sharma A, Guha G, Mukherjee D, Frankel R. Comparing newer oral anti-platelets prasugrel and ticagrelor in reduction of ischemic events-evidence from a network meta-analysis. *J Thromb Thrombolysis* 2013;36(3):223-32.

[D149] Chatterjee S, Sardar P, Mukherjee D, Lichstein E, Aikat S. Timing and route of amiodarone for prevention of postoperative atrial fibrillation after cardiac surgery: a network regression meta-analysis. *Pacing Clin Electrophysiol* 2013;36(8):1017-23.

[D150] Landoni G, Greco T, Biondi-Zoccai G, Nigro Neto C, Febres D, Pintaudi M, et al. Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery. *Br J Anaesth* 2013;111(6):886-96.

[D151] Sardar P, Chatterjee S, Wu WC, Lichstein E, Ghosh J, Aikat S, Muhkerjee D. New oral anticoagulants are not superior to warfarin in secondary prevention of stroke or transient ischemic attacks, but lower the risk of intracranial bleeding: insights from a meta-analysis and indirect treatment comparisons. *PLoS One* 2013;8(10):e77694.

[D152] Testa L, Agnifili M, Latini RA, Mattioli R, Lanotte S, De Marco F, et al. Adjusted indirect comparison of new oral anticoagulants for stroke prevention in atrial fibrillation. *QJM* 2012;105(10):949-57.

[D153] Chen JM, Heran BS, Wright JM. Blood pressure lowering efficacy of diuretics as second-line therapy for primary hypertension. *Cochrane Database Syst Rev* 2009;(4):CD007187.

[D154] Chen JM, Heran BS, Perez MI, Wright JM. Blood pressure lowering efficacy of beta-blockers as second-line therapy for primary hypertension. *Cochrane Database Syst Rev* 2010;(1):CD007185.

[D155] Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin converting enzyme (ACE) inhibitors for primary hypertension. *Cochrane Database Syst Rev* 2008;(4):CD003823.

[D156] Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin receptor blockers for primary hypertension. *Cochrane Database Syst Rev* 2008;(4):CD003822.

[D157] Heran BS, Galm BP, Wright JM. Blood pressure lowering efficacy of alpha blockers for primary hypertension. *Cochrane Database Syst Rev* 2009;(4):CD004643.

[D158] Heran BS, Chen JM, Wang JJ, Wright JM. Blood pressure lowering efficacy of potassium-sparing diuretics (that block the epithelial sodium channel) for primary hypertension. *Cochrane Database Syst Rev* 2010;(1):CD008167.

[D159] Heran BS, Galm BP, Wright JM. Blood pressure lowering efficacy of alpha blockers for primary hypertension. *Cochrane Database Syst Rev* 2012;(8):CD004643.

[D160] Heran BS, Chen JM, Wang JJ, Wright JM. Blood pressure lowering efficacy of potassium-sparing diuretics (that block the epithelial sodium channel) for primary hypertension. Cochrane Database Syst Rev 2012;(11):CD008167.

[D161] Dewilde S, Hawkins N. Investigating incoherence gives insight: clopidogrel is equivalent to extended-release dipyridamole plus aspirin in secondary stroke prevention. *J Clin Epidemiol* 2012;65(8):835-45.

[D162] Gross JL, Kramer CK, Leitão CB, Hawkins N, Viana LV, Schaan BD, et al. Effect of antihyperglycemic agents added to metformin and a sulfonylurea on glycemic control and weight gain in type 2 diabetes: a network meta-analysis. *Ann Intern Med* 2011;154(10):672-9.

[D163] Khan N, Shah D, Tongbram V, Verdian L, Hawkins N. The efficacy and tolerability of perampanel and other recently approved anti-epileptic drugs for the treatment of refractory partial onset seizure: a systematic review and Bayesian network meta-analysis. *Curr Med Res Opin* 2013;29(8):1001-13.

[D164] Mealing S, Barcena L, Hawkins N, Clark J, Eaton V, Hirji I, Davis C. The relative efficacy of imatinib, dasatinib and nilotinib for newly diagnosed chronic myeloid leukemia: a systematic review and network meta-analysis. *Exp Hematol Oncol* 2013;2(1):5.

[D165] Reich K, Burden AD, Eaton JN, Hawkins NS. Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials. *Br J Dermatol* 2012;166(1):179-88.

[D166] Scott DA, Boye KS, Timlin L, Clark JF, Best JH. A network meta-analysis to compare glycaemic control in patients with type 2 diabetes treated with exenatide once weekly or liraglutide once daily in comparison with insulin glargine, exenatide twice daily or placebo. *Diabetes Obes Metab* 2013;15(3):213-23.

[D167] Desai RJ, Hansen RA, Rao JK, Wilkins TM, Harden EA, Yuen A, et al. Mixed treatment comparison of the treatment discontinuations of biologic disease-modifying antirheumatic drugs in adults with rheumatoid arthritis. *Ann Pharmacother* 2012;46(11):1491-505.

[D168] Gartlehner G, Hansen RA, Jonas BL, Thieda P, Lohr KN. The comparative efficacy and safety of biologics for the treatment of rheumatoid arthritis: a systematic review and metaanalysis. *J Rheumatol* 2006;33(12):2398-408.

[D169] Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, et al. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. *Ann Intern Med* 2011;155(11):772-85.

[D170] Hansen RA, Gartlehner G, Webb AP, Morgan LC, Moore CG, Jonas DE. Efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease: a systematic review and meta-analysis. *Clin Interv Aging* 2008;3(2):211-25.

[D171] Hansen RA, Gaynes BN, Gartlehner G, Moore CG, Tiwari R, Lohr KN. Efficacy and tolerability of second-generation antidepressants in social anxiety disorder. *Int Clin Psychopharmacol* 2008;23(3):170-9.

[D172] Signorovitch JE, Wu EQ, Yu AP, Gerrits CM, Kantor E, Bao Y, et al. Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept. *Pharmacoeconomics* 2010;28(10):935-45.

[D173] Signorovitch JE, Wu EQ, Swallow E, Kantor E, Fan L, Gruenberger JB. Comparative efficacy of vildagliptin and sitagliptin in Japanese patients with type 2 diabetes mellitus: a matching-adjusted indirect comparison of randomized trials. *Clin Drug Investig* 2011;31(9):665-74.

[D174] Signorovitch JE, Wu EQ, Betts KA, Parikh K, Kantor E, Guo A, et al. Comparative efficacy of nilotinib and dasatinib in newly diagnosed chronic myeloid leukemia: a matching-adjusted indirect comparison of randomized trials. *Curr Med Res Opin* 2011;27(6):1263-71.

[D175] Signorovitch J, Erder MH, Xie J, Sikirica V, Lu M, Hodgkins PS, Wu EQ. Comparative effectiveness research using matching-adjusted indirect comparison: an application to treatment with guanfacine extended release or atomoxetine in children with attention-deficit/hyperactivity disorder and comorbid oppositional defiant disorder. *Pharmacoepidemiol Drug Saf* 2012;21 Suppl 2:130-7.

[D176] Sikirica V, Findling RL, Signorovitch J, Erder MH, Dammerman R, Hodgkins P, et al. Comparative efficacy of guanfacine extended release versus atomoxetine for the treatment of attention-deficit/hyperactivity disorder in children and adolescents: applying matching-adjusted indirect comparison methodology. *CNS Drugs* 2013;27(11):943-53.

[D177] Ribeiro RA, Ziegelmann PK, Duncan BB, Stella SF, da Costa Vieira JL, Restelatto LM, et al. Impact of statin dose on major cardiovascular events: a mixed treatment comparison meta-analysis involving more than 175,000 patients. *Int J Cardiol* 2013;166(2):431-9.

[D178] Rotta I, Ziegelmann PK, Otuki MF, Riveros BS, Bernardo NL, Correr CJ. Efficacy of topical antifungals in the treatment of dermatophytosis: a mixed-treatment comparison meta-analysis involving 14 treatments. *JAMA Dermatol* 2013;149(3):341-9.

[D179] Sanches AC, Correr CJ, Venson R, Pontarolo R. Revisiting the efficacy of long-acting insulin analogues on adults with type 1 diabetes using mixed-treatment comparisons. *Diabetes Res Clin Pract* 2011;94(3):333-9.

[D180] Sanches ACC, Correr CJ, Venson R, Gonçalves PR, Garcia MM, Piantavini S, et al. Insulin analogues versus human insulin in type 1 diabetes: direct and indirect meta-analyses of efficacy and safety. *Braz J Pharm Sci* 2013;49(3):501-9.

[D181] Wiens A, Lenzi L, Venson R, Correr CJ, Rotta I, Pedroso ML, et al. Comparative efficacy of oral nucleoside or nucleotide analog monotherapy used in chronic hepatitis B: a mixed-treatment comparison meta-analysis. *Pharmacotherapy* 2013;33(2):144-51.

[D182] Anothaisintawee T, Attia J, Nickel JC, Thammakraisorn S, Numthavaj P, McEvoy M, et al. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. *JAMA* 2011;305(1):78-86.

[D183] Jones LJ, Craven PD, Attia J, Thakkinstian A, Wright I. Network meta-analysis of indomethacin versus ibuprofen versus placebo for PDA in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2011;96(1):F45-52.

[D184] Numthavaj P, Thakkinstian A, Dejthevaporn C, Attia J. Corticosteroid and antiviral therapy for Bell's palsy: a network meta-analysis. *BMC Neurol* 2011;11:1.

[D185] Thakkinstian A, Attia J, Anothaisintawee T, Nickel JC. α-blockers, antibiotics and anti-inflammatories have a role in the management of chronic prostatitis/chronic pelvic pain syndrome. *BJU Int* 2012;110(7):1014-22.

[D186] Vejakama P, Thakkinstian A, Lertrattananon D, Ingsathit A, Ngarmukos C, Attia J. Reno-protective effects of renin-angiotensin system blockade in type 2 diabetic patients: a systematic review and network meta-analysis. *Diabetologia* 2012;55(3):566-78.

[D187] Dranitsaris G, Jelincic V, Choe Y. Meta regression analysis to indirectly compare dalteparin to enoxaparin for the prevention of venous thromboembolic events following total hip replacement. *Thromb J* 2011;9(1):3.

[D188] Dranitsaris G, Jelincic V, Choe Y. Meta-regression analysis to indirectly compare prophylaxis with dalteparin or enoxaparin in patients at high risk for venous thromboembolic events. *Clin Appl Thromb Hemost* 2012;18(3):233-42.

[D189] Dranitsaris G, Schmitz S, Broom RJ. Small molecule targeted therapies for the second-line treatment for metastatic renal cell carcinoma: a systematic review and indirect comparison of safety and efficacy. *J Cancer Res Clin Oncol* 2013;139(11):1917-26.

[D190] Kieran J, Schmitz S, O'Leary A, Walsh C, Bergin C, Norris S, et al. The relative efficacy of boceprevir and telaprevir in the treatment of hepatitis C virus genotype 1. *Clin Infect Dis* 2013;56(2):228-35.

[D191] Schmitz S, Adams R, Walsh CD, Barry M, FitzGerald O. A mixed treatment comparison of the efficacy of anti-TNF agents in rheumatoid arthritis for methotrexate non-responders demonstrates differences between treatments: a Bayesian approach. *Ann Rheum Dis* 2012;71(2): 225-30.

[D192] Chou R, Fu R, Huffman LH, Korthuis PT. Initial highly-active antiretroviral therapy with a protease inhibitor versus a non-nucleoside reverse transcriptase inhibitor: discrepancies between direct and indirect meta-analyses. *Lancet* 2006;368(9546):1503-15.

[D193] Chou R, Carson S, Chan BK. Pegylated interferons for chronic hepatitis C virus infection: an indirect analysis of randomized trials. *J Viral Hepat* 2008;15(8):551-70.

[D194] Chou R, Carson S, Chan BK. Gabapentin versus tricyclic antidepressants for diabetic neuropathy and post-herpetic neuralgia: discrepancies between direct and indirect meta-analyses of randomized controlled trials. *J Gen Intern Med* 2009;24(2):178-88.

[D195] Norris SL, Carson S, Roberts C. Comparative effectiveness of pioglitazone and rosiglitazone in type 2 diabetes, prediabetes, and the metabolic syndrome: a meta-analysis. *Curr Diabetes Rev* 2007;3(2):127-40.

[D196] Peterson K, McDonagh MS, Fu R. Comparative benefits and harms of competing medications for adults with attention-deficit hyperactivity disorder: a systematic review and indirect comparison meta-analysis. *Psychopharmacology* 2008;197(1):1-11.

[D197] Chang JWC, Thongprasert S, Wright E, Tsang K, Kim HT, Ahn MJ, et al. An indirect comparison of bevacizumab plus cisplatin-gemcitabine and cisplatin plus pemetrexed treatment for patients with advanced first-line non-squamous non-small cell lung cancer in East Asia. *Asia Pac J Clin Oncol* 2011;7 Suppl 2:13-21.

[D198] Mickisch GHJ, Schwander B, Escudier B, Bellmunt J, Maroto Jp, Porta C, et al. Indirect treatment comparison of bevacizumab + interferon-α-2a vs tyrosine kinase inhibitors in first-line metastatic renal cell carcinoma therapy. *Clinicoecon Outcomes Res* 2011;3(1):19-27.

[D199] Nuijten M, Heigener DF, Bischoff HG, Chouaid C, Vergnenègre A, de Castro Carpeño J, et al. Effectiveness of bevacizumab- and pemetrexed-cisplatin treatment for patients with advanced non-squamous non-small cell lung cancer. *Lung Cancer* 2010;69 Suppl 1):S4-10.

[D200] Nuijten MJ, Aultman R, Carpeño Jde C, Vergnenègre A, Chouaid C, Walzer S, et al. An indirect comparison of the efficacy of bevacizumab plus carboplatin and paclitaxel versus pemetrexed with cisplatin in patients with advanced or recurrent non-squamous adenocarcinoma non-small cell lung cancer. *Curr Med Res Opin* 2011;27(11):2193-201.

[D201] Liao WC, Chien KL, Lin YL, Wu MS, Lin JT, Wang HP, et al. Adjuvant treatments for resected pancreatic adenocarcinoma: a systematic review and network meta-analysis. *Lancet Oncol* 2013;14(11):1095-103.

[D202] Liu SC, Tu YK, Chien MN, Chien KL. Effect of antidiabetic agents added to metformin on glycaemic control, hypoglycaemia and weight change in patients with type 2 diabetes: a network meta-analysis. *Diabetes Obes Metab* 2012;14(9):810-20.

[D203] Wu HY, Huang JW, Lin JH, Liao WC, Peng YS, Hung KY, et al. Comparative effectiveness of renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes: systematic review and bayesian network meta-analysis. *BMJ* 2013;347:f6008.

[D204] Wu MS, Tan SC, Xiong T. Indirect comparison of randomised controlled trials: comparative efficacy of dexlansoprazole vs. esomeprazole in the treatment of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2013;38(2):190-201.

[D205] Bakalos G, Miligkos M, Doxani C, Mpoulimari I, Rodopoulou P, Zintzaras E. Assessing the relative effectiveness and tolerability of treatments in small cell lung cancer: a network meta-analysis. *Cancer Epidemiol* 2013;37(5):675-82.

[D206] Hadjigeorgiou GM, Doxani C, Miligkos M, Ziakas P, Bakalos G, Papadimitriou D, et al. A network meta-analysis of randomized controlled trials for comparing the effectiveness and safety profile of treatments with marketing authorization for relapsing multiple sclerosis. *J Clin Pharm Ther* 2013;38(6):433-9.

[D207] Zintzaras E, Doxani Mprotsis T, Schmid CH, Hadjigeorgiou GM. Network analysis of randomized controlled trials in multiple sclerosis. *Clin Ther* 2012;34(4):857-69.e9.

[D208] Ziogas DC, Voulgarelis M, Zintzaras E. A network meta-analysis of randomized controlled trials of induction treatments in acute myeloid leukemia in the elderly. *Clin Ther* 2011;33(3):254-79.

[D209] Kumar A, Hozo I, Wheatley K, Djulbegovic B. Thalidomide versus bortezomib based regimens as first-line therapy for patients with multiple myeloma: a systematic review. *Am J Hematol* 2011;86(1):18-24.

[D210] Mhaskar R, Redzepovic J, Wheatley K, Clark OA, Miladinovic B, Glasmacher A, et al. Bisphosphonates in multiple myeloma. *Cochrane Database Syst Rev* 2010;(3):CD003188.

[D211] Mhaskar R, Redzepovic J, Wheatley K, Clark OA, Miladinovic B, Glasmacher A, et al., Bisphosphonates in multiple myeloma: a network meta-analysis. *Cochrane Database Syst Rev* 2012;(5):CD003188.

[D212] Terasawa T, Trikalinos NA, Djulbegovic B, Trikalinos TA. Comparative efficacy of first-line therapies for advanced-stage chronic lymphocytic leukemia: a multiple-treatment meta-analysis. *Cancer Treat Rev* 2013;39(4):340-9.

[D213] Cheng MM, Goulart B, Veenstra Dl, Blough DK, Devine EB. A network meta-analysis of therapies for previously untreated chronic lymphocytic leukemia. *Cancer Treat Rev* 2012;38(8):1004-11.

[D214] Devine EB, Alfonso-Cristancho R, Sullivan SD. Effectiveness of biologic therapies for rheumatoid arthritis: an indirect comparisons approach. *Pharmacotherapy* 2011;31(1):39-51.

