BMJ Open

Multiple chemical sensitivity scoping review protocol: overview of research and MCS construct

Susanne Hempel ,[1] Margie Danz,[1] Karen A Robinson,[2] Maria Bolshakova,[1] Jesus Rodriguez,[1] Alanna Mears,[1] Cindy Pham,[1] Sachi Yagyu,[1] Aneesa Motala,[1] Danica Tolentino,[3] Omid Akbari,[4] Jill Johnston[3]

To cite: Hempel S, Danz M, Robinson KA, *et al*. Multiple chemical sensitivity scoping review protocol: overview of research and MCS construct. *BMJ Open* 2023;**13**:e072098. doi:10.1136/bmjopen-2023-072098

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2023-072098).

Received 27 January 2023
Accepted 16 August 2023

[1]Southern California Evidence Review Center, University of Southern California, Los Angeles, California, USA
[2]Division of Health Science Informatics, John Hopkins Medicine, Baltimore, Maryland, USA
[3]Keck School of Medicine, University of Southern California, Los Angeles, California, USA
[4]Molecular Microbiology and Immunology, University of Southern California, Los Angeles, California, USA

Correspondence to
Dr Susanne Hempel;
susanne.hempel@med.usc.edu

ABSTRACT

Introduction Multiple chemical sensitivity (MCS) has been characterised by reported adverse responses to environmental exposures of common chemical agents (eg, perfumes, paint, cleaning products and other inhaled or ingested agents) in low doses considered non-toxic for the general population. There is currently no consensus on whether MCS can be established as a distinct disorder.

Methods and analysis The scoping review of the literature will be guided by five questions: How is MCS defined and which diagnostic criteria have been proposed? What methods are used to report prevalence and incidence estimates of MCS? What are the characteristics of the body of scientific evidence that addresses whether MCS is a distinct disorder or syndrome? What underlying mechanisms for MCS have been proposed in the scientific literature? Which treatment and management approaches for MCS have been evaluated in empirical research studies? We will conduct a comprehensive search in 14 research databases. Citation screening will be supported by machine learning algorithms. Two independent reviewers will assess eligibility of full-text publications against prespecified criteria. Data abstraction will support concise evidence tables. A formal consultation exercise will elicit input regarding the review results and presentation. The existing research evidence will be documented in a user-friendly visualisation in the format of an evidence map.

Ethics and dissemination Determined to be exempt from review (UP-22-00516). Results will be disseminated through a journal manuscript and data will be publicly accessible through an online data repository.

Registration details The protocol is registered in Open Science Framework (osf.io/4a3wu).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This scoping review will cast a wide net capturing multiple important aspects of the complex construct *multiple chemical sensitivity* (MCS).
⇒ A formal consultation exercise will provide input from experts and stakeholders.
⇒ The existing research evidence will be documented in a user-friendly visualisation in the format of an evidence map.
⇒ A scoping review can only provide a broad overview of the existing MCS research.
⇒ The lack of standardised terminology for the MCS construct makes identifying and documenting relevant research challenging.

INTRODUCTION

Multiple chemical sensitivity (MCS) has been characterised by reported adverse responses to environmental exposures of common chemical agents in low doses considered non-toxic for the general population. These may be solvents such as paint and cleaning products, odorants such as perfume and scented soaps, air pollutants such as cigarette smoke and smog, or materials such as new furnishings or new carpets. Symptoms are non-specific, involve multiple organ systems, and may include nausea, dizziness, headache, abdominal pain, fatigue and depression, among others.[1–3] Responses generalise from individual to sets of often unrelated chemical agents and limit social and occupational functioning.[2 4–8] Terminology varies and some authors describe the condition more broadly as an idiopathic environmental intolerance.[2 9 10] Other researchers have called for a paradigm shift, moving away from terms that characterise the symptoms (eg, as a sensitivity or intolerance) to a more neutral description of *symptoms associated with environmental factors*.[11 12]