[D215] Lin VW, Ringold S, Devine EB. Comparison of ustekinumab with other biological agents for the treatment of moderate to severe plaque psoriasis: a Bayesian network meta-analysis. *Arch Dermatol* 2012;148(12):1403-10.

[D216] Ney JP, Devine EB, Watanabe JH, Sullivan SD. Comparative efficacy of oral pharmaceuticals for the treatment of chronic peripheral neuropathic pain: meta-analysis and indirect treatment comparisons. *Pain Med* 2013;14(5):706-19.

[D217] Migliore A, Bizzi E, Broccoli S, Laganà B. Indirect comparison of etanercept, infliximab, and adalimumab for psoriatic arthritis: mixed treatment comparison using placebo as common comparator. *Clin Rheumatol* 2012;31(1):133-7.

[D218] Migliore A, Broccoli S, Massafra U, Bizzi E, Frediani B. Mixed-treatment comparison of anabolic (teriparatide and PTH 1-84) therapies in women with severe osteoporosis. *Curr Med Res Opin* 2012;28(3):467-73.

[D219] Migliore A, Broccoli S, Bizzi E, Laganà B. Indirect comparison of the effects of anti-TNF biological agents in patients with ankylosing spondylitis by means of a mixed treatment comparison performed on efficacy data from published randomised, controlled trials. *J Med Econ* 2012;15(3):473-80.

[D220] Migliore A, Broccoli S, Massafra U, Cassol M, Frediani B. Ranking antireabsorptive agents to prevent vertebral fractures in postmenopausal osteoporosis by mixed treatment comparison meta-analysis. *Eur Rev Med Pharmacol Sci* 2013;17(5):658-67.

[D221] Wilhelmus KR. The treatment of herpes simplex virus epithelial keratitis. *Trans Am Ophthalmol Soc* 2000;98:505-32.

[D222] Wilhelmus KR. Therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Reviews* 2007;(1):CD002898.

[D223] Wilhelmus KR. Therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev* 2008;(1):CD002898.

[D224] Wilhelmus KR. Antiviral treatment and other therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev* 2010;(12):CD002898.

[D225] Coomarasamy A, Knox EM, Gee H, Song F, Khan KS. Effectiveness of nifedipine versus atosiban for tocolysis in preterm labour: a meta-analysis with an indirect comparison of randomised trials. *BJOG* 2003;110(12):1045-9.

[D226] Lim E, Ali Z, Ali A, Routledge T, Edmonds L, Altman DG, et al. Indirect comparison meta-analysis of aspirin therapy after coronary surgery. *BMJ* 2003;327(7427):1309-11.

[D227] Lim E, Harris G, Patel A, Adachi I, Edmonds L, Song F. Preoperative versus postoperative chemotherapy in patients with resectable non-small cell lung cancer systematic review and indirect comparison meta-analysis of randomized trials. *J Thorac Oncol* 2009;4(11): 1380-8.

[D228] Bansback N, Sizto S, Sun H, Feldman S, Willian MK, Anis A. Efficacy of systemic treatments for moderate to severe plaque psoriasis: systematic review and meta-analysis. *Dermatology* 2009;219(3):209-18.

[D229] Nixon R, Bansback N, Brennan A. The efficacy of inhibiting tumour necrosis factor alpha and interleukin 1 in patients with rheumatoid arthritis: a meta-analysis and adjusted indirect comparisons. *Rheumatology* 2007;46(7):1140-7.

[D230] Nixon RM, Bansback N, Brennan A. Using mixed treatment comparisons and meta-regression to perform indirect comparisons to estimate the efficacy of biologic treatments in rheumatoid arthritis. *Stat Med* 2007;26(6):1237-54.

[D231] Jandhyala R. Relative potency of incobotulinumtoxinA vs onabotulinumtoxinA a meta-analysis of key evidence. *J Drugs Dermatol* 2012;11(6):731-6.

[D232] Jandhyala R, Fullarton JR, Bennett MI. Efficacy of rapid-onset oral fentanyl formulations vs. oral morphine for cancer-related breakthrough pain: a meta-analysis of comparative trials. *J Pain Symptom Manage* 2013;46(4):573-80.

[D233] Palmieri C, Fullarton JR, Brown J. Comparative efficacy of bisphosphonates in metastatic breast and prostate cancer and multiple myeloma: a mixed-treatment meta-analysis. *Clin Cancer Res* 2013;19(24):6863-72.

[D234] Di Lorenzo G, Casciano R, Malangone E, Buonerba C, Sherman S, Willet J, et al. An adjusted indirect comparison of everolimus and sorafenib therapy in sunitinib-refractory metastatic renal cell carcinoma patients using repeated matched samples. *Expert Opin Pharmacother* 2011;12(10):1491-7.

[D235] Thompson Coon JS, Liu Z, Hoyle M, Rogers G, Green C, Moxham T, et al. Sunitinib and bevacizumab for first-line treatment of metastatic renal cell carcinoma: a systematic review and indirect comparison of clinical effectiveness. *Br J Cancer* 2009;101(2):238-43.

[D236] Bodalia PN, Grosso AM, Sofat R, Macallister RJ, Smeeth L, Dhillon S, et al. Comparative efficacy and tolerability of anti-epileptic drugs for refractory focal epilepsy: systematic review and network meta-analysis reveals the need for long term comparator trials. *Br J Clin Pharmacol* 2013;76(5):649-67.

[D237] Samarasekera EJ, Sawyer L, Wonderling D, Tucker R, Smith CH. Topical therapies for the treatment of plaque psoriasis: systematic review and network meta-analyses. *Br J Dermatol* 2013;168(5):954-67.

[D238] Yuan J, Liu Y, Yang Z, Qin X, Yang K, Mao C. The efficacy and safety of alpha-1 blockers for benign prostatic hyperplasia: an overview of 15 systematic reviews. *Curr Med Res Opin* 2013;29(3):279-87.

[D239] Yuan JQ, Zhang R, Yang Z, Lee J, Liu Y, Tian J, et al. Comparative effectiveness and safety of oral phosphodiesterase type 5 inhibitors for erectile dysfunction: a systematic review and network meta-analysis. *Eur Urol* 2013;63(5):902-12.

[D240] Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, et al. Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. *JAMA* 2003;289(19):2534-44.

[D241] van der Valk R, Webers CA, Lumley T, Hendrikse F, Prins MH, Schouten JS. A network meta-analysis combined direct and indirect comparisons between glaucoma drugs to rank effectiveness in lowering intraocular pressure. *J Clin Epidemiol* 2009;62(12):1279-83.

[D242] Ford JA, Elders A, Shyangdan D, Royle P, Waugh N. The relative clinical effectiveness of ranibizumab and bevacizumab in diabetic macular oedema: an indirect comparison in a systematic review. *BMJ* 2012;345:e5182.

[D243] Ford JA, Jones R, Elders A, Mulatero C, Royle P, Sharma P, et al. Denosumab for treatment of bone metastases secondary to solid tumours: systematic review and network meta-analysis. *Eur J Cancer* 2013;49(2):416-30.

[D244] Dretzke J, Meadows A, Novielli N, Huissoon A, Fry-Smith A, Meads C. Subcutaneous and sublingual immunotherapy for seasonal allergic rhinitis: a systematic review and indirect comparison. *J Allergy Clin Immunol* 2013;131(5):1361-6.

[D245] Virgili G, Novielli N, Menchini F, Murro V, Giacomelli G. Pharmacological treatments for neovascular age-related macular degeneration: can mixed treatment comparison meta-analysis be useful? *Curr Drug Targets* 2011;12(2):212-20.

[D246] Fénix-Caballero S, Alegre-del Rey EJ, Castaño-Lara R, Puigventós-Latorre F, Borrero-Rubio JM, López-Vakkehi JF. Direct and indirect comparison of the efficacy and safety of adalimumab, etanercept, infliximab and golimumab in psoriatic arthritis. *J Clin Pharm Ther* 2013;38(4):286-93.

[D247] Gallego-Galisteo M, Villa-Rubio A, Alegre-del Rey E, Márquez-Fernáandez E, Ramos-Báez JJ. Indirect comparison of biological treatments in refractory rheumatoid arthritis. *J Clin Pharm Ther* 2012;37(3):301-7.

[D248] Germani G, Pleguezuelo M, Gurusamy K, Meyer T, Isgrò G, Burroughs AK. Clinical outcomes of radiofrequency ablation, percutaneous alcohol and acetic acid injection for hepatocelullar carcinoma: a meta-analysis. *J Hepatol* 2010;52(3):380-8.

[D249] Gurusamy KS, Pissanou T, Pikhart H, Vaughan J, Burroughs AK, Davidson BR. Methods to decrease blood loss and transfusion requirements for liver transplantation. *Cochrane Database Syst Rev* 2011;(12):CD009052.

[D250] Sultana A, Ghaneh P, Cunningham D, Starling N, Neoptolemos JP, Smith CT. Gemcitabine based combination chemotherapy in advanced pancreatic cancer-indirect comparison. *BMC Cancer* 2008;8:192.

[D251] Tudur Smith C, Marson AG, Chadwick DW, Williamson PR. Multiple treatment comparisons in epilepsy monotherapy trials. Trials 2007;8:34.

[D252] Caldeira D, Alarcão J, Vaz-Carneiro A, Costa J. Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. *BMJ* 2012;345:e4260.

[D253] Costa J, Fareleira F, Ascenção R, Borges M, Sampaio C, Vaz-Carneiro A. Clinical comparability of the new antiepileptic drugs in refractory partial epilepsy: a systematic review and meta-analysis. *Epilepsia* 2011;52(7):1280-91.

[D254] Del Santo F, Maratea D, Fadda V, Trippoli S, Messori A. Treatments for relapsing-remitting multiple sclerosis: summarising current information by network meta-analysis. *Eur J Clin Pharmacol* 2012;68(4):441-8.

[D255] Zaccara G, Giovannelli F, Maratea D, Fadda V, Verrotti A. Neurological adverse events of new generation sodium blocker antiepileptic drugs. Meta-analysis of randomized, double-blinded studies with eslicarbazepine acetate, lacosamide and oxcarbazepine. *Seizure* 2013;22(7):528-36.

[D256] Dumville JC, Soares MO, O'Meara S, Cullum N. Systematic review and mixed treatment comparison: dressings to heal diabetic foot ulcers. *Diabetologia* 2012;55(7):1902-10.

[D257] Dumville JC, McFarlane E, Edwards P, Lipp A, Holmes A. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev 2013;(3):CD003949.

[D258] Gagne JJ, Bykov K, Choudhry NK, Toomey TJ, Connolly JG, Avorn J. Effect of smoking on comparative efficacy of antiplatelet agents: Systematic review, meta-analysis, and indirect comparison. *BMJ* 2013;347(7927):f5307.

[D259] Schneeweiss S, Gagne JJ, Patrick AR, Choudhry NK, Avorn J. Comparative efficacy and safety of new oral anticoagulants in patients with atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2012;5(4):480-6.

[D260] Sun F, Yu K, Wu S, Zhang Y, Yang Z, Shi L, et al. Cardiovascular safety and glycemic control of glucagon-like peptide-1 receptor agonists for type 2 diabetes mellitus: a pairwise and network meta-analysis. *Diabetes Res Clin Pract* 2012;98(3):386-95.

[D261] Sun F, Yu K, Yang Z, Wu S, Zhang Y, Shi L, et al. Impact of GLP-1 receptor agonists on major gastrointestinal disorders for type 2 diabetes mellitus: a mixed treatment comparison meta-analysis. *Exp Diabetes Res* 2012;2012:230624.

[D262] Levi Marpillat N, Macquin-Mavier I, Tropeano AI, Bachoud-Levi AC, Maison P. Antihypertensive classes, cognitive decline and incidence of dementia: a network meta-analysis. *J Hypertens* 2013;31(6):1073-82.

[D263] Tropeano AI, Saleh N, Hawajri N, Macquin-Mavier I, Maison P. Do all antihypertensive drugs improve carotid intima-media thickness? A network meta-analysis of randomized controlled trials. *Fundam Clin Pharmacol* 2011;25(3):395-404.

[D264] Assiri A, Al-Majzoub O, Kanaan AO, Donovan JL, Silva M. Mixed treatment comparison meta-analysis of aspirin, warfarin, and new anticoagulants for stroke prevention in patients with nonvalvular atrial fibrillation. *Clin Ther* 2013;35(7):967-84.

[D265] Malloy RJ, Kanaan AO, Silva MA, Donovan JL. Evaluation of antiplatelet agents for secondary prevention of stroke using mixed treatment comparison meta-analysis. *Clin Ther* 2013;35(10):1490-500.

[D266] Lee YH, Ji JD, Song GG. Adjusted indirect comparison of celecoxib versus rofecoxib on cardiovascular risk. *Rheumatol Int* 2007;27(5):477-82.

[D267] Lee YH, Woo JH, Rho YH, Choi SJ, Ji JD, Song GG. Meta-analysis of the combination of TNF inhibitors plus MTX compared to MTX monotherapy, and the adjusted indirect comparison of TNF inhibitors in patients suffering from active rheumatoid arthritis. *Rheumatol Int* 2008;28(6):553-9.

[D268] Bolaños R, Francia J. Isoflavones versus hormone therapy for reduction of vertebral fracture risk: indirect comparison. Menopause 2010;17(6):1201-5.

[D269] Bolaños-Diaz R, Zavala-Gonzales JC, Mezones-Holguín E, Francia-Romero J. Soy extracts versus hormone therapy for reduction of menopausal hot flushes: indirect comparison. *Menopause* 2011;18(7):825-9.

[D270] Kabra SK, Lodha R, Pandey RM. Antibiotics for community acquired pneumonia in children. *Cochrane Database Syst Rev* 2006;(3):CD004874.

[D271] Kabra SK, Lodha R, Pandey RM. Antibiotics for community-acquired pneumonia in children. *Cochrane Database Syst Rev* 2010;(3):CD004874.

[D272] Abdullah AK, Khan S. Relative oral corticosteroid-sparing effect of 7 inhaled corticosteroids in chronic asthma: a meta-analysis. *Ann Allergy Asthma Immunol* 2008;101(1):74-81.

[D273] Baldwin D, Woods R, Lawson R, Taylor D. Efficacy of drug treatments for generalised anxiety disorder: systematic review and meta-analysis. *BMJ* 2011;342:d1199.

[D274] Bally M, Dendukuri N, Sinclair A, Ahern SP, Poisson M, Brophy J. A network meta-analysis of antibiotics for treatment of hospitalised patients with suspected or proven meticillin-resistant Staphylococcus aureus infection. *Int J Antimicrob Agents* 2012;40(6):479-95.

[D275] Bangalore S, Kumar S, Kjeldsen SE, Makani H, Grossman E, Wettersley J, et al. Antihypertensive drugs and risk of cancer: network meta-analyses and trial sequential analyses of 324,168 participants from randomised trials. *Lancet Oncol* 2011;12(1):65-82.

[D276] Bansal M, Farrugia A, Balboni S, Martin G. Relative survival benefit and morbidity with fluids in severe sepsis - a network meta-analysis of alternative therapies. *Curr Drug Saf* 2013;8(4):236-45.

[D277] Bash LD, Buono JL, Davies GM, Martin A, Fahrbach K, Phatak H, et al. Systematic review and meta-analysis of the efficacy of cardioversion by vernakalant and comparators in patients with atrial fibrillation. *Cardiovasc Drugs Ther* 2012;26(2):167-79.

[D278] Berner MM, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2006;18(3):229-35.

[D279] Bicket MC, Gupta A, Brown CH 4th, Cohen SP. Epidural injections for spinal pain: a systematic review and meta-analysis evaluating the "control" injections in randomized controlled trials. *Anesthesiology* 2013;119(4):907-31.

[D280] Blanchard P, Hill C, Guihenneuc-Jouyaux C, Baey C, Bourhis J, Pignon JP, et al. Mixed treatment comparison meta-analysis of altered fractionated radiotherapy and chemotherapy in head and neck cancer. *J Clin Epidemiol* 2011;64(9):985-92.

[D281] Boonen S, Lips P, Bouillon R, Bischoff-Ferrari HA, Vanderschueren D, Haentjens P. Need for additional calcium to reduce the risk of hip fracture with vitamin d supplementation: evidence from a comparative metaanalysis of randomized controlled trials. *J Clin Endocrinol Metab* 2007;92(4):1415-23.

[D282] Brigo F, Igwe SC, Nardone R, Tezzon F, Bongiovanni LG, Trinka E. A common reference-based indirect comparison meta-analysis of intravenous valproate versus intravenous phenobarbitone for convulsive status epilepticus. *Epileptic Disord* 2013;15(3):314-23.

[D283] Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev* 2013;(5):CD009329.

[D284] Carter B, Fedorowicz Z. Antiemetic treatment for acute gastroenteritis in children: an updated Cochrane systematic review with meta-analysis and mixed treatment comparison in a Bayesian framework. *BMJ Open* 2012;2(4):e000622.

[D285] Cates CJ, Oleszczuk M, Stovold E, Wieland LS. Safety of regular formoterol or salmeterol in children with asthma: an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2012;10:CD010005.

[D286] Cawston H, Davie A, Paget MA, Sklijarevski V, Happich M. Efficacy of duloxetine versus alternative oral therapies: an indirect comparison of randomised clinical trials in chronic low back pain. *Eur Spine J* 2013;22(9):1996-2009.

[D287] Chapell R, Gould AL, Alexander CM. Baseline differences in A1C explain apparent differences in efficacy of sitagliptin, rosiglitazone and pioglitazone. Diabetes Obes Metab 2009;11(11):1009-16.

[D288] Coleman KA, Xavier VY, Palmer TL, Meaney JV, Randalj LM, Canny LM. An indirect comparison of the efficacy and safety of desvenlafaxine and venlafaxine using placebo as the common comparator. *CNS Spectr* 2012;17(3):131-41.

[D289] Conde-Agudelo A, Romero R, Nicolaides K, Chaiworapongsa T, O'Brien JM, Cetingoz E, et al. Vaginal progesterone vs. cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. *Am J Obstet Gynecol* 2013;208(1):42.e1-42.e18.

[D290] Cooper KL, Fitzgerald P, Dillingham K, Helme K, Akehurst R. Romiplostim and eltrombopag for immune thrombocytopenia: methods for indirect comparison. *Int J Technol Assess Health Care* 2012;28(3):249-58.

[D291] Cota GF, de Sousa MR, Fereguetti TO, Rabello A. Efficacy of anti-leishmania therapy in visceral leishmaniasis among HIV infected patients: a systematic review with indirect comparison. *PLoS Negl Trop Dis* 2013;7(5):e2195.

[D292] Cure S, Diels J, Gavart S, Bianic F, Jones E. Efficacy of telaprevir and boceprevir in treatment-naive and treatment-experienced genotype 1 chronic hepatitis C patients: an indirect comparison using Bayesian network meta-analysis. *Curr Med Res Opin* 2012;28(11):1841-56.

[D293] Danchin N, Marzilli M, Parkhomenko A, Ribeiro JP. Efficacy comparison of trimetazidine with therapeutic alternatives in stable angina pectoris: a network meta-analysis. *Cardiology* 2011;120(2):59-72.

[D294] Datto C, Hellmund R, Siddiqui MK. Efficacy and tolerability of naproxen/esomeprazole magnesium tablets compared with non-specific NSAIDs and COX-2 inhibitors: a systematic review and network analyses. *Open Access Rheumatol* 2013;5:1-19.

[D295] de Menezes GB, Coutinho ES, Fontenelle LF, Vigne P, Figueira I, Versiani M. Second-generation antidepressants in social anxiety disorder: meta-analysis of controlled clinical trials. *Psychopharmacology* 2011;215(1):1-11.

[D296] Delahoy P, Thompson S, Marschner IC. Pregabalin versus gabapentin in partial epilepsy: a meta-analysis of dose-response relationships. *BMC Neurol* 2010;10:104.

[D297] Dong YH, Lin HH, Shau WY, Wu YC, Chang CH, Lai MS. Comparative safety of inhaled medications in patients with chronic obstructive pulmonary disease: systematic review and mixed treatment comparison meta-analysis of randomised controlled trials. *Thorax* 2013;68(1):48-56.

[D298] Elliott WJ, Meyer PM. Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis. Lancet 2007;369(9557):201-7.

[D299] Engelman E, Salengros JC, Barvais L. How much does pharmacologic prophylaxis reduce postoperative vomiting in children? Calculation of prophylaxis effectiveness and expected incidence of vomiting under treatment using Bayesian meta-analysis. *Anesthesiol* 2008;109(6):1023-35.

[D300] Fang Y, Ding Y, Guo Q, Xing J, Long Y, Zong Z. Radioiodine therapy for patients with differentiated thyroid cancer after thyroidectomy: direct comparison and network meta-analyses. *J Endocrinol Invest* 2013;36(10):896-902.

[D301] Fountoulakis KN, Veroniki AA, Siamouli M, Möller HJ. No role for initial severity on the efficacy of antidepressants: results of a multi-meta-analysis. *Ann Gen Psychiatry* 2013;12(1):26.

[D302] Fretheim A, Odgaard-Jensen J, Brørs O, Madsen S, Njølstad I, Norheim OF, et al. Comparative effectiveness of antihypertensive medication for primary prevention of

cardiovascular disease: systematic review and multiple treatments meta-analysis. *BMC Med* 2012;10:33.

[D303] Galvan-Banqueri M, Marin Gil R, Santos Ramos B, Bautista Paloma FJ. Biological treatments for moderate-to-severe psoriasis: indirect comparison. *J Clin Pharm Ther* 2013;38(2):121-30.

[D304] Gao L, Xia L, Zhao FL, Li SC. Clinical efficacy and safety of the newer antiepileptic drugs as adjunctive treatment in adults with refractory partial-onset epilepsy: a meta-analysis of randomized placebo-controlled trials. *Epilepsy Res* 2013;103(1):31-44.

[D305] Ginés J, Sabater E, Martorell C, Grau M, Monroy M, Casado MA. Efficacy of taxanes as adjuvant treatment of breast cancer: a review and meta-analysis of randomised clinical trials. Clin Transl Oncol 2011;13(7):485-98.

[D306] Gómez-Outes A, Terleira-Fernández AI, Suárez-Gea ML, Vargas-Castrillón E. Dabigatran, rivaroxaban, or apixaban versus enoxaparin for thromboprophylaxis after total hip or knee replacement: systematic review, meta-analysis, and indirect treatment comparisons. *BMJ* 2012;344(7863):e3675.

[D307] Goralczyk AD, Cameron S, Amanzada A. Treatment of chronic HCV genotype 1 infection with telaprevir: a Bayesian mixed treatment comparison of fixed-length and response-guided treatment regimens in treatment-naive and -experienced patients. *BMC Gastroenterol* 2013;13(1):148.

[D308] Gupta AK, Paquet M. Network meta-analysis of the outcome 'participant complete clearance' in nonimmunosuppressed participants of eight interventions for actinic keratosis: a follow-up on a Cochrane review. *Br J Dermatol* 2013;169(2):250-9.

[D309] Hoaglin DC, Filonenko A, Glickman ME, Wasiak R, Gidwani R. Use of mixed-treatment-comparison methods in estimating efficacy of treatments for heavy menstrual bleeding. *Eur J Med Res* 2013;18(1):17.

[D310] Hofmeyr GJ, Gülmezoglu AM, Novikova N, Linder V, Ferreira S, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. *Bull World Health Organ* 2009;87(9):666-77.

[D311] Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, et al. Prevention of pain on injection of propofol: systematic review and meta-analysis. *BMJ* 2011;342:d1110.

[D312] Kalil AC, Mindru C, Florescu DF. Effectiveness of valganciclovir 900 mg versus 450 mg for cytomegalovirus prophylaxis in transplantation: direct and indirect treatment comparison meta-analysis. *Clin Infect Dis* 2011;52(3):313-21.

[D313] Karabis A, Lindner L, Mocarski M, Huisman E, Greening A. Comparative efficacy of aclidinium versus glycopyrronium and tiotropium, as maintenance treatment of moderate to severe COPD patients: a systematic review and network meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2013;8:405-23.

[D314] Klemp M, Tvete IF, Skomedal T, Gaasemyr J, Natvig B, Aursnes I. A review and Bayesian meta-analysis of clinical efficacy and adverse effects of 4 atypical neuroleptic drugs compared with haloperidol and placebo. *J Clin Psychopharmacol* 2011;31(6):698-704.

[D315] Kotzé A, Scally A, Howell S. Efficacy and safety of different techniques of paravertebral block for analgesia after thoracotomy: a systematic review and metaregression. Br J Anaesth 2009;103(5):626-36.

[D316] Launois R, Avouac B, Berenbaum F, Blin O, Bru I, Fautrel B, et al. Comparison of certolizumab pegol with other anticytokine agents for treatment of rheumatoid arthritis: a multiple-treatment Bayesian metaanalysis. *J Rheumatol* 2011;38(5):835-45.

[D317] Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *BMJ* 2003;326(7404):1427-31.

[D318] Leung HW, Chan AL. Multikinase inhibitors in metastatic renal cell carcinoma: indirect comparison meta-analysis. *Clin Ther* 2011;33(6):708-16.

[D319] Levy AR, Johnston KM, Sambrook J, Donato B, Penrod JR, Corral M, et al. Indirect comparison of the efficacy of cetuximab and cisplatin in squamous cell carcinoma of the head and neck. *Curr Med Res Opin* 2011;27(12):2253-9.

[D320] Liu JL, Dong J, Wang L, Su Y, Yan P, Sun S. Comparative efficacy and acceptability of antidepressants in Parkinson's disease: a network meta-analysis. *Plos One* 2013;8(10):e76651.

[D321] Mantha S, Ansell J. An indirect comparison of dabigatran, rivaroxaban and apixaban for atrial fibrillation. *Thromb Haemost* 2012;108(3):476-84.

[D322] Martyn-St James M, Glanville J, McCool R, Duffy S, Cooper J, Hugel P, et al. The efficacy and safety of retigabine and other adjunctive treatments for refractory partial epilepsy: a systematic review and indirect comparison. *Seizure* 2012;21(9):665-78.

[D323] Maund E, McDaid C, Rice S, Wright K, Jenkins B, Woolacott N. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review. *Br J Anaesth* 2011;106(3):292-7.

[D324] Meader N. A comparison of methadone, buprenorphine and alpha2 adrenergic agonists for opioid detoxification: a mixed treatment comparison meta-analysis. Drug Alcohol Depend 2010;108(1-2):110-4.

[D325] Menzies D, Benedetti A, Paydar A, Martin I, Royce S, Pai M, et al. Effect of duration and intermittency of rifampin on tuberculosis treatment outcomes: a systematic review and meta-analysis. *PLoS Med* 2009;6(9):e1000146.

[D326] Mösges R, Nematian-Samani M, Hellmich M, Shah-Hosseini K. A meta-analysis of the efficacy of quinolone containing otics in comparison to antibiotic-steroid combination drugs in the local treatment of otitis externa. *Curr Med Res Opin* 2011;27(10):2053-60.

[D327] Ollendorf DA, Colby JA, Pearson SD. Comparative effectiveness of anti-vegf agents for diabetic macular edema. *Int J Technol Assess Health Care* 2013;29(4):392-401.

[D328] Otoul C, Arrigo C, van Rijckevorsel K, French JA. Meta-analysis and indirect comparisons of levetiracetam with other second-generation antiepileptic drugs in partial epilepsy. *Clin Neuropharmacol* 2005;28(2):72-8.

[D329] Otten MH, Anink J, Spronk S, van Suijlekom-Smit LW. Efficacy of biological agents in juvenile idiopathic arthritis: a systematic review using indirect comparisons. Ann Rheum Dis 2013;72(11):1806-12.

[D330] Owen A. Antithrombotic treatment for the primary prevention of stroke in patients with non valvular atrial fibrillation: a reappraisal of the evidence and network meta analysis. *Int J Cardiol* 2010;142(3):218-23.

[D331] Packer M, Antonopoulos GV, Berlin JA, Chittams J, Konstam MA, Udelson JE. Comparative effects of carvedilol and metoprolol on left ventricular election fraction in heart failure: results of a meta-analysis. *Am Heart J* 2001;141(6):899-907.

[D332] Piccini JP, Hasselblad V, Peterson ED, Washam JB, Califf RM, Kong DF. Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation. *J Am Coll Cardiol* 2009;54(12):1089-95.

[D333] Pink J, Pirmohamed M, Hughes DA. Comparative effectiveness of dabigatran, rivaroxaban, apixaban, and warfarin in the management of patients with nonvalvular atrial fibrillation. Clin Pharmacol Ther 2013;94(2):269-76.

[D334] Qi WX, Tang LN, He AN, Shen Z, Lin F, Yao Y. Erlotinib and pemetrexed as maintenance therapy for advanced non-small-cell lung cancer: a systematic review and indirect comparison. *Curr Med Res Opin* 2012;28(4):643-50.

[D335] Robenshtok E, Gafter-Gvili A, Goldberg E, Weinberger M, Yeshurun M, Leibovici L, et al. Antifungal prophylaxis in cancer patients after chemotherapy or hematopoietic stem-cell transplantation: systematic review and meta-analysis. *J Clin Oncol* 2007;25(34):5471-89.

[D336] Ronellenfitsch U, Schwarzbach M, Hofheinz R, Kienle P, Kieser M, Slanger TE, et al. Preoperative chemo(radio)therapy versus primary surgery for gastroesophageal adenocarcinoma: systematic review with meta-analysis combining individual patient and aggregate data. *Eur J Cancer* 2013;49(15):3149-58.

[D337] Roush GC, Holford TR, Guddati AK. Chlorthalidone compared with hydrochlorothiazide in reducing cardiovascular events: systematic review and network meta-analyses. *Hypertension* 2012;59(6):1110-7.

[D338] Rudroju N, Bansal D, Talakokkula ST, Gudala K, Hota D, Bhansali A, et al. Comparative efficacy and safety of six antidepressants and anticonvulsants in painful diabetic neuropathy: a network meta-analysis. *Pain Physician* 2013;16(6):E705-14.

[D339] Sauriol L, Laporta M, Edwardes MD, Deslandes M, Ricard N, Suissa S. Meta-analysis comparing newer antipsychotic drugs for the treatment of schizophrenia: evaluating the indirect approach. *Clin Ther* 2001;23(6):942-56.

[D340] Schoels M, Aletaha D, Smolen JS, Wong JB. Comparative effectiveness and safety of biological treatment options after tumour necrosis factor alpha inhibitor failure in rheumatoid arthritis: systematic review and indirect pairwise meta-analysis. *Ann Rheum Dis* 2012;71(8):1303-8.

[D341] Sciarretta S, Palano F, Tocci G, Baldini R, Volpe M. Antihypertensive treatment and development of heart failure in hypertension: a Bayesian network meta-analysis of studies in patients with hypertension and high cardiovascular risk. *Arch Intern Med* 2011;171(5):384-94.

[D342] Shamliyan TA, Choi JY, Ramakrishnan R, Miller JB, Wang SY, Taylor FR, et al. Preventive pharmacologic treatments for episodic migraine in adults. *J Gen Intern Med* 2013;28(9):1225-37.

[D343] Shi KQ, Liu WY, Pan ZZ, Ling XF, Chen SL, Chen YP, et al. Secondary prophylaxis of variceal bleeding for cirrhotic patients: a multiple-treatments meta-analysis. *Eur J Clin Invest* 2013;43(8):844-54.

[D344] Shu T, Chen GH, Rong L, Feng F, Yang B, Chen R, et al. Indirect comparison of anti-TNF-alpha agents for active ankylosing spondylitis: mixed treatment comparison of randomised controlled trials. Clin Exp Rheumatol 2013;31(5):717-22.

[D345] Stegeman BH, de Bastos M, Rosendaal FR, van Hylckama Vlieg A, Helmerhorst FM, Stijnen T, et al. Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis. *BMJ* 2013;347(7925):f5298.

[D346] Stevens JW, Simpson E, Harnan S, Squires H, Meng Y, Thomas S, et al. Systematic review of the efficacy of cilostazol, naftidrofuryl oxalate and pentoxifylline for the treatment of intermittent claudication. *Br J Surg* 2012;99(12):1630-8.

[D347] Szegedi A, Verweij P, van Duijnhoven W, Mackle M, Cazorla P, Fennema H. Meta-analyses of the efficacy of asenapine for acute schizophrenia: comparisons with placebo and other antipsychotics. J Clin Psychiatry 2012;73(12):1533-40.

[D348] Tang DH, Malone DC. A network meta-analysis on the efficacy of serotonin type 3 receptor antagonists used in adults during the first 24 hours for postoperative nausea and vomiting prophylaxis. *Clin Ther* 2012;34(2):282-94.

[D349] Thijs V, Lemmens R, Fieuws S. Network meta-analysis: simultaneous meta-analysis of common antiplatelet regimens after transient ischaemic attack or stroke. *Eur Heart J* 2008;29(9):1086-92.

[D350] Tonelli M, Lloyd A, Clement F, Conly J, Husereau D, Hemmelgarn B, et al. Efficacy of statins for primary prevention in people at low cardiovascular risk: a meta-analysis. *CMAJ* 2011;183(16):E1189-202.

[D351] Trkulja V, Kolundzic R. Rivaroxaban vs dabigatran for thromboprophylaxis after joint-replacement surgery: exploratory indirect comparison based on metaanalysis of pivotal clinical trials. *Croat Med J* 2010;51(2):113-23.

[D352] Turkstra E, Ng SK, Scuffham PA. A mixed treatment comparison of the short-term efficacy of biologic disease modifying anti-rheumatic drugs in established rheumatoid arthritis. *Curr Med Res Opin* 2011;27(10):1885-97.

[D353] Tzellos TG, Toulis KA, Goulis DG, Papazisis G, Zampeli VA, Vakfari A, et al. Gabapentin and pregabalin in the treatment of fibromyalgia: a systematic review and a meta-analysis. *J Clin Pharm Ther* 2010;35(6):639-56.

[D354] Uthman OA, Abdulmalik J. Comparative efficacy and acceptability of pharmacotherapeutic agents for anxiety disorders in children and adolescents: a mixed treatment comparison meta-analysis. Curr Med Res Opin 2010;26(1):53-9.

[D355] Verduyn SC, Biesma B, Schramel FM, van der Scheer FW, Langenfeld MK, de Peuter MA, et al. Estimating quality adjusted progression free survival of first-line treatments for EGFR mutation positive non small cell lung cancer patients in The Netherlands. *Health Qual Life Outcomes* 2012;10:108.

[D356] Whegang Youdom S, Samson A, Basco LK, Thalabard JC. Multiple treatment comparisons in a series of anti-malarial trials with an ordinal primary outcome and repeated treatment evaluations. *Malar J* 2012;11:147.

[D357] Woo G, Tomlinson G, Nishikawa Y, Kowgier M, Sherman M, Wong DK, et al. Tenofovir and entecavir are the most effective antiviral agents for chronic hepatitis B: a systematic review and Bayesian meta-analyses. *Gastroenterology* 2010;139(4):1218-29.