To date, tens of thousands of publications have addressed MCS in the international lay and scientific literature.[13] However, little consensus exists regarding MCS, including its defining characteristics.[14–19] Prevalence estimates vary considerably, suggesting differences in operationalisations of the definition and diagnostic criteria for MCS.[20–23] Individual symptoms reported by patients are not unique to MCS and the lack of consensus, including whether MCS should be considered a distinct disorder, hinders the

identification and differential diagnosis of MCS in clinical practice.[24–26] Much debate centres around the underlying nature of the condition as toxigenic or psychogenic.[27–29] A large number of potentially underlying mechanisms of action for MCS have been described (eg, immune system dysregulation, neural sensitisation and hyperresponsivity, neurogenic inflammation, limbic system dysfunction, oxidative stress hypothesis, genetic theories, pyschological theories, panic and post-traumatic stress disorder symptoms, somatisation disorder symptoms, psychological beliefs and expectancies or classical conditioning).[5] Regardless of the challenges in operationalising definitions and establishing its aetiology, MCS is an internationally recognised phenomenon that has been described in different formats and terms for decades.[5] It is a distressing and puzzling condition for patients as well as their healthcare providers.[30–32] Some hypotheses about mechanisms of action have resulted in proposed interventions for patients; however, no comprehensive review of the evaluated treatment and management options exists that currently successfully supports patients describing MCS symptoms.[33 34] Few attempts have been made to establish consensus on how patients presenting with MCS should be assessed or treated in clinical practice and new guidelines highlight the need for a complex multidisciplinary approach.[35] Surveys describe multiple, often not evidence-based treatment approaches that have been tried by patients, and the lack of clinical guidance leaves healthcare practitioners guessing how to best address MCS in their patients.[8 34 36 37]

Despite the large number of publications addressing MCS, there is a lack of research syntheses that provide an overview of the existing evidence base on the condition. We believe that the existing evidence base needs to be mapped as a first step in order to advance research and practice in this complex field. Before trying to establish the most salient case definition of MCS or the most plausible underlying mechanism(s) leading to MCS in a systematic review, a scoping review should systematically identify, explore and characterise the existing research literature. The proposed work will be based on this type of review. Scoping reviews are systematic literature review approaches that explore research fields to capture the volume and content of scientific literature that is relevant to guiding questions for the review.[38–40] To address the complexity of the topic, it is critical that a comprehensive review cast a wide net, incorporating research from different disciplines and conceptual positions. Our planned scoping review will use extensive literature searches to map the existing literature. The review will provide an overview of proposed definitions of and diagnostic criteria for MCS, identify prevalence and incidence research, document the body of evidence addressing the question of whether MCS is a distinct disorder, compile a compendium of suggested underlying mechanisms of MCS aetiology and processes, and provide an overview of the literature on MCS treatment and management that has been published to date.

This scoping review was prospectively registered and will be conducted according to established procedures to provide a systematic and transparent exploration of the literature.[41] The findings of the scoping review will be presented as an evidence map. Evidence maps are an evidence synthesis tool that provide a visualisation of a large evidence base to provide readers with a concise overview.[42 43] They allow a visual and user-friendly research overview suitable for a large and diverse research field, effectively mapping the existing evidence.[42 44–51] The evidence map will document the presence and absence of research on MCS for the five questions guiding the review in a user-friendly format.

Guiding questions

The following review questions will guide the scoping review:

- GQ1: How is MCS defined and which diagnostic criteria have been proposed?
- GQ2: What methods are used to report prevalence and incidence estimates of MCS?
- GQ3: What are the characteristics of the body of scientific evidence that addresses whether MCS is a distinct disorder or syndrome?
- GQ4: What underlying mechanisms for MCS have been proposed in the scientific literature?
- GQ5: Which treatment and management approaches for MCS have been evaluated in empirical research studies?

Review aim

The review will answer the guiding questions with the identified scientific literature in a user-friendly format. A systematic evidence map will provide a visualisation of the existing evidence and research gaps.

METHODS AND ANALYSIS

The review is registered in the Open Science Framework (OSF).[13] The scoping review will follow the steps for scoping reviews outlined by Arksey and Malloy: stage 1: identifying the research question; stage 2: identifying relevant studies; stage 3: study selection; stage 4: charting the data; stage 5: collating, summarising and reporting the results. In addition, a consultation exercise to inform and validate findings from the scoping review will be conducted. The planned duration is April 2022 to December 2023. The following outlines the steps in detail. The reporting will follow established guidelines.[39 52]

Search strategy

We will search the international literature on MCS using different taxonomy and nomenclature. Literature searches will be designed, executed and documented by an experienced evidence review centre librarian. The scoping review addresses multiple aspects of MCS, and the search strategy covers multiple databases to ensure that all scientific literature relevant to MCS will be identified.

The use of multiple sources is a key method to minimise selection bias being introduced into the review. We plan on searching the following databases to obtain a diverse set of citations potentially relevant to MCS from different disciplines:

- PubMed (biomedical)
- CINAHL (nursing)
- Embase (biomedical)
- Web of Science (general scientific database)
- Scopus (health sciences)
- PsycINFO (behavioural and social sciences)
- Healthcare Administration Database (public health administration)
- Current Contents Connect (multidisciplinary)
- BIOSIS Citation Index (life sciences)
- Environment Index (environmental research)
- Environmental Science Database
- HERO (Health & Environmental Research Online)
- SciFinder (chemical literature)
- Agricultural & Environmental Science Collection (includes AGRICOLA, environmental research)

The search strategy is shown in online supplemental appendix 1. Content experts provided input regarding individual search terms and databases.

In addition, our review will be informed by existing comprehensive reviews on the topic.[4 12 16 17 24 35 53–61] Reviews will be systematically identified through the systematic review filter in PubMed and the Cochrane Database of Systematic Review. We will screen the international registry PROSPERO for ongoing efforts that could inform this project during the update search period; currently, the registry includes only two ongoing efforts that address selected aspects of MCS.[62 63]

For individual guiding questions, we will search additional sources, including selected and prespecified grey literature sources. For definitions and diagnostic criteria (GQ1), we will search the website of global organisations such as the WHO. Searches for prevalence research (GQ2) will reference-mine existing reviews.[5] We will review reports identified in PubMed Health regarding consensus statements on MCS as a distinct disorder (GQ3) and regarding published suggested underlying mechanisms (GQ4). For intervention studies (GQ5), we will search repositories of practice guidelines including G-I-N[64] and the ECRI-maintained guideline database.[65] In addition, we will search the US trial registry clinicaltrials.gov[66] and the International Clinical Trials Registry Platform maintained by the WHO.[67]

In addition, we will reference-mine relevant reviews and included studies and consult with content experts to ensure that all relevant literature has been captured.

Eligibility criteria and screening

We will use a PICOTSO (population, intervention/exposure, comparator, outcome, timing, setting and other limiter) framework to structure the eligibility criteria. For each guiding question, we will determine detailed inclusion and exclusion criteria. The criteria, thus far, are as follows:

- Population:
  - Publications reporting definitions (GQ1) and studies reporting on the prevalence and incidence (GQ2) of MCS will be limited to those that explicitly state *MCS*, *chemical intolerance* or *idiopathic environmental intolerance* with a reference to *chemical* sensitivities (rather than electromagnetic sensitivity or other conditions not associated with perceived exposure to chemical agents, solvents, odorants, air pollutants or materials). Publications reporting exclusively on the prevalence of individual sick building syndrome symptoms or electromagnetic hypersensitivity will be excluded.
  - Eligible populations for GQ3 and GQ4 will include those that either state *MCS* or those that are characterised by symptoms of idiopathic environmental intolerance or exposure to environmental factors with a reference to chemical agents, solvents, odorants, air pollutants or materials . Populations will not be restricted to human participants diagnosed with MCS, and will instead include a wide range of research that may contribute to establishing MCS as a diagnosis and exploring relevant underlying mechanisms.
  - GQ5 will be limited to samples of human participants where some participants are characterised by MCS, idiopathic environmental intolerance for chemicals, the equivalent of the ICD-10-CM Code F45.9 (somatoform disorder, unspecified) or studies that report on a subgroup of the patients of interest.
- Intervention/exposure/independent variable:
  - We will accept definitions of MCS and descriptions that include diagnostic criteria (GQ1).
  - Prevalence and incidence measures need to state the criteria of MCS clearly to be eligible (GQ2).
  - GQ3 studies assessing whether MCS is a distinct disorder (ie, distinct from other 'physical' disorders or 'psychiatric' disorders) need to provide empirical evidence of discriminatory power to support the authors' conclusions or need to be based on formal expert consensus methods. Opinions of individual authors will not be eligible.
  - Eligible publications suggesting underlying mechanisms (GQ4) may include evidence for the onset of MCS or the course of the disease, including TILT (toxicant-induced loss of tolerance describing an initiation and a triggering stage).
  - Studies evaluating interventions (GQ5) to prevent, manage or treat MCS will be eligible. Interventions will not be restricted by the content or treatment approach and may include interventions aiming to avoid triggers, focusing on coping with MCS symptoms, desensitisation or addressing the causes of MCS. In addition, interventions in patients diagnosed with MCS will be eligible regardless of

the intervention focus (patient-centred rather than intervention-centred approach). Case studies of individual patients will be included if focused on intervention rather than the natural course of the condition and the description is published in a peer-reviewed scientific journal.