[D358] Yang Q, Wei Y, Chen YX, Zhou SW, Jiang ZM, Xie DR. Indirect comparison showed survival benefit from adjuvant chemoradiotherapy in completely resected gastric cancer with d2 lymphadenectomy. *Gastroenterol Res Pract* 2013;2013:634929.

[D359] Zagmutt FJ, Tarrants ML. Indirect comparisons of adverse events and dropout rates in early Parkinson's disease trials of pramipexole, ropinirole, and rasagiline. Int J Neurosci 2012;122(7):345-53.

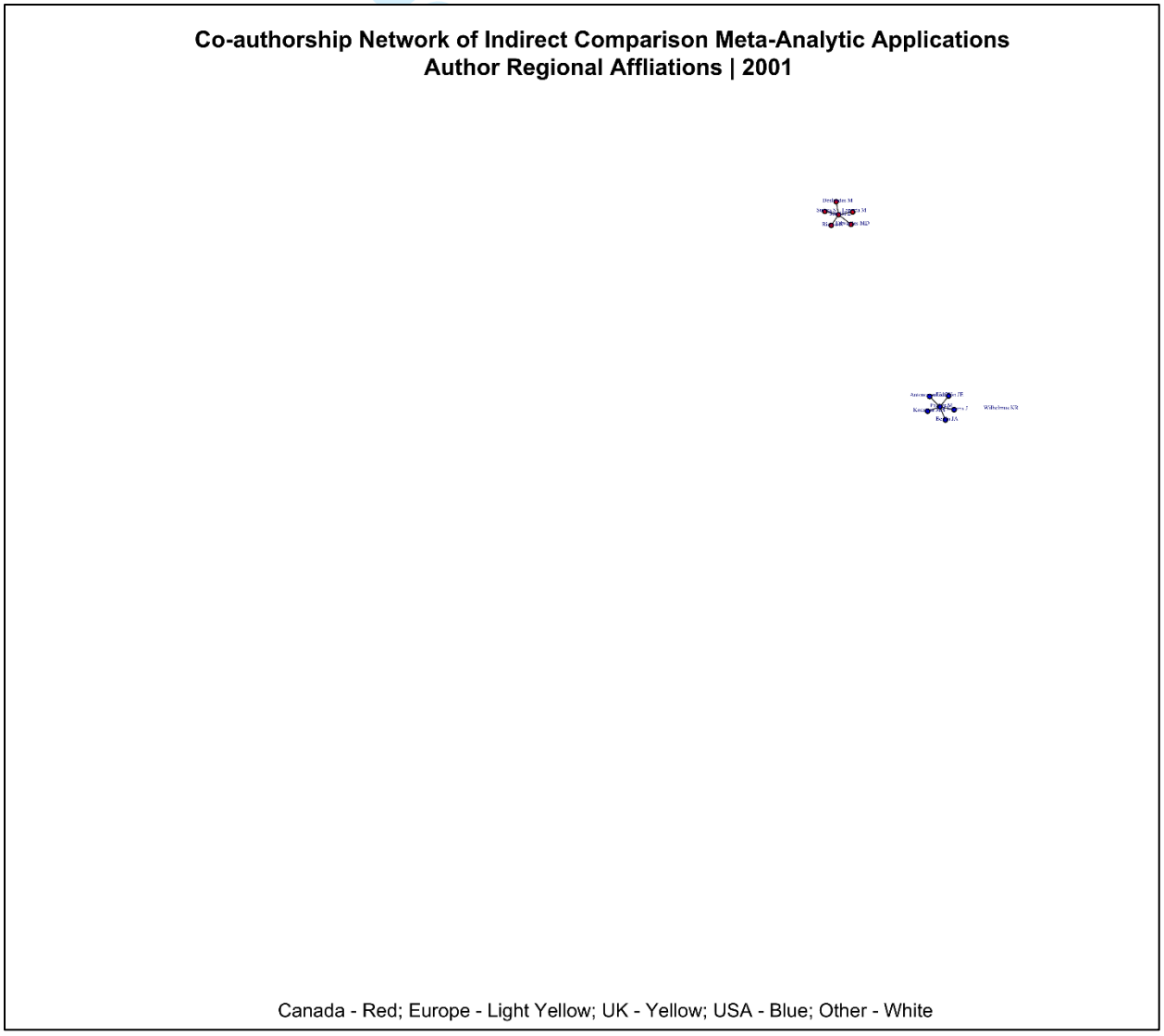
[D360] Zeng L, Luo R, Zhang L. Efficacy of high-dose ACTH versus low-dose ACTH in infantile spasms: a meta-analysis with direct and indirect comparison of randomized trials. *J Pediatr Neurol* 2011;9(2):141-9.

[D361] Zou YD, Sheng Z, Niu S, Wang H, Yu J, Xu J. Lenalidomide versus thalidomide based regimens as first-line therapy for patients with multiple myeloma. *Leuk Lymphoma* 2013;54(10):2219-25.

# Appendix E: Co-authorship of indirect comparison meta-analytic methods by country over time

Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000 to 2013. Colour based on country: Canada (red), the United States (blue), the United Kingdom (yellow), all other Europe (light yellow), and all other regions (white). Authors publishing on papers with more than one country affiliation were coloured based on combinations of the primary colours and white, thereby yielding secondary and tertiary colours. For example, authors on papers with affiliations from Canada and the United States were coloured purple (a combination of red and blue), authors on papers with affiliations from the United States and the United Kingdom were coloured green (a combination of blue and yellow), and authors on papers with affiliations from Canada and the United Kingdom were coloured orange (a combination of red and yellow). Authors on papers affiliated with Canada, the United States, and the United Kingdom were coloured grey (a combination of red, blue, and yellow). The addition of other European countries (light yellow) and all other regions (white) into the mix, lightened these colour combinations. For example, authors on papers affiliated with Canada, the United States, and all other regions were coloured light purple (a combination of red, blue, and white).