- Comparator: Studies will be eligible regardless of the presence of a comparator.
- Outcome: GQ1 publications will need to provide sufficiently detailed descriptions that can be operationalised as a definition or diagnostic criteria. GQ2 studies will need to report a numerical estimate of the prevalence or incidence of MCS. GQ3 and GQ4 will not be limited by reported outcomes. GQ5 studies may report on patient health (self or clinician report), physiological or psychosocial measures assessing the effect of the intervention (effectiveness as well as safety indicators); quantitative and qualitative data will be eligible. Studies reporting only on treatment uptake, patient or provider acceptability of treatments, or treatment costs will be excluded.
- Timing: GQ1 studies will be included regardless of the publication year (eg, definitions from the 1980s are eligible). GQ2 studies will be eligible regardless of the timing of the exposure or assessment (eg, childhood exposure, symptoms tested in adults). GQ3 and GQ4 studies will not be restricted by time of exposure or follow-up, and retrospective, concurrent and prospective studies will be eligible. GQ5 studies will be included regardless of the intervention duration and follow-up.
- Setting: Studies will not be restricted by setting and will be drawn from the international literature.
- Other limiters: English-language publications disseminated to a wide audience through a scientific journal will be eligible. Studies published in abbreviated form (eg, conference abstracts) will not be eligible for inclusion.

Systematic reviews and relevant narrative reviews will be retained for reference-mining. Multiple publications on the same study (ie, studies defined by the included participants) will be consolidated into one study record to ensure that a given study is not counted multiple times regardless of the number of publications reported on the study. The literature flow will be transparently documented in a citation management programme.

Inclusion screening process

We will use an online database (DistillerSR) designed for literature reviews to screen the search output. The team will design detailed citation and full-text screening forms to ensure a transparent, consistent and unambiguous approach. Citations found to be potentially relevant by at least one reviewer will be obtained as full text. Citations screening will be supported by machine learning algorithms to reduce reviewer errors and bias. All citations excluded by a human reviewer will be screened for relevance by the machine learning algorithm to ensure that no potentially relevant publication has been missed.

Full-text screening will apply the detailed eligibility criteria. Training will ensure a shared understanding of all inclusion and exclusion criteria across reviewers. Full-text publications will be screened by two independent reviewers and any discrepancies will be resolved through discussion in the review team. Dual screening reduces reviewer bias and errors and is critical for this complex topic. The screening decisions and reasons for exclusion of studies will be tracked in the online database and citation management software. This allows us to reconstruct a detailed literature flow and facilitates the documentation of included and excluded publications. Reasons for exclusion will match the exclusion criteria dimensions to orient the reader. The literature flow will be documented in a flow diagram.

Studies excluded at full text will be documented in the online supplemental appendix 1 of the review together with a reason for exclusion. We will retain background papers, that is, papers to cite or reviews to reference-mine. We will report the number of included studies and the number of publications reporting on each study across the review and for each guiding question.

Data abstraction

The data abstraction will provide a concise overview of the evidence.

For *GQ1* (definitions and diagnostic criteria), we will document the suggested definitions and the approach to establish it. We will document published diagnostic criteria of MCS and for diagnostic accuracy studies, the type (eg, self-report questionnaire, objective test such as exposure chamber and challenge test) and name of the test will be recorded.

For *GQ2* (prevalence and incidence), we will document the data type (eg, prevalence or incidence), the method of assessment (eg, self-report, medical record) and the operationalisation of MCS (definition, criteria). We will distinguish general, unselected populations (eg, students) from targeted samples with potentially increased risk (eg, Gulf War veterans). For each study, we will record the country, sample size and year of estimate, and identify any published prospective studies.

For *GQ3* (MCS as a distinct disorder), we will document the aim of the study, the employed study design, and the analytic approach to evaluate MCS as a distinct disorder. We will record the type of research approach used to determine whether MCS should or should not be considered a distinct disorder or syndrome (eg, establishing a unique biomarker, analysing symptom clusters, documenting explained variance)[26] and differentiate the use of direct, mechanistic and parallel evidence by the authors.[68–70] We will abstract the authors' conclusion regarding their conceptual agreement with MCS as a distinct disorder with a differential clinical diagnosis.

For *GQ4* (underlying mechanisms), we will broadly categorise the study type and approach to indicate which

aspect of the condition the study addresses (eg, the general aetiology or a specific process such as the mechanism of generalising across agents) and whether the approach assumes a biological, psychological or other (eg, multiple processes) hypothesis. For each study, we will categorise the suggested mechanisms (eg, neurogenic inflammation).[5] This will involve collating and reviewing all identified mechanisms and establishing a categorisation system based on the published literature and identified approaches. We will also establish a compendium of frameworks and diagrams reported by the authors. For this, figures published under a Creative Commons license will be included in the compendium; for all others, the publisher will be contacted to request permission to use the figure.

GQ5 (therapy and management for MCS) will collate all identified interventions and broadly categorise interventions as prevention, management or treatment. We will document the focus of the intervention (eg, aiming to alter the course of the condition, coping strategies) together with the broad therapeutic approach (removing triggers from environment, diet, supplements, masks, devices, (off-label) medication, psychological approaches). The categorisation system will built on existing reviews and the identified empirical research.[26] We will also abstract the author group, publication year and country.

Data will be abstracted by one reviewer and checked by an experienced literature review methodologist. We will export data into tables and figures or data files for further analysis.

Consultation exercise

The last step of the scoping review process will be a consultation exercise. We will ask multidisciplinary technical experts and stakeholders in MCS research, practice and advocacy to review the results of the scoping review. These reviewers will not have been involved in the review process and will assess the review de novo. Previous experiences have shown that this last step of stakeholder involvement provides invaluable input and adds to the usefulness and validity of the end product.[41 71 72] The consultation exercise will be conducted as an online survey sent to participants together with the review to elicit structured feedback on the content and presentation of the review. The input will contribute to the presentation of the scoping review results.

Patient and public involvement

The planned review was presented at a stakeholder meeting organised by the funding agency that included a patient representative. Several stakeholders are also part of the scientific steering committee that reviewed this protocol (see the Acknowledgement section). The results of the review will be distributed to stakeholders in a formal consultation exercise as outlined earlier. This step will be instrumental in ensuring a user-friendly presentation of results that is useful to patients and the public.

RESULT PRESENTATION

Characteristics of all studies meeting inclusion criteria will be documented in concise evidence tables to provide a broad documentation of the underlying evidence base. Findings across studies will be documented in an evidence map. This visual and user friendly research overview will map the existing evidence on MCS.

The evidence map will use a limited number of dimensions to display the existing research. Displaying the evidence as a bubble plot, each bubble in the plot will represent a study and the size of the bubble will represent the size of the study. The plot will use the x-axis to display existing types of research studies to characterise the evidence base further. The y-axis can be used to characterise the guiding question addressed by the research. In addition, the shape of the bubble and/or shading may represent different study designs and methodological characteristics. The optimal display will be selected based on input from the consultation exercise.

The tables and figures will be accompanied by a narrative that summarises the identified evidence base. This scoping review and evidence map will provide a broad overview of the existing research on MCS. It also aims to facilitate a future systematic review of the literature that will answer definitive research questions (eg, what is the prevalence of MCS and the effectiveness of treatments for MCS). Scoping and mapping has become increasingly useful to prepare more definitive systematic reviews that answer closed questions, in particular for large and controversial topics.[42 43 48 52 73 74] The scoping review will provide context and information on which topic areas are to date amenable to a formal systematic review of the literature. The future systematic review will address a narrower scope of approaches that have been identified in this scoping review, assess the quality of evidence for distinct topics of interest, and synthesise the evidence.

In addition to documenting the existing evidence base, we will clearly outline gaps in the literature identified in this scoping review. The gap presentation will use the scoping review's eligibility framework to transparently document existing gaps and future research needs. The gap analysis will make concrete recommendations to facilitate future research.

Ethics and dissemination and data availability

The scoping review was determined to be exempt from further review by the University of Southern California Institutional Review Board review in July 2022 (ID UP-22-00516). The results of the review will be disseminated through a journal manuscript. Data of the scoping review will be publicly available through an online data repository (SRDR+).

Acknowledgements We thank Dori Germolec, Howard Hu, Jon Samet and Roberta White for their thoughtful comments. We also thank Tatjana Walker at the at the Marilyn Brachman Hoffman Foundation for her feedback and support.

Contributors SH obtained funding; SH, MD, KAR, OA and JJ designed the study, SH, MD, MB, JR, AIM and CP screened literature to develop this manuscript;

AnM and DT manage the data; SY conducted the literature searches; all authors contributed conceptually to the work and edited this manuscript.