## 2001



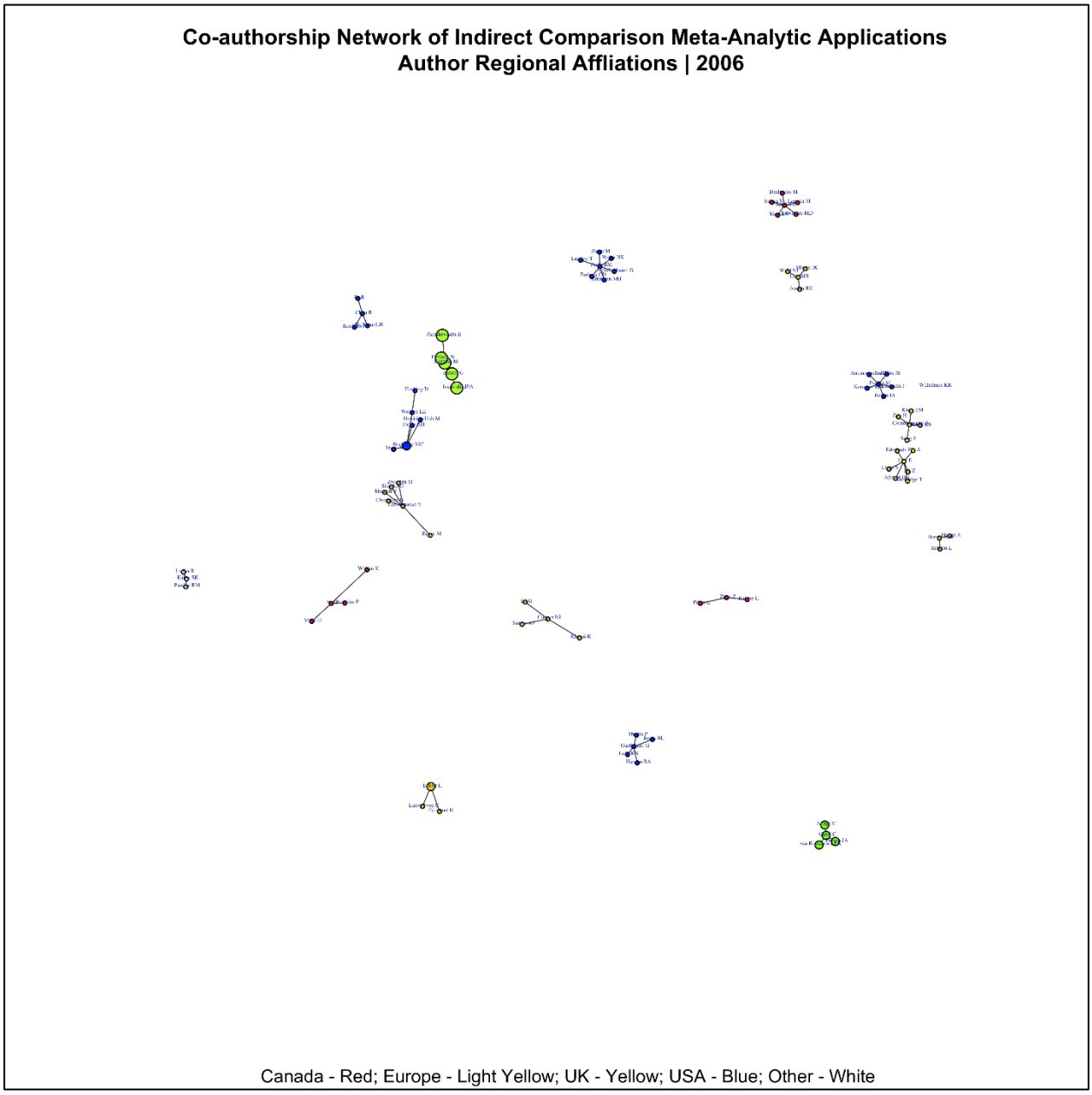
## 2002

## 2003

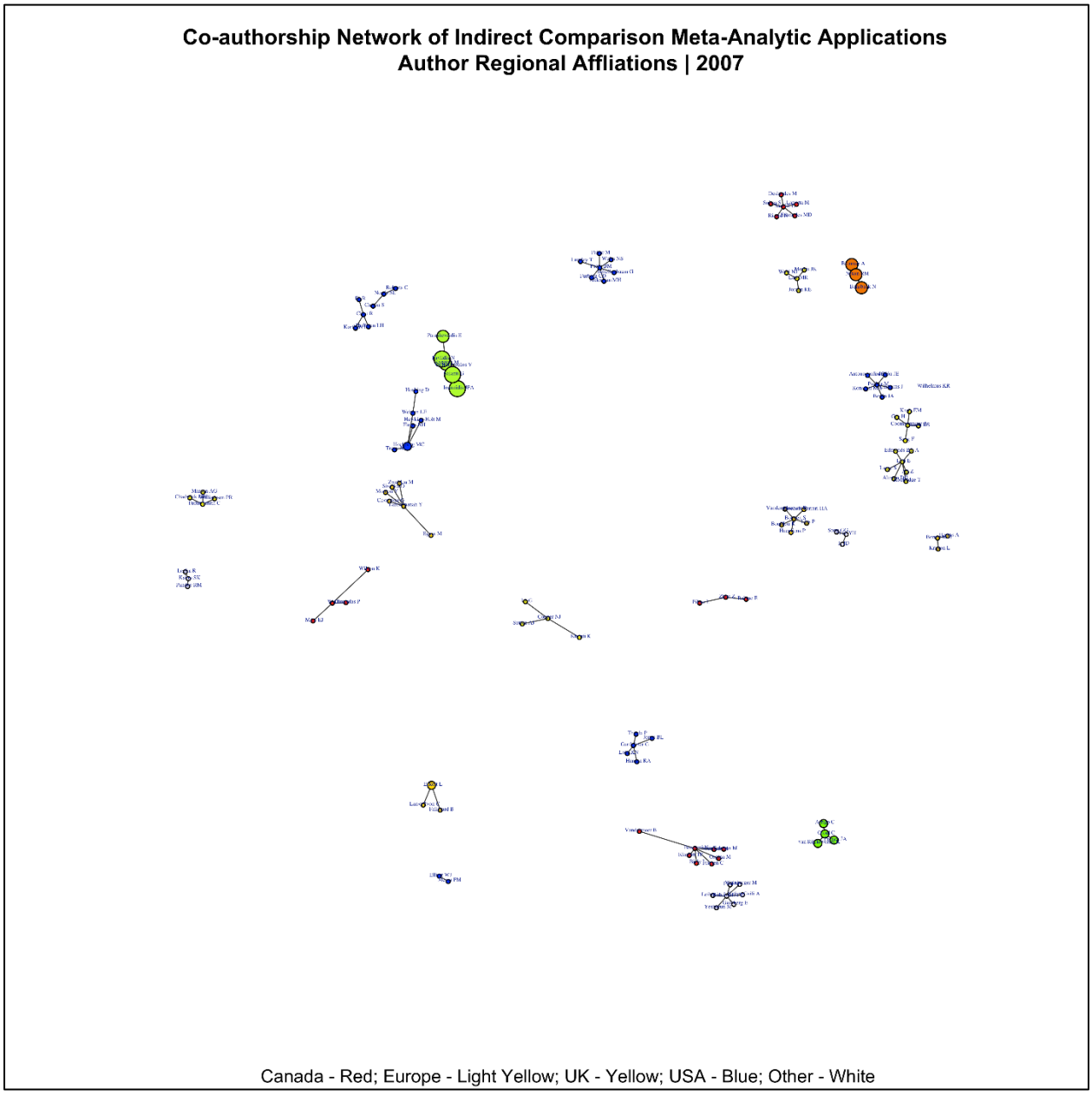
## 2004

## 2005

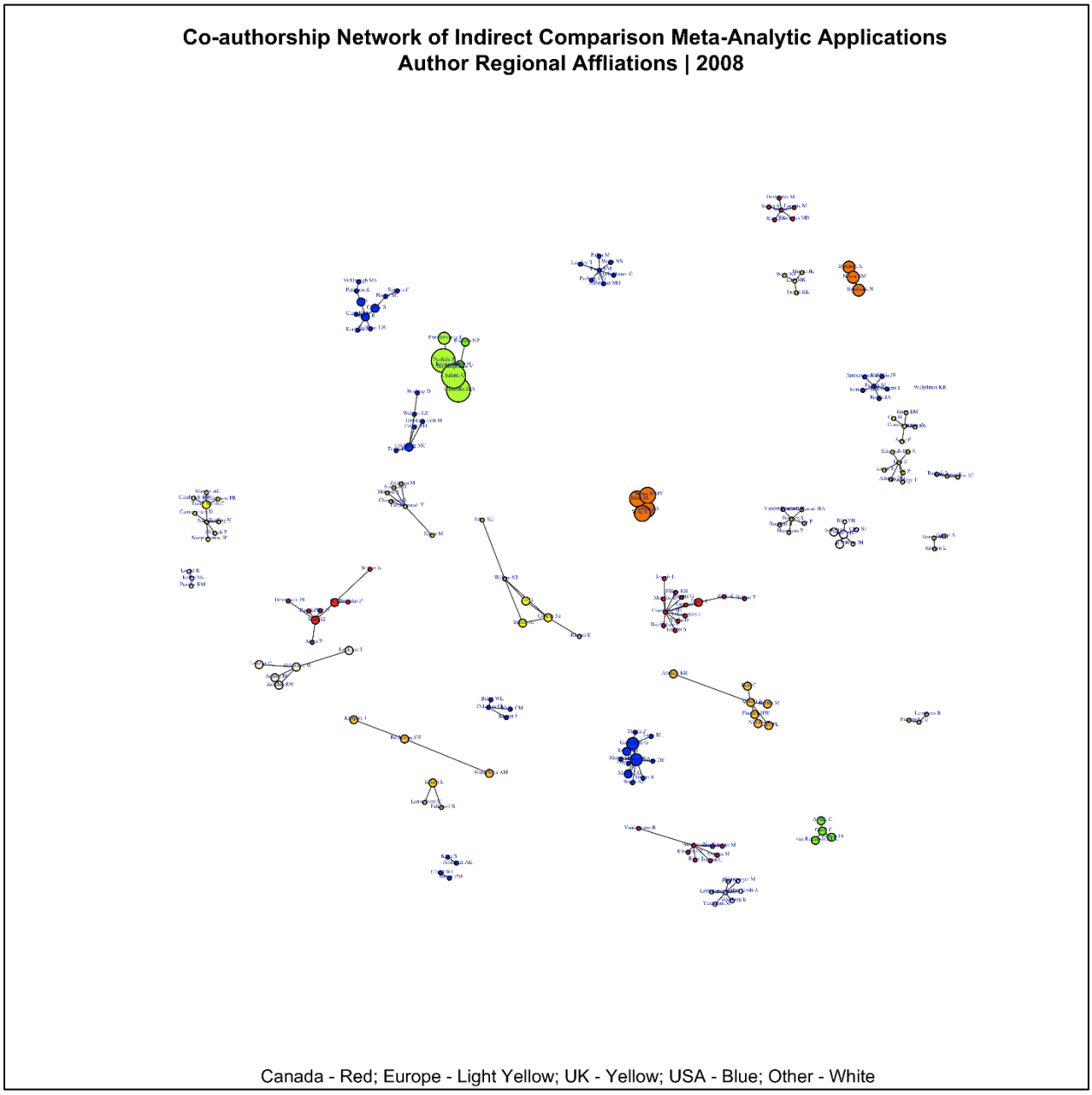
## 2006



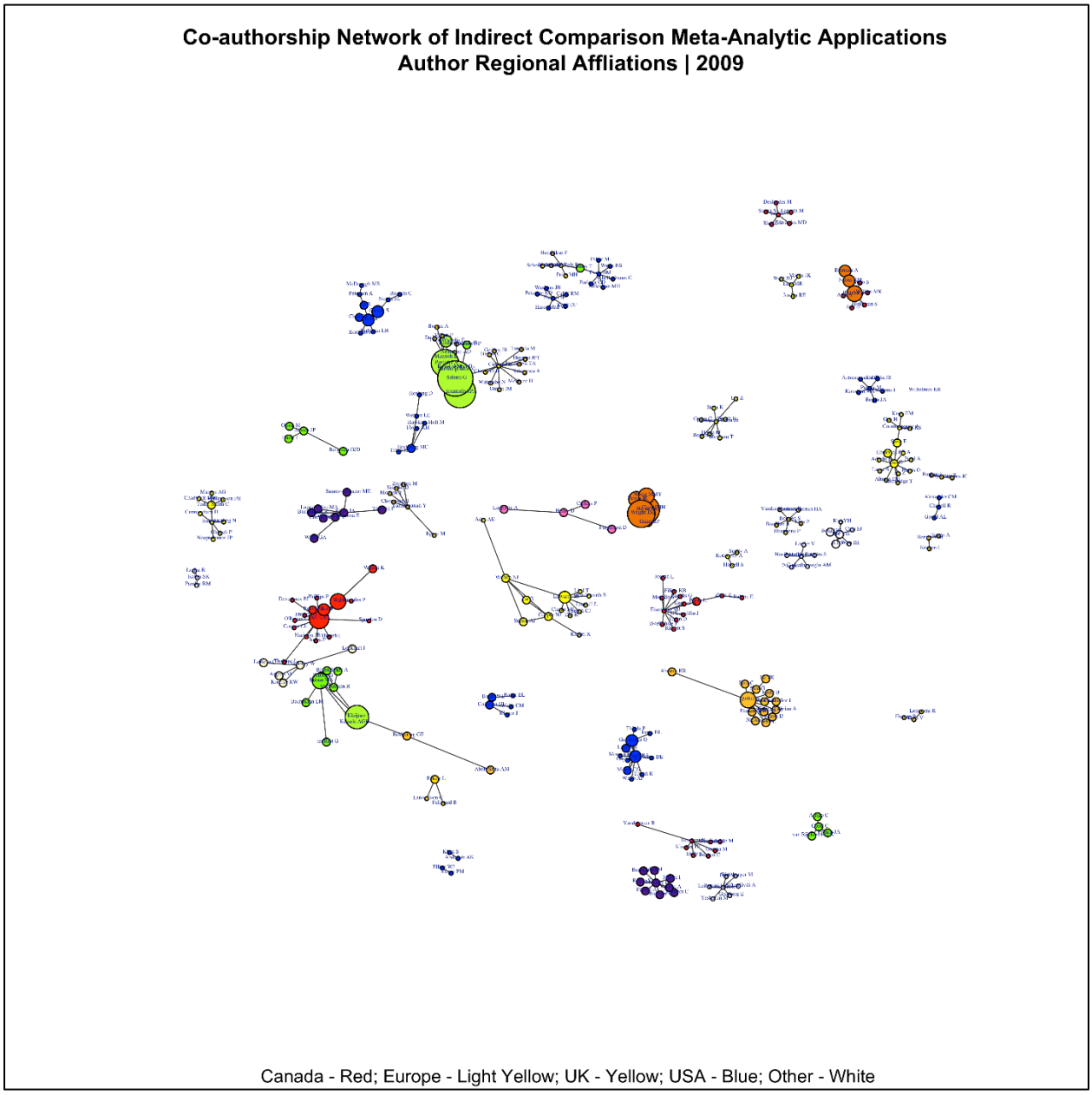
## 2007



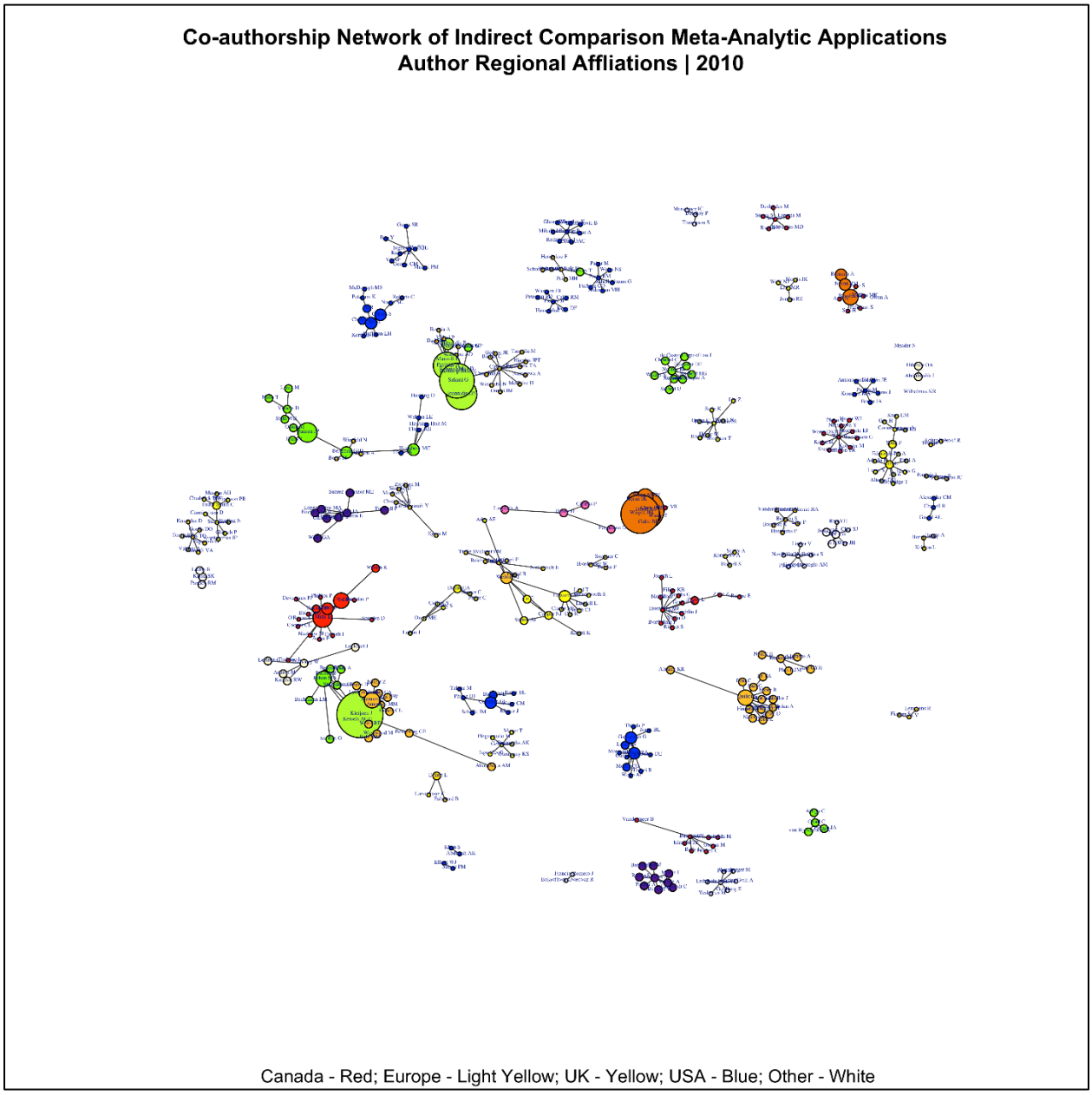
## 2008



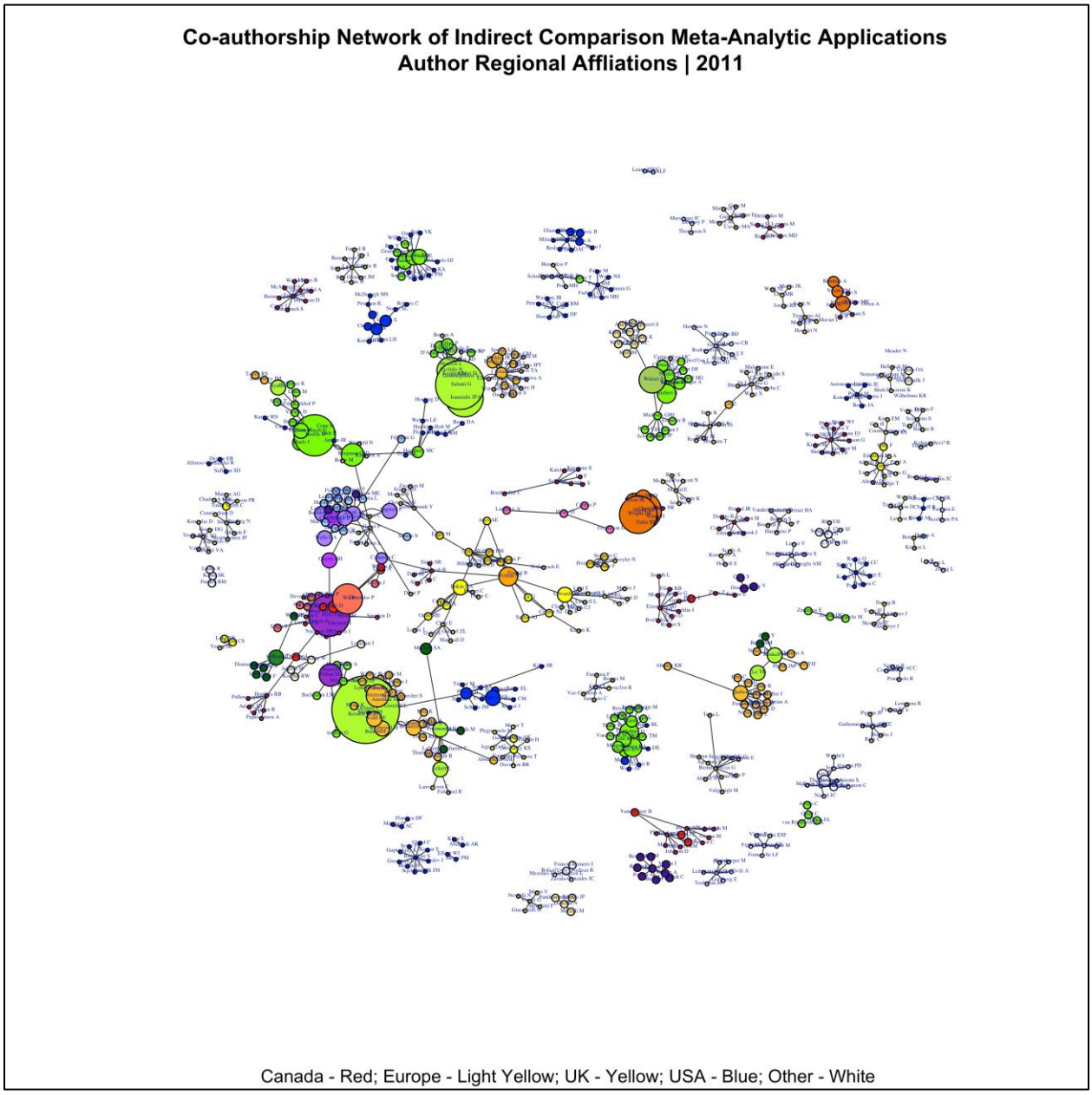
## 2009



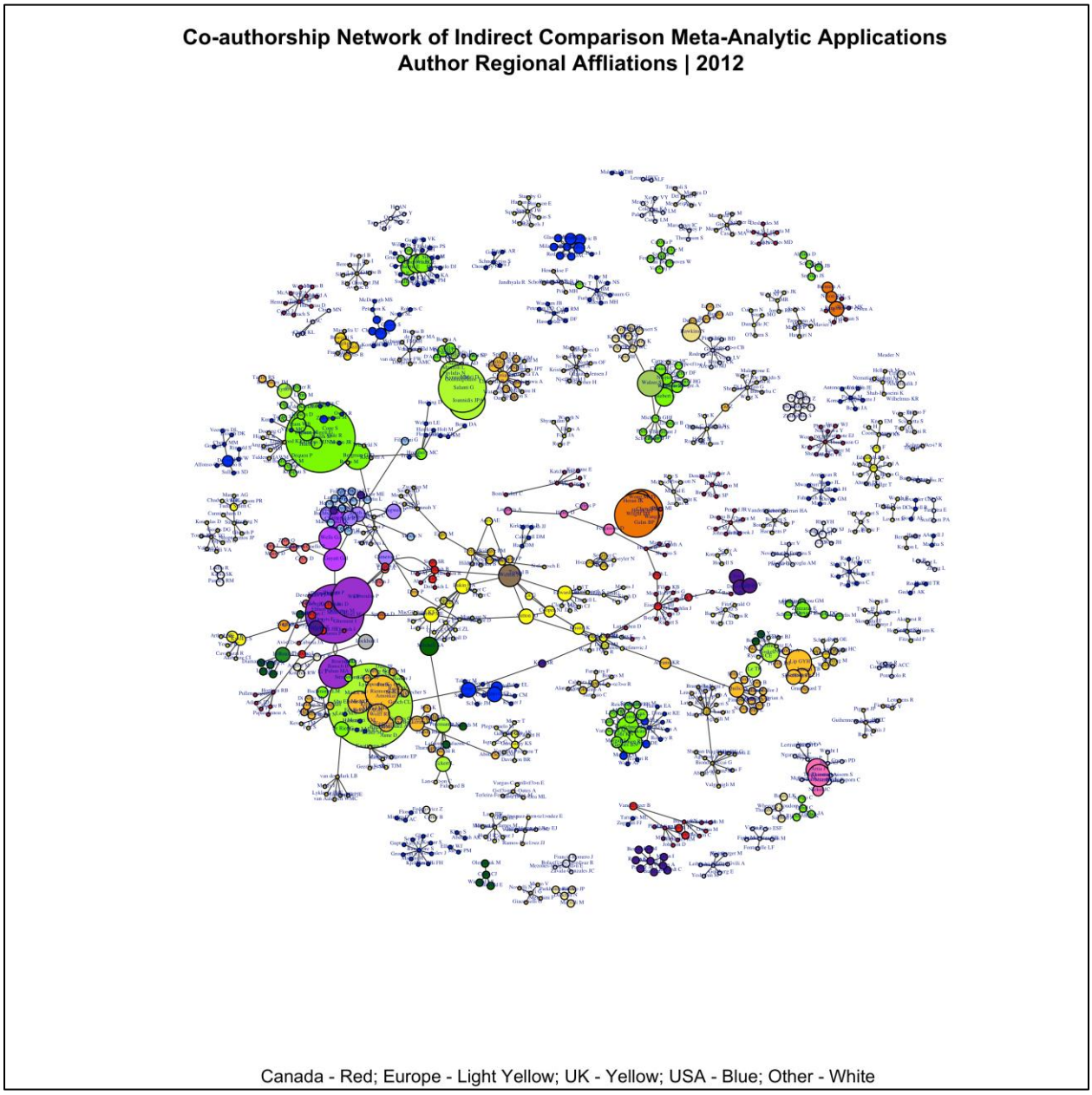
## 2010



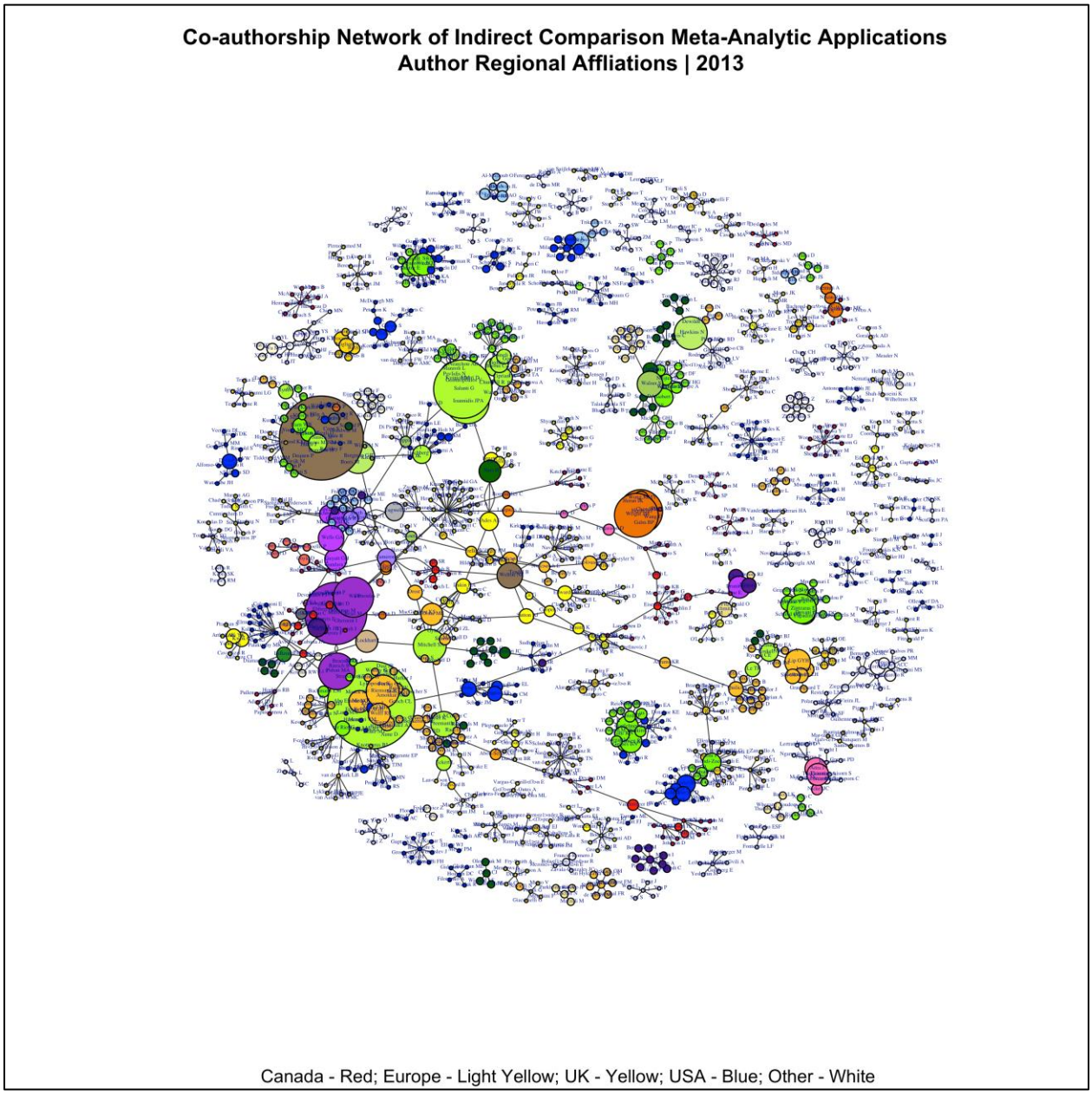
## 2011



## 2012



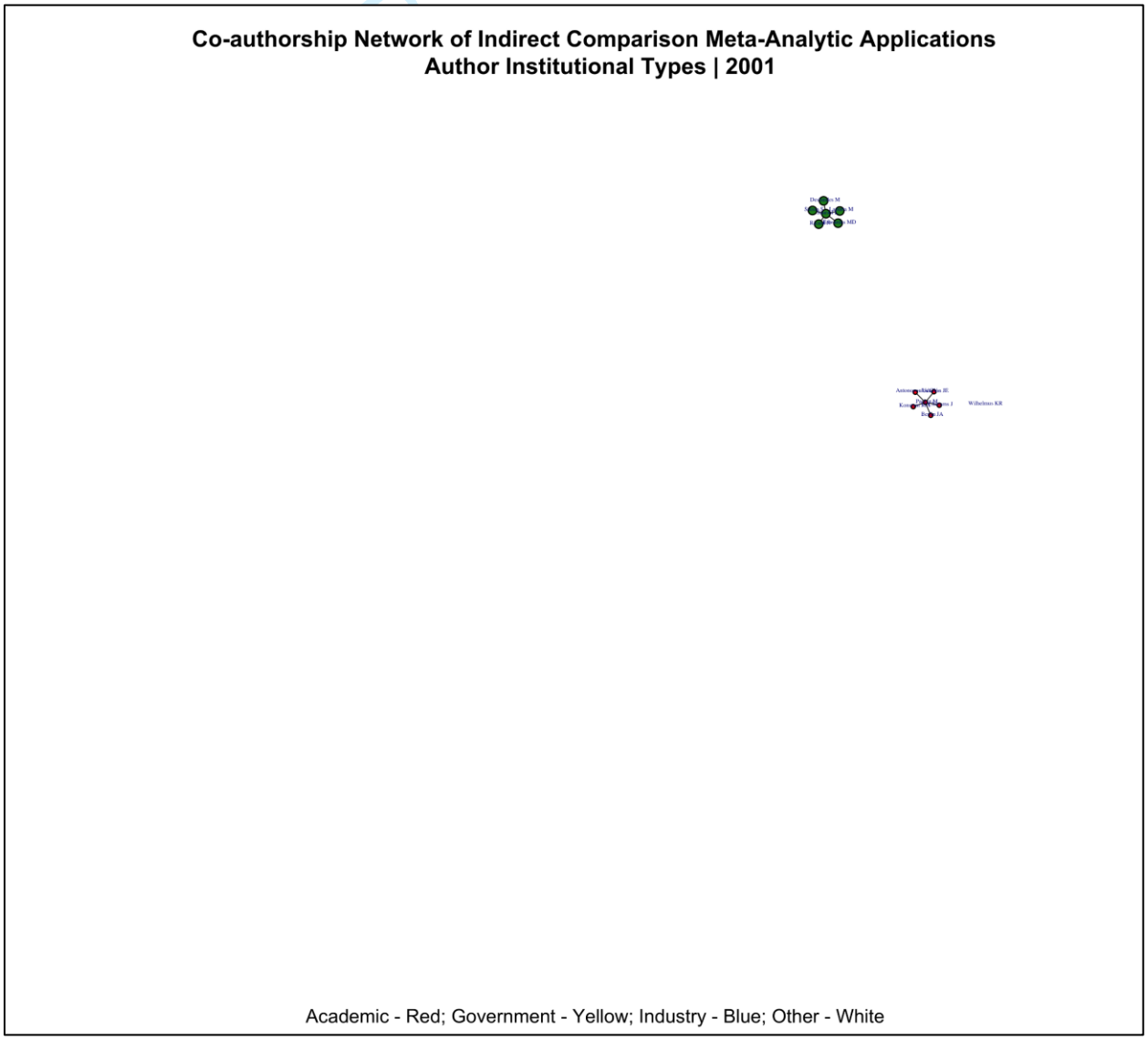
## 2013



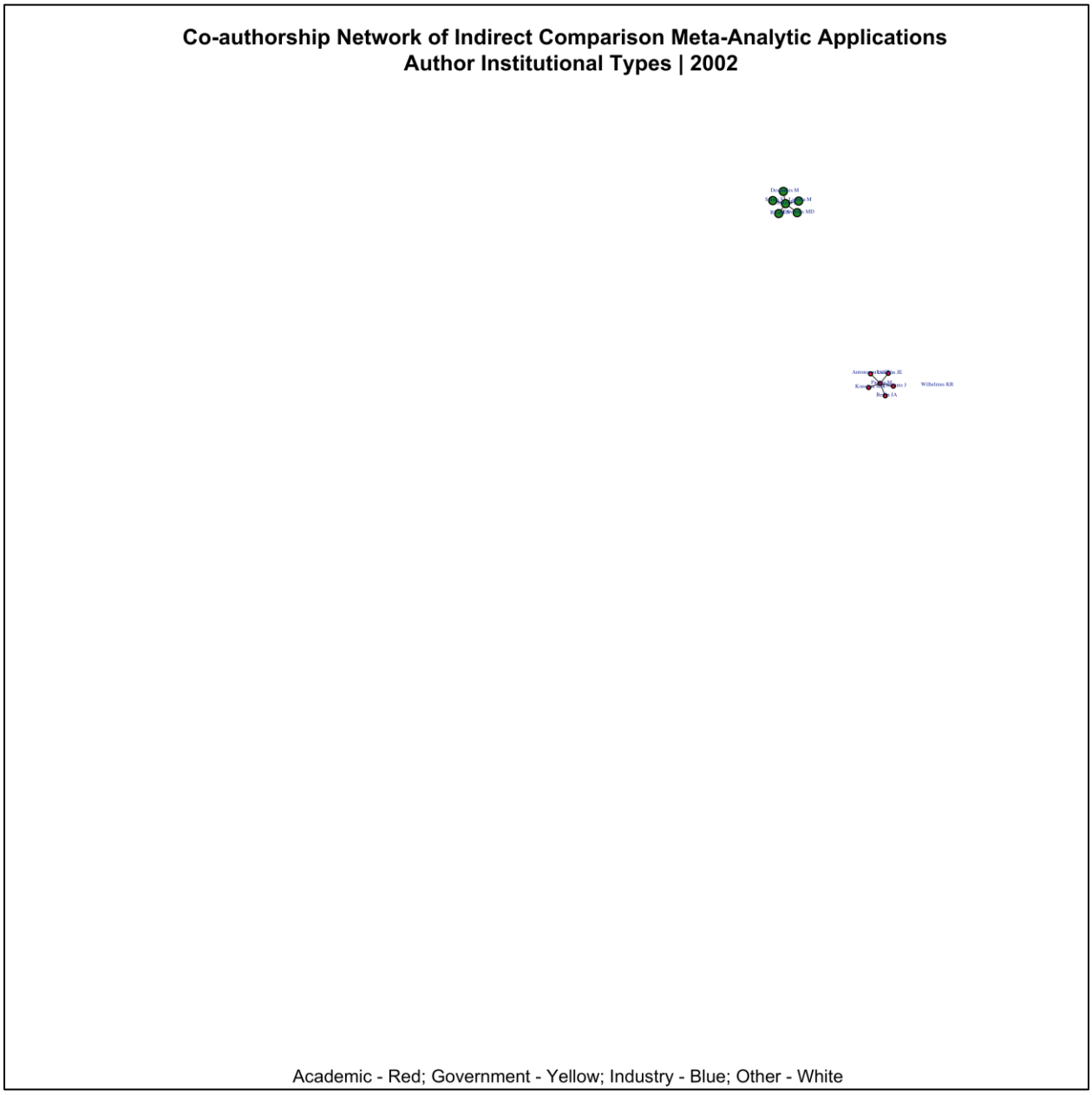
# Appendix F: Co-authorship of indirect comparison meta-analytic methods by affiliation type over time

Directed co-authorship network of the 361 indirect comparison meta-analytic applications, 129 components, 1513 authors, 2000-2013. Colour based on affiliation type: academic (red), government (yellow), industry (blue), and all other affiliation types (white). Authors publishing on papers with more than one affiliation type were coloured based on combinations of the primary colours and white, thereby yielding secondary and tertiary colours. For example, authors on papers with affiliated with academia and government were coloured orange (a combination of red and yellow), authors on papers affiliated with government and industry were coloured green (a combination of yellow and blue), authors on papers affiliated with academia and industry were coloured purple (a combination of red and blue), and authors on papers affiliated with academic, government, and industry were coloured grey (a combination of red, yellow, and blue). The addition of other affiliation types into the mix, which were represented by the colour white, lightened these colour combinations. For example, authors on papers affiliated with academia, government, and other were coloured light orange (a combination of red, yellow, and white).