Funding This work was supported by the Marilyn Brachman Hoffman Foundation (ID 015153-00001).

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD

Susanne Hempel http://orcid.org/0000-0003-1597-5110

REFERENCES

1 Consensus on multiple chemical sensitivity. Multiple chemical sensitivity: a 1999 consensus. *Arch Environ Health* 1999;54:147–9.
2 Workshop on Multiple Chemical S. World health organization. programme for the promotion of chemical safety, international programme for chemical safety. In: *Report of the Workshop on Multiple Chemical Sensitivities (MCS)*. Berlin, Germany Geneva: World Health Organization, 1996.
3 Cone JE, Harrison R, Reiter R. Patients with multiple chemical sensitivities: clinical diagnostic Subsets among an occupational health clinic population. *Occup Med* 1987;2:721–38.
4 Driesen L, Patton R, John M. The impact of multiple chemical sensitivity on people's social and occupational functioning; a systematic review of qualitative research studies. *J Psychosom Res* 2020;132:109964.
5 Zucco GM, Doty RL. Multiple chemical sensitivity. *Brain Sci* 2021;12:46.
6 Winder C. Mechanisms of multiple chemical sensitivity. *Toxicol Lett* 2002;128:85–97.
7 Cullen MR. The worker with multiple chemical sensitivities - an overview. *Occup Med-State Art Rev* 1987;2:655–61.
8 Alameda Cuesta A, Pazos Garciandía Á, Oter Quintana C, *et al*. Chronic fatigue syndrome, and multiple chemical sensitivity: illness experiences. *Clin Nurs Res* 2021;30:32–41.
9 American Academy of allergy asthma and Immunology (AAAAI) board of directors. idiopathic environmental Intolerances. *J Allergy Clin Immunol* 1999;103(1 Pt 1):36–40.
10 ACOEM position statement. Multiple chemical sensitivities: idiopathic environmental intolerance. *Journal of Occupational and Environmental Medicine* 1999;41:940–2.
11 Van den Bergh O, Brown RJ, Petersen S, *et al*. Idiopathic environmental intolerance: A comprehensive model. *Clinical Psychological Science* 2017;5:551–67.
12 Haanes JV, Nordin S, Hillert L, *et al*. ""symptoms associated with environmental factors" (SAEF) - towards a paradigm shift regarding "idiopathic environmental intolerance" and related phenomena". *J Psychosom Res* 2020;131:109955.
13 Hempel S, Danz M, Robinson KA, *et al*. Multiple chemical sensitivity. Secondary Multiple Chemical Sensitivity; 2022.
14 Gad SC. Multiple chemical sensitivity: A moderator's viewpoint. *Int J Toxicol* 1999;18:379–81.
15 Hyams KC. Developing case definitions for symptom-based conditions: the problem of specificity. *Epidemiol Rev* 1998;20:148–56.
16 Kreutzer R. Idiopathic environmental intolerance: case definition issues. *Occup Med* 2000;15:511–7.
17 Lacour M, Zunder T, Schmidtke K, *et al*. Multiple chemical sensitivity syndrome (MCS)--Suggestions for an extension of the U.S. MCS-case definition. *Int J Hyg Environ Health* 2005;208:141–51.
18 Rossi S, Pitidis A. Multiple chemical sensitivity: review of the state of the art in epidemiology, diagnosis, and future perspectives. *J Occup Environ Med* 2018;60:138–46.
19 Sparks PJ, Daniell W, Black DW, *et al*. Multiple chemical sensitivity syndrome: a clinical perspective. I. case definition, theories of pathogenesis, and research needs. *J Occup Med* 1994;36:718–30.
20 Heo Y, Kim SH, Lee SK, *et al*. Factors contributing to the self-reported prevalence of multiple chemical sensitivity in public facility workers and the general population of Korea. *J UOEH* 2017;39:249–58.
21 Cui X, Lu X, Hiura M, *et al*. Prevalence and Interannual changes in multiple chemical sensitivity in Japanese workers. *Environ Health Prev Med* 2014;19:215–9.
22 Kipen HM, Hallman W, Kelly-McNeil K, *et al*. Measuring chemical sensitivity prevalence: a questionnaire for population studies. *Am J Public Health* 1995;85:574–7.
23 Dupas D, Dagorne M-A. Multiple chemical sensitivity: a diagnosis not to be missed. *Rev Mal Respir* 2013;30:99–104.
24 Dantoft TM, Andersson L, Nordin S, *et al*. Chemical intolerance. *Curr Rheumatol Rev* 2015;11:167–84.
25 Herr C, Eikmann T. Environmental-medical diagnosis and therapy. hasty diagnosis of unspecified environmental syndromes should be avoided. *Fortschr Med* 1998;116:26–9.
26 Watanabe M, Tonori H, Aizawa Y. Multiple chemical sensitivity and idiopathic environmental intolerance (part two). *Environ Health Prev Med* 2003;7:273–82.
27 Regal Ramos RJ. Can we rule out that Fibromyalgia, chronic fatigue syndrome and multiple chemical sensitivity are psychosomatic diseases? *Semergen* 2015;41:349–53.
28 Staudenmayer H. "Clinical consequences of the EI/MCS "diagnosis": two paths". *Regul Toxicol Pharmacol* 1996;24(1 Pt 2):S96–110.
29 Gots RE. Multiple chemical sensitivities: distinguishing between psychogenic and Toxicodynamic. *Regul Toxicol Pharmacol* 1996;24(1 Pt 2):S8–15.
30 Sparks PJ, Daniell W, Black DW, *et al*. Multiple chemical sensitivity syndrome: a clinical perspective. II. evaluation, diagnostic testing, treatment, and social considerations. *J Occup Med* 1994;36:731–7.
31 Gibson PR, Lindberg A. Physicians' perceptions and practices regarding patient reports of multiple chemical sensitivity. *ISRN Nurs* 2011;2011:838930.
32 Phillips T, Rees T. In)Visibility online: the benefits of online patient forums for people with a hidden illness: the case of multiple chemical sensitivity (MCS. *Med Anthropol Q* 2018;32:214–32.
33 Ross GH. Treatment options in multiple chemical sensitivity. *Toxicol Ind Health* 1992;8:87–94.
34 Gibson PR, Elms AN-M, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity. *Environ Health Perspect* 2003;111:1498–504.
35 Damiani G, Alessandrini M, Caccamo D, *et al*. Italian expert consensus on clinical and therapeutic management of multiple chemical sensitivity (MCS). *Int J Environ Res Public Health* 2021;18:11294.
36 Skovbjerg S, Johansen JD, Rasmussen A, *et al*. General practitioners' experiences with provision of Healthcare to patients with self-reported multiple chemical sensitivity. *Scand J Prim Health Care* 2009;27:148–52.
37 Rest KM. A survey of AOEC physician practices and attitudes regarding multiple chemical sensitivity. *Toxicol Ind Health* 1992;8:51–65.
38 McGowan J, Straus S, Moher D, *et al*. Reporting Scoping reviews-PRISMA SCR extension. *J Clin Epidemiol* 2020;123:177–9.
39 Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for Scoping reviews (PRISMA-SCR): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
40 Peters MDJ, Marnie C, Colquhoun H, *et al*. Scoping reviews: reinforcing and advancing the methodology and application. *Syst Rev* 2021;10:263.
41 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol 2005;8:19–32.
42 Miake-Lye IM, Hempel S, Shanman R, *et al*. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. *Syst Rev* 2016;5:28.
43 Hempel S. Conducting your literature review. In: *Conducting Your Literature Review*. Washington: American Psychological Association, 2019.