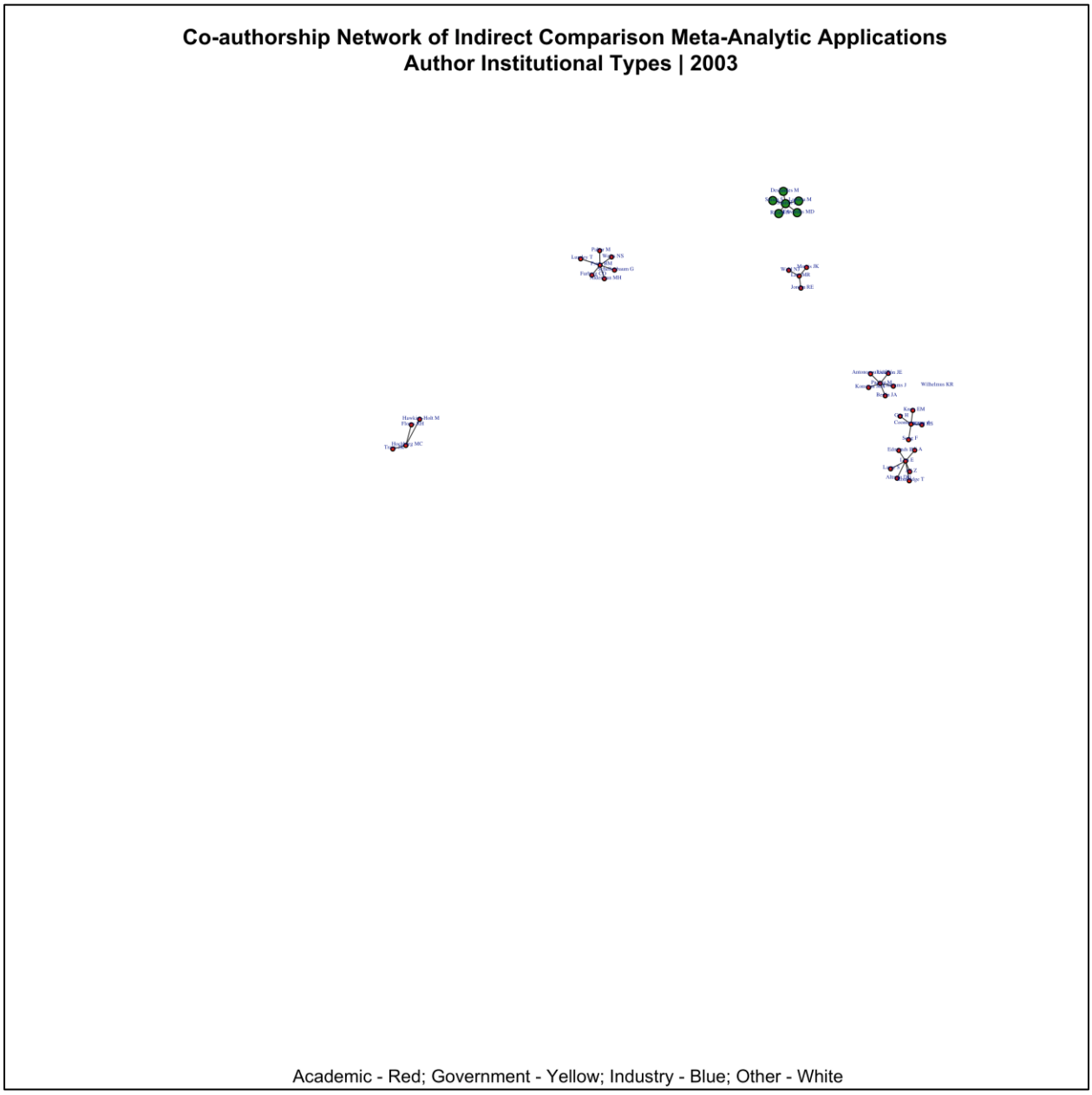
## 2001



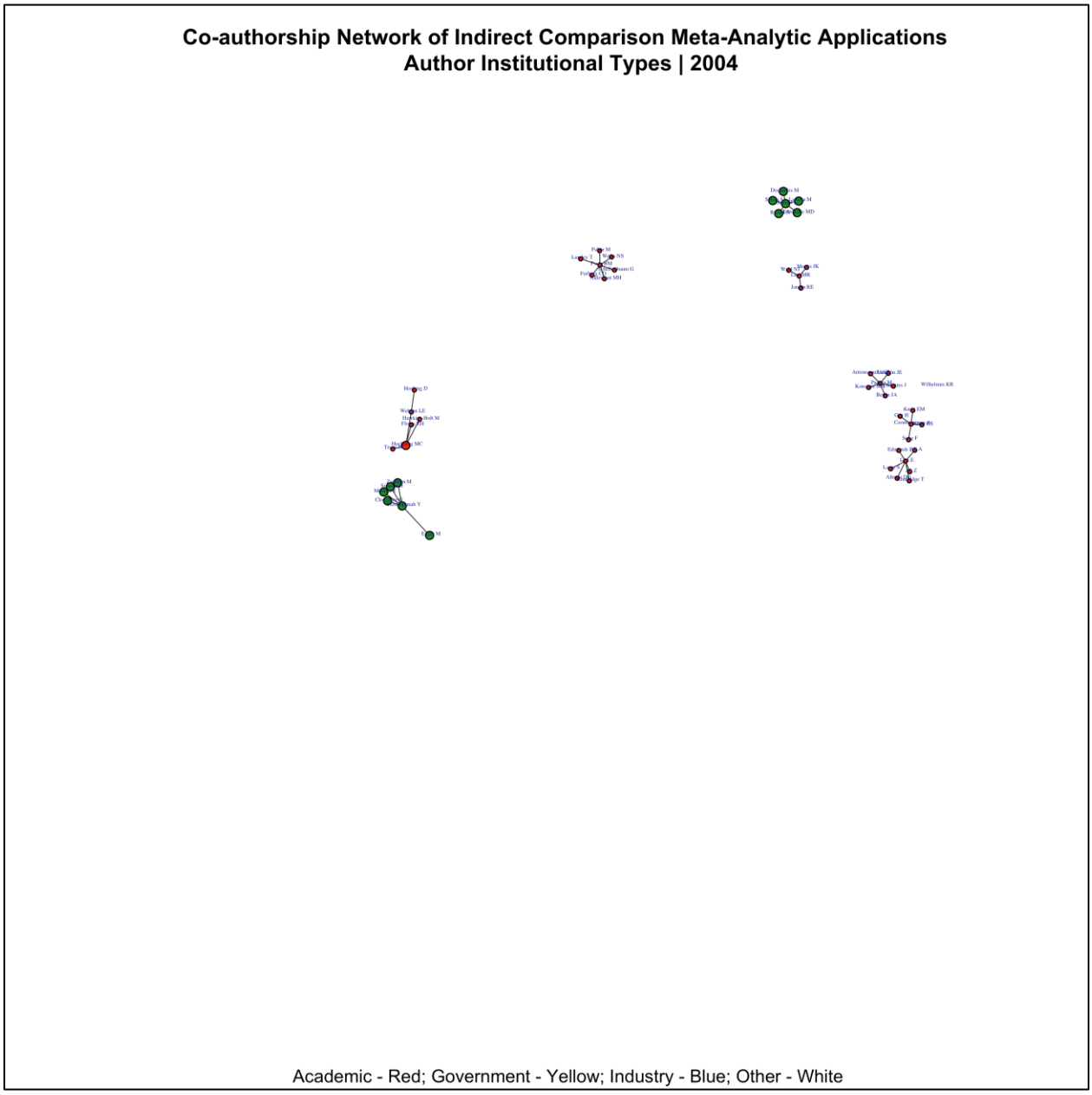
## 2002



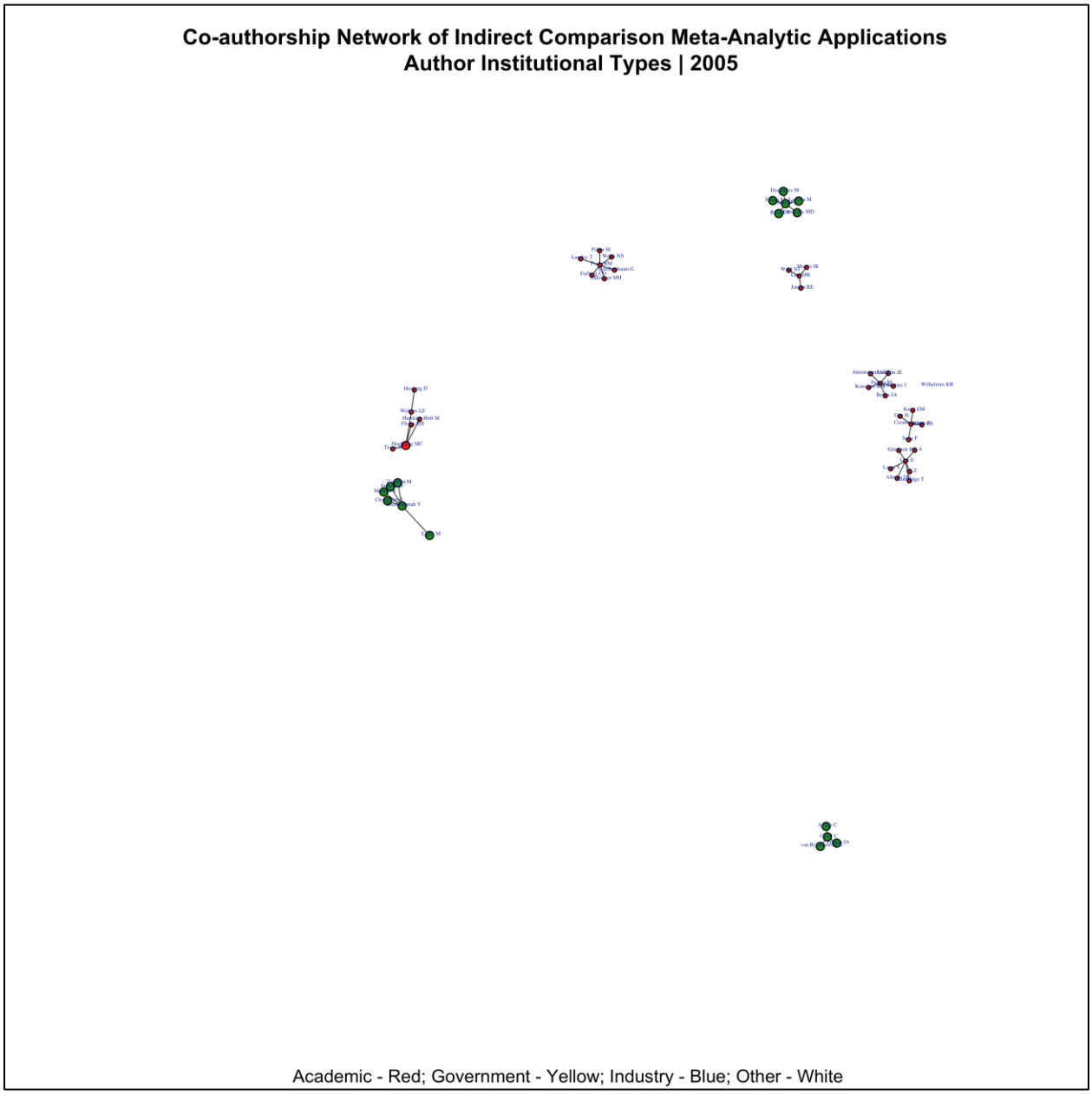
## 2003



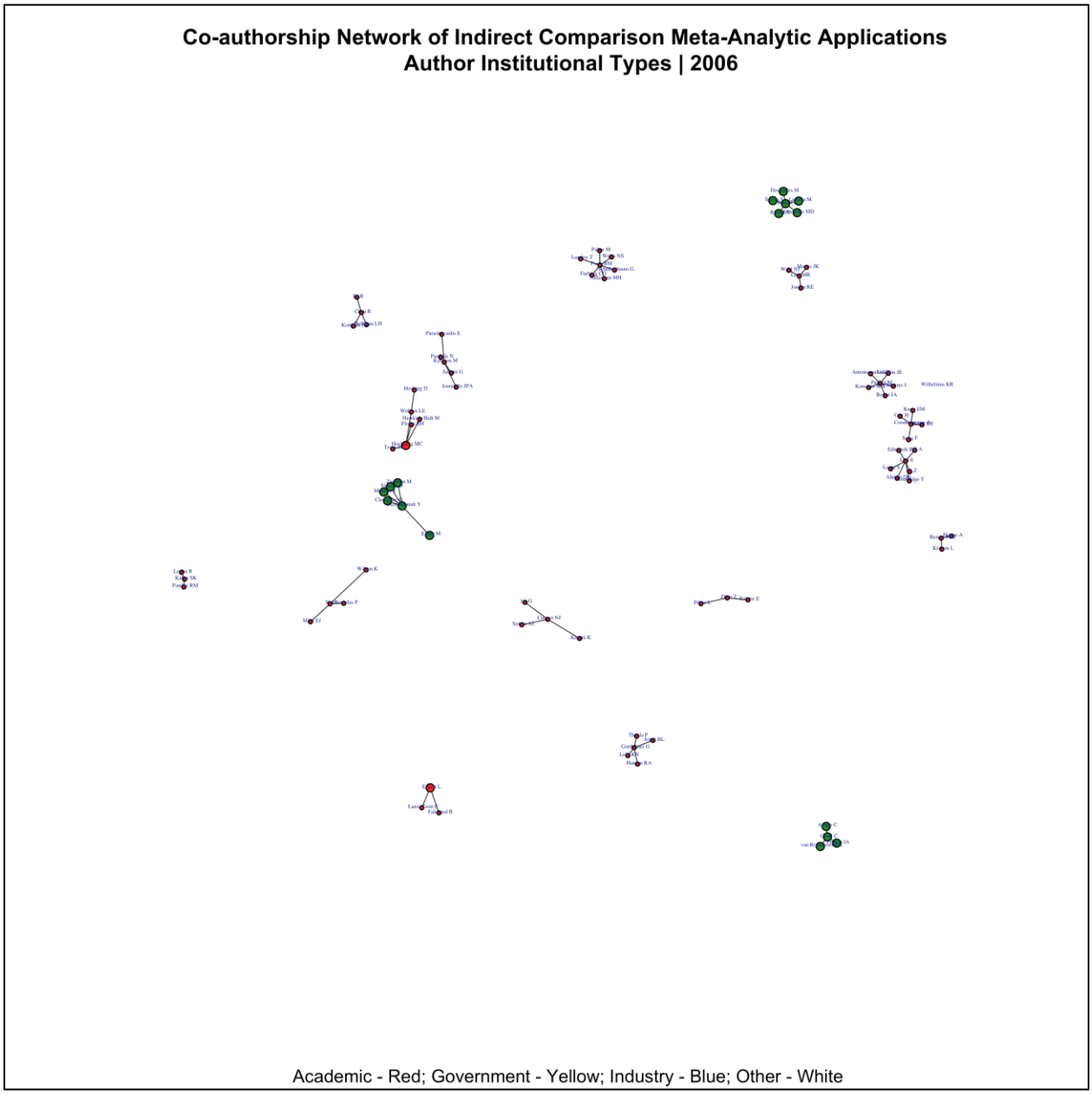
## 2004



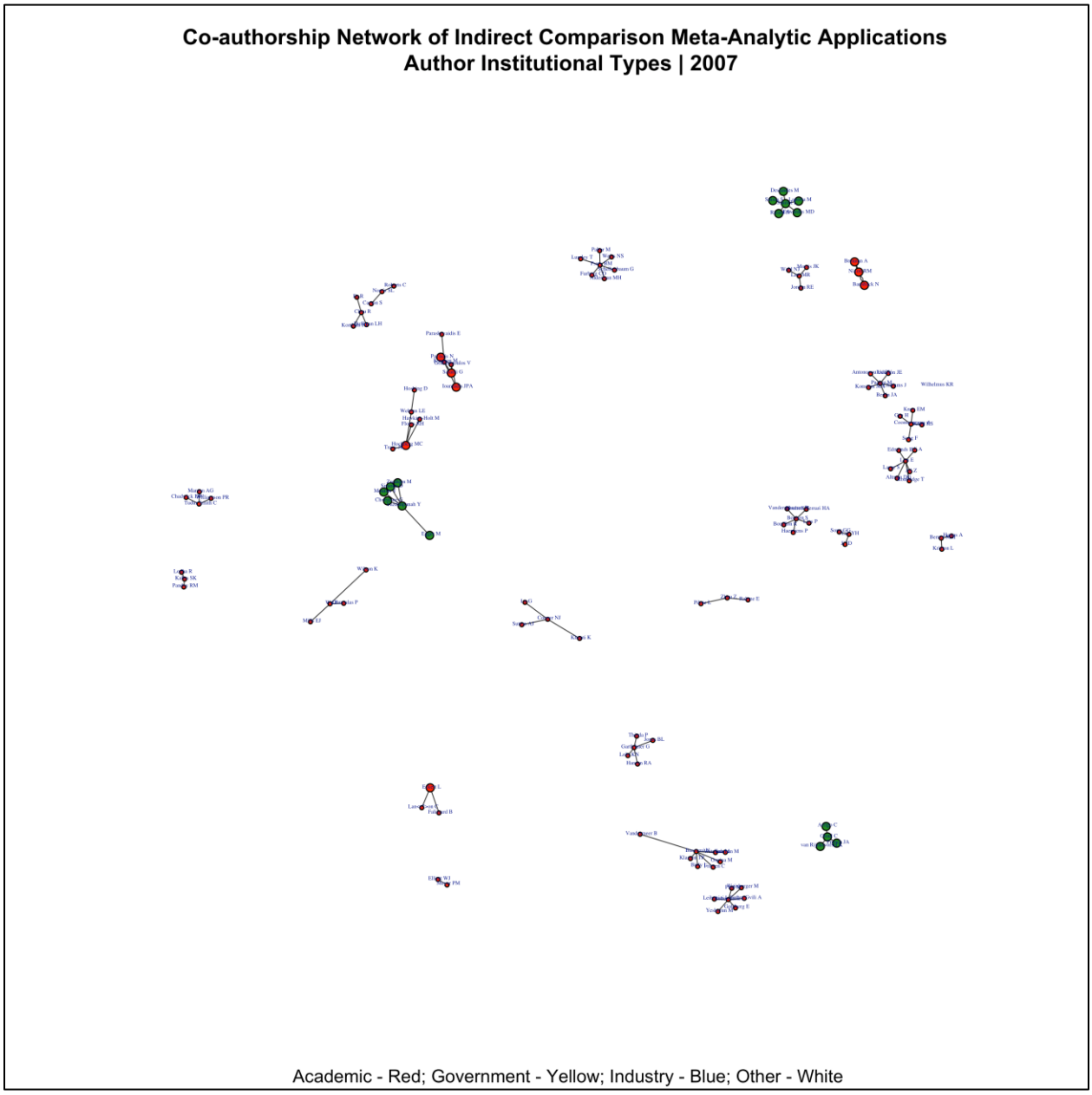
## 2005



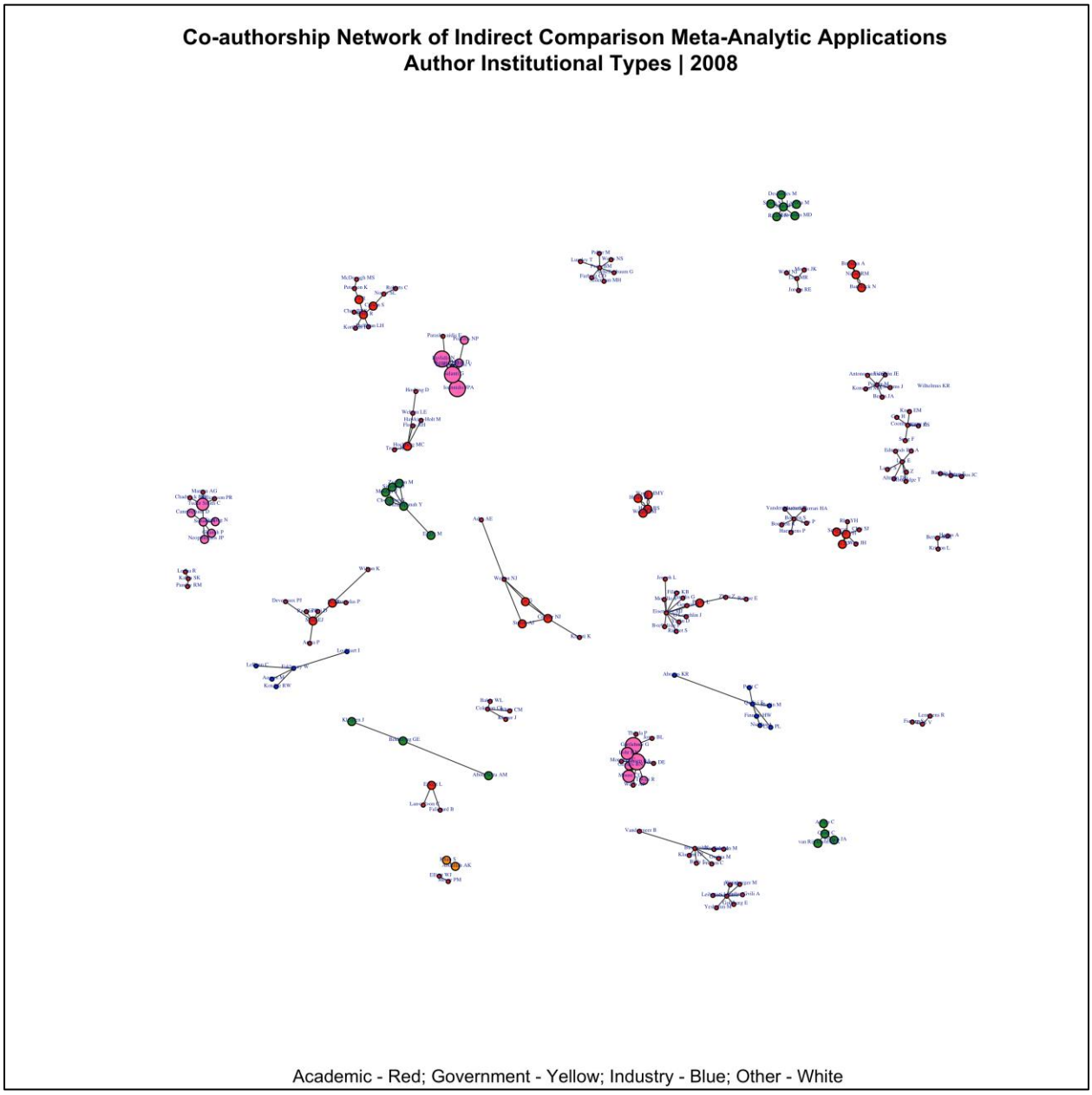
## 2006



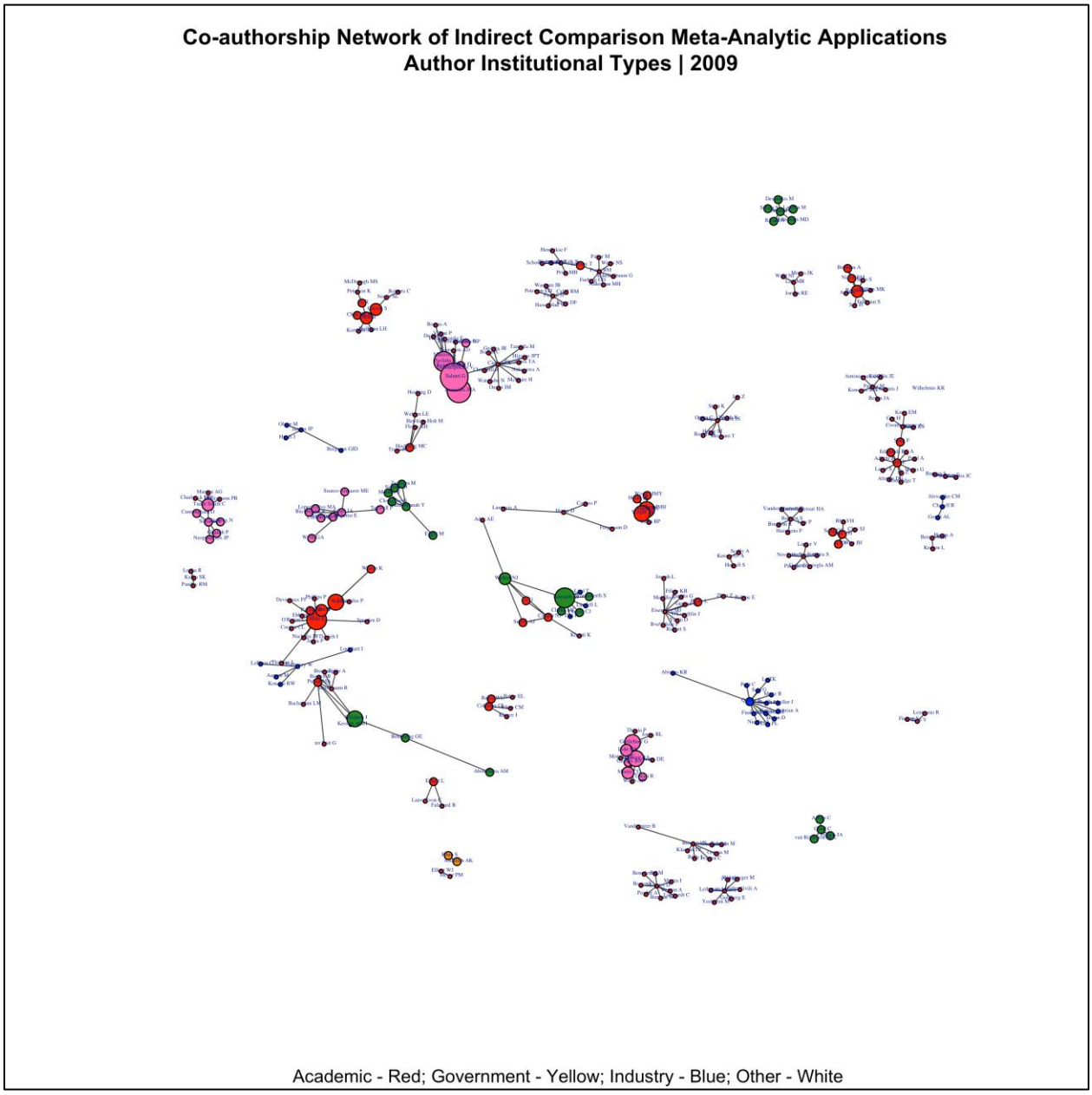
## 2007



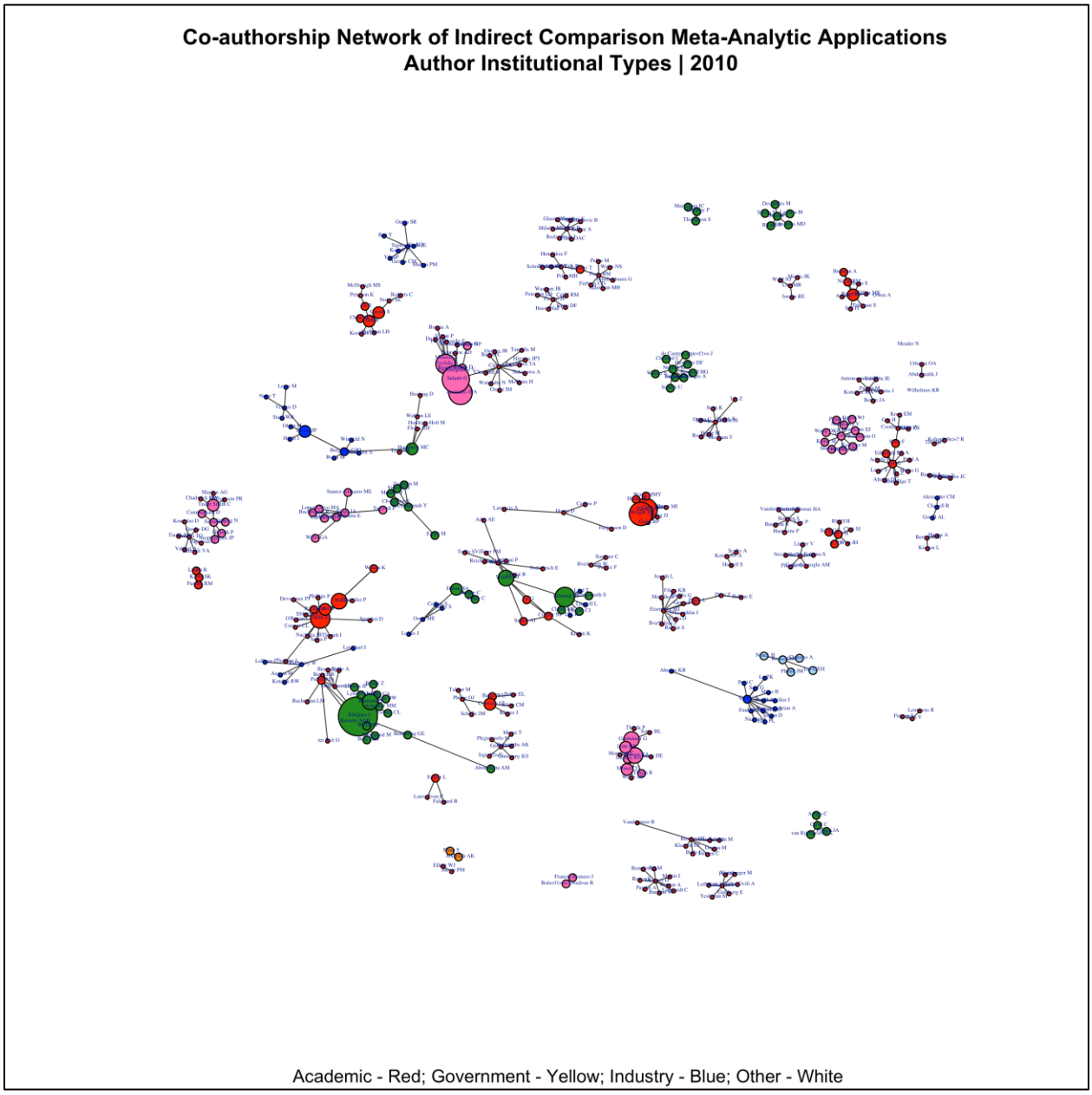
## 2008



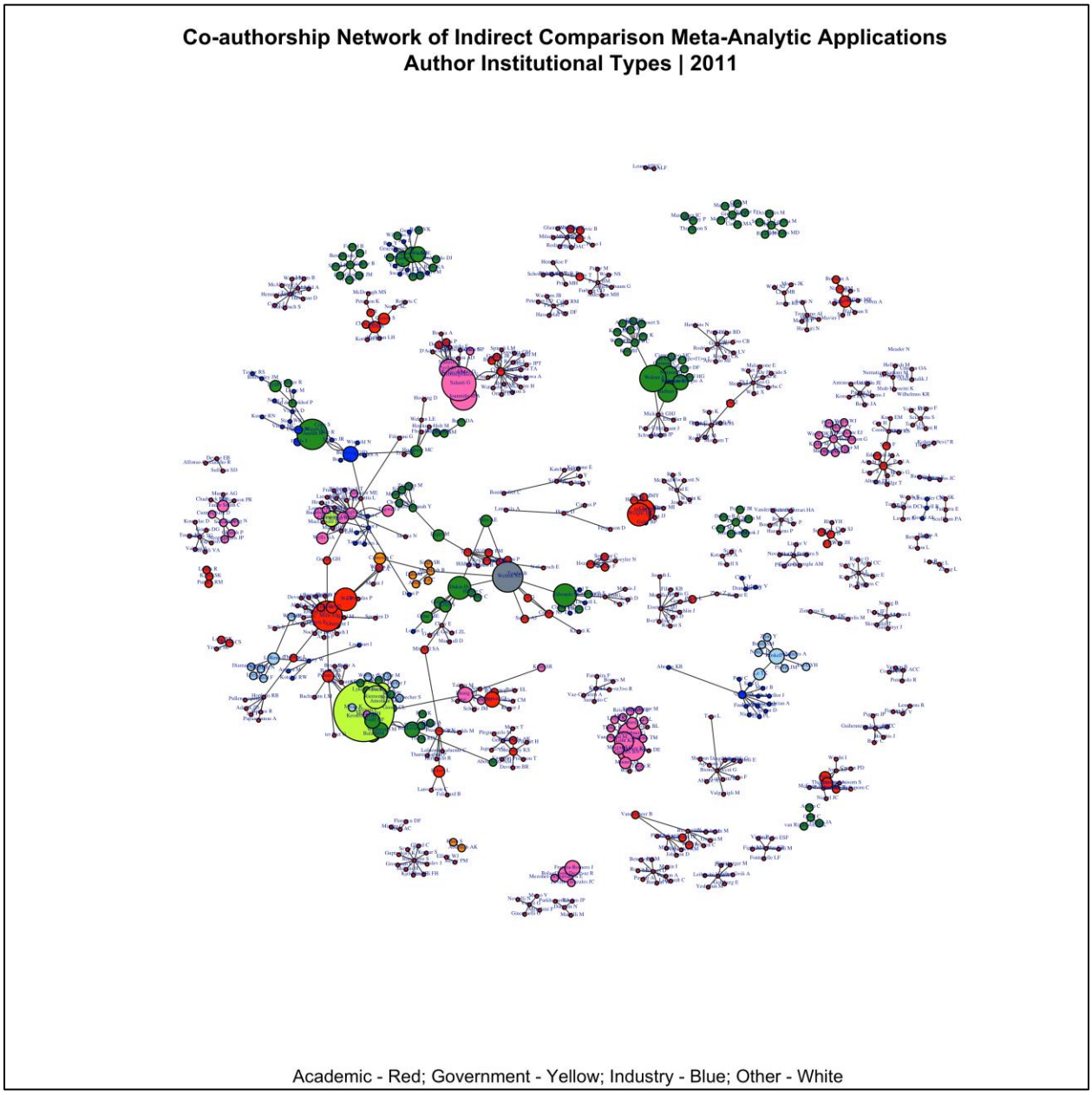
## 2009



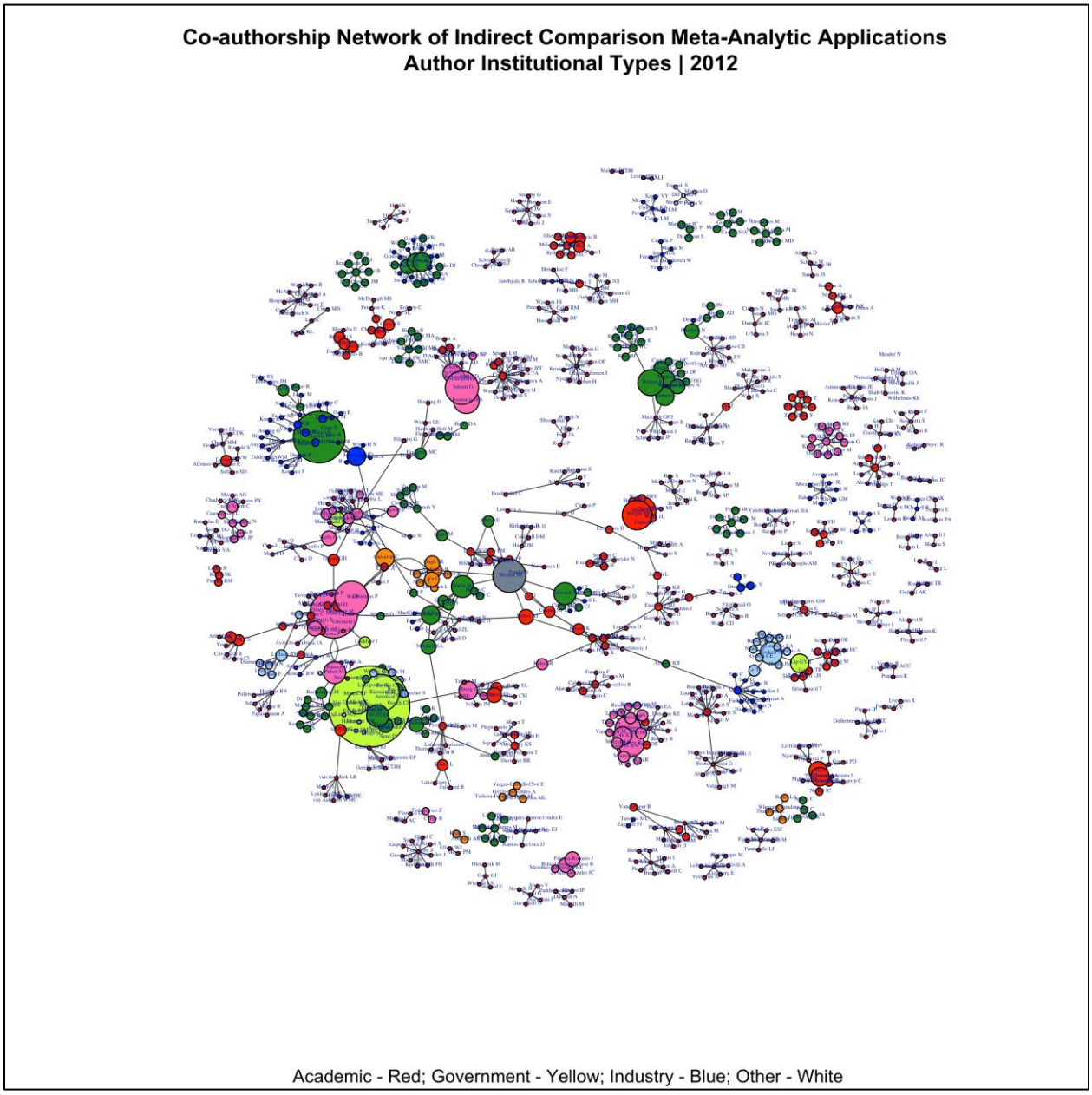
## 2010



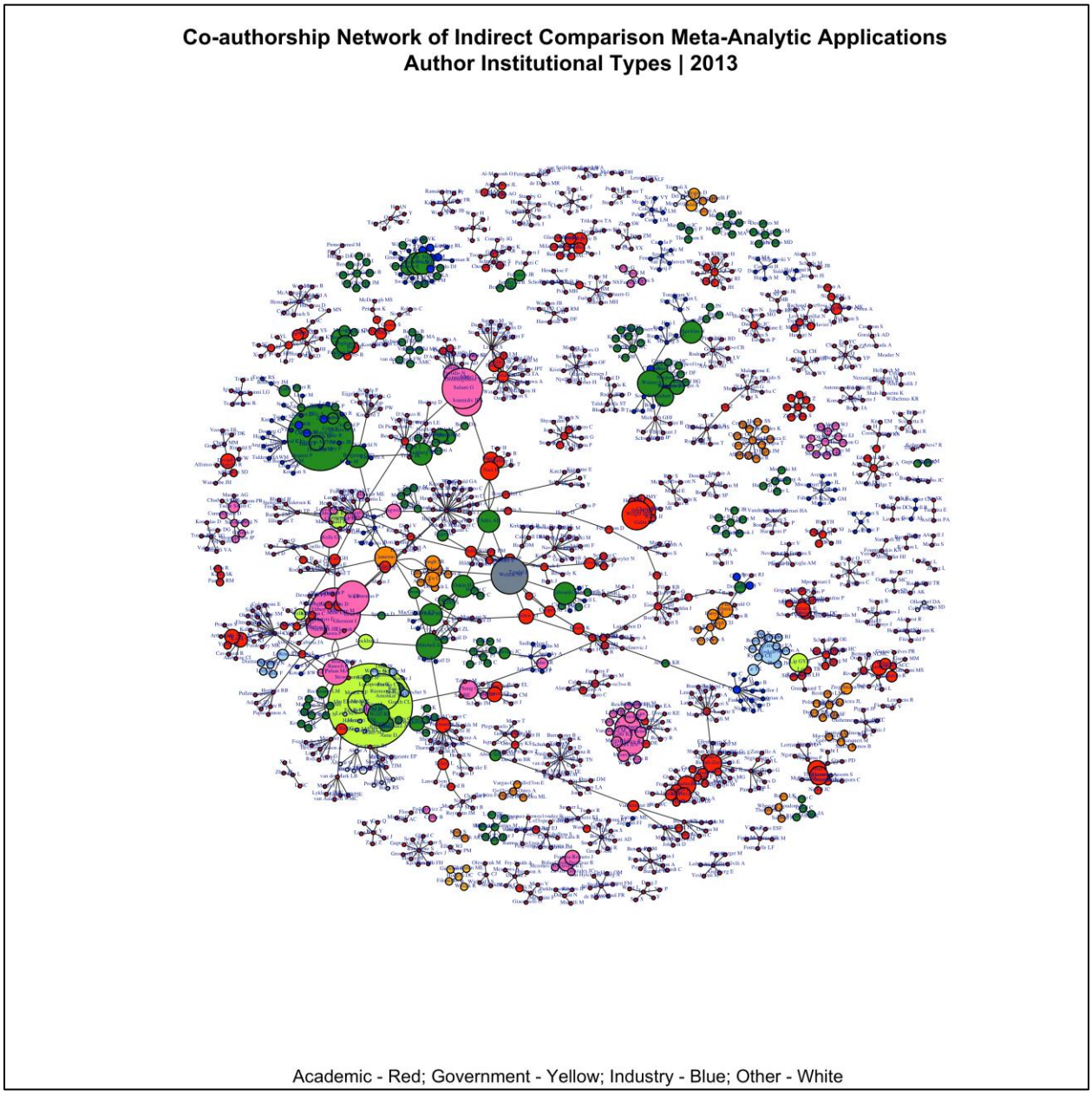
## 2011



## 2012



## 2013



# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2-3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5-6 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | N/A |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7-8 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 7-8 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 7-8 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 8 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 8 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 8 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | N/A |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | N/A |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | N/A |

# PRISMA 2009 Checklist



| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | N/A |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 10, 28 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 10-11, 25-27 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | N/A |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | N/A |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | N/A |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | N/A |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 13-16 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 16-18 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 18-19 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 20 |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.