44 Apaydin EA, Maher AR, Raaen L, *et al*. The use of technology in the clinical care of depression: an evidence map. *J Clin Psychiatry* 2018;79:18r12118.
45 Apaydin EA, Partikian A, Rollison J, *et al*. An evidence map of treatments for infantile epilepsy. *Epilepsy Res* 2021;178:106781.
46 Apaydin EA, Richardson AS, Baxi S, *et al*. An evidence map of randomised controlled trials evaluating genetic therapies. *BMJ Evid Based Med* 2020;26:bmjebm-2020-111448.
47 Bouskill K, Hempel S, Richardson A, *et al*. Evidence map of Ductal carcinoma in situ management options. *Menopause* 2019;26:1250–8.
48 Hempel S, Taylor SL, Solloway MR, *et al*. Evidence map of Acupuncture. Washington (DC), 2014.
49 Hilton LG, Marshall NJ, Motala A, *et al*. Mindfulness meditation for workplace wellness: an evidence map. *Work* 2019;63:205–18.
50 Maher AR, Apaydin EA, Raaen L, *et al*. The use of technology in the clinical care of anxiety: an evidence map. *Psychiatr Serv* 2021;72:195–9.
51 Solloway MR, Taylor SL, Shekelle PG, *et al*. An evidence map of the effect of Tai Chi on health outcomes. *Syst Rev* 2016;5:126.
52 Haddaway N, Macura B, Whaley P, *et al*. ROSES for systematic review protocols Version 1.0. 2018.
53 De Luca C, Raskovic D, Pacifico V, *et al*. The search for reliable biomarkers of disease in multiple chemical sensitivity and other environmental Intolerances. *Int J Environ Res Public Health* 2011;8:2770–97.
54 Das-Munshi J, Rubin GJ, Wessely S. Multiple chemical sensitivities: A systematic review of provocation studies. *J Allergy Clin Immunol* 2006;118:1257–64.
55 Viziano A, Micarelli A, Pasquantonio G, *et al*. Perspectives on Multisensory perception disruption in idiopathic environmental intolerance: a systematic review. *Int Arch Occup Environ Health* 2018;91:923–35.
56 Driesen L, Patton R, John M. The impact of multiple chemical sensitivity on people's social and occupational functioning; a systematic review of qualitative research studies. *J Psychosom Res* 2020;132:109964.
57 Romero Pérez P. A first Urological approach to the Genitourinary manifestations of multiple chemical sensitivity. *Arch Esp Urol* 2022;75:584–611.
58 Kurt TL. Multiple chemical sensitivities--a syndrome of Pseudotoxicity manifest as exposure perceived symptoms. *J Toxicol Clin Toxicol* 1995;33:101–5.
59 Sparks PJ. Idiopathic environmental Intolerances: overview. *Occup Med* 2000;15:497–510.
60 Clinical ecology. American college of physicians. *Ann Intern Med* 1989;111:168–78.
61 Decker JT, Aarestad D, Elliott W, *et al*. Chemical sensitivity in the workplace. J Soc Work Disabil Rehabil 2002;1:45–61.
62 Toft M, Sani RN, Gasevic D, *et al*. Multiple chemical sensitivity: prevalence, triggers, symptoms, and impact on lifestyle. A systematic review of Epidemiological studies; 2018.
63 Vohra S, Karkhaneh M, Punja S, *et al*. Systematic review of evidence for the effectiveness of mind-body interventions to treat multiple chemical sensitivity (MCS); 2017.
64 Guidelines International Network. Welcome to guidelines international network. In: *Secondary Welcome to Guidelines International Network*. Available: https://g-i-n.net/
65 ECRI. ECRI guidelines trust. Secondary ECRI Guidelines Trust. n.d. Available: https://www.ecri.org/solutions/ecri-guidelines-trust
66 U.S. National Library of Medicine. Clinicaltrials Homepage. Secondary ClinicalTrials Homepage. n.d. Available: https://clinicaltrials.gov/
67 World Health Organization. In: *International Clinical Trials Registry Platform. Secondary International Clinical Trials Registry Platform*. Available: https://trialsearch.who.int/
68 Fedak KM, Bernal A, Capshaw ZA, *et al*. Applying the Bradford hill criteria in the 21st century: how data integration has changed causal inference in molecular epidemiology. *Emerg Themes Epidemiol* 2015;12:14.
69 HILL AB. The environment and disease: Association or causation *Proc R Soc Med* 1965;58:295–300.
70 Howick J, Glasziou P, Aronson JK. "The evolution of evidence hierarchies: what can Bradford hill's 'guidelines for causation' contribute" *J R Soc Med* 2009;102:186–94.
71 Hempel S, Bolshakova M, Turner BJ, *et al*. Evidence-based quality improvement: a Scoping review of the literature. *J Gen Intern Med* 2022;37:4257–67.
72 Torriani-Pasin C, Demers M, Polese JC, *et al*. mHealth Technologies used to capture walking and arm use behavior in adult stroke survivors: a Scoping review beyond measurement properties. *Disabil Rehabil* 2022;44:6094–106.
73 United States Environmental Protection Agency (EPA). ORD staff Handbook for developing IRIS assessments (public comment draft, Nov. 2020). secondary ORD staff Handbook for developing IRIS assessments (public comment draft, Nov. 2020). 2020. Available: https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=350086
74 Hempel S, Xenakis L, Danz M. Systematic reviews for occupational safety and health questions: resources for evidence synthesis. In: *Systematic Reviews for Occupational Safety and Health Questions: Resources for Evidence*. Synthesis: RAND Corporation, 2016.