PEER REVIEW HISTORY

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ARTICLE DETAILS

Title (Provisional)

Analysis of the Patient-sharing Network in Hypertension Management: A Retrospective Study in China

Authors

Gong, Zhiwen; Wang, Ruilin; Hu, Huajie; Huang, Tao; Li, Huangqianyu; Han, Sheng; Shi, Luwen; Guan, Xiaodong

VERSION 1 - REVIEW

Reviewer	**1**
Name	**Elovainio, Marko**
Affiliation	**university of helsinki, psychology**
Date	**18-Nov-2024**
COI	**None**

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The authors examined the persistence of the patient-sharing relationships in physicians taking care of patients with hypertension diagnose. They also analysed the associations of patient-sharing relationship persistence with the strength of ties, whether the physicians worked in the same hospitals and the physician specialty. The authors found that the patient-sharing relationships were relatively stable and that the strength of the relationships and working in the same hospital were associated with the persistence.

My suggestions for improving the manuscript are as follows:

The authors use "causal" language and I think that should be tuned down.

Much more information is needed about the process how the authors formed their (be-partite) network.

The authors use network analyses, but they basically do not report any network characteristics (density, transitivity...)?

The authors should justify using logistic regression instead of using ERGM, that may be more appropriate

The one – year time frame for the patient sharing relationship may be rather long, so I suggest that the authors also test shorter time frames.

The persistency of the patient sharing relationship may dependent on the length of stay or the number of different episodes of the patient. Did the authors take into account the severity of the hypertension or potential co-morbidities?

Similarly, how many of the patients had episodes in multiple years and thus would increase the persistence?

It would be interesting to see in the future studies whether the persistence of the patient sharing relationships would be associated with patient outcomes.

In sum, an interesting paper, that needs further clarifications.

Reviewer	**2**
Name	**Ishikawa, Tomoki**
Affiliation	**Hokkaido University**
Date	**31-Dec-2024**
COI	**None**

Introduction:

- Specificity of the research question: While the objectives are stated, the research question could be articulated more explicitly. For example, what specific factors do they hypothesize will influence the persistence of patient-sharing networks?

-Theoretical framework: While the introduction mentions the importance of persistence and strength of relationships, it could benefit from explicitly stating a theoretical framework or model guiding the analysis. This would strengthen the study's conceptual foundation.

Justification for focusing on hypertension: While the introduction provides statistics on hypertension prevalence, it could elaborate on why hypertension was chosen as the focus of this study. Are there specific characteristics of hypertension management that make it particularly relevant to study through the lens of patient-sharing networks?

-Clarity on "persistence": While the introduction defines persistence as stability, it could benefit from further clarifying how "persistence" will be measured and analyzed in the study.

Methods:

While the methods are generally well-described, there are some areas where more detail would be beneficial. For example, the justification for the specific threshold values used in the analysis could be more precise. Additionally, a more detailed explanation of the variable selection process for the logistic regression model would be helpful.

-Ethical considerations: While the authors mention data de-identification, they could elaborate on the ethical approvals obtained for this study. This is crucial when dealing with patient data.

-Justification for threshold selection: The authors mention using a threshold to identify stable relationships. -However, they could provide more justification for the specific threshold values used in the analysis. How did they determine the optimal threshold to balance inclusivity and identifying meaningful relationships?

-Potential limitations of YHIS data: While YHIS seems comprehensive, the authors could acknowledge any potential limitations, such as missing data or potential biases in data collection.

-Explanation of variable selection: While Table 1 likely provides details, the methods section could briefly explain the rationale behind selecting the specific variables in the logistic regression model.

-Addressing potential confounding factors: The authors could discuss potential confounding factors that might influence the persistence of relationships and how they plan to address them in the analysis.

Results:

-Interpretation of threshold analysis: While the authors describe the persistence patterns across different thresholds, they could further elaborate on the implications of these findings. How do these patterns inform our understanding of knowledge diffusion in the network?

-Further exploration of specialty effects: The analysis shows differences in persistence based on physician specialty. The authors could explore these differences further and offer potential explanations.

-Discussion of physician characteristics: The authors acknowledge the limitation of not analyzing physician characteristics. They could expand on this point by discussing which factors might be relevant and how they could be incorporated in future research.

VERSION 1 - AUTHOR RESPONSE

Reviewer #1:

1. The authors use "causal" language and I think that should be tuned down.

Thank you for your comment. We have thoroughly reviewed the manuscript and reduced the use of causal language. For example:

*"We conducted a patient-sharing network analysis to describe the persistence of patient-sharing relationships and logistic regression to analyze factors ~~influencing~~ **associating with** the persistence of patient-sharing relationships…"* (page 2, line 8-9)

~~"The persistence of the relationships increased significantly as the strength of the relationships increased.~~ We found the increase of strength of the relationships was associating with the increase of persistence of the relationships." (page 11, line 206-207)

*"The strength of the relationship, tie characteristics, and physician specialty were important factors ~~influencing~~ **associating with** the persistence of the physician's patient-sharing relationships"* (page 12, line 223-224)

2. Much more information is needed about the process how the authors formed their (be-partite) network.

Thank you for your comment. In response, we have added a section - "**Networks Construction**" in the **Methods** part to explain how we construct the patient-sharing network in detail:

"We constructed physician networks by identified relationships between physicians if one patient had visit both of them within the same year. Specifically, we first constructed the bipartite network composed of physician-patient connections by extract the outpatient visit records within a year and generated the adjacency matrix of bipartite network (Figure 1-a).[40] Then, we constructed the physician-physician unipartite network by multiplying the adjacency matrix of bipartite network with its transpose.[45] The elements in the matrix of unimodal network were the number of patients shared between two physicians, which represented the strength of their relationship (Figure 1-b) …" (page 8, line 126-132)

3. The authors use network analyses, but they basically do not report any network characteristics (density, transitivity…)?

Thank you for your comment. In response,

a) We have reported the network characteristics for each network thresholds we tested, including number of network nodes, number of network edges, diameter, density, and clustering coefficient (transitivity), in the **Supplementary Materials** as **eTable 3**.

b) We also added the description in the **Result** part in the **Manuscript**:

"… The network characteristics at different thresholds were reported in the eTable 3. Overall, the network diameter from 2010 to 2018 ranged from 6 to 9 for thresholds from 1 to 9; the network density ranged from 0.18 to 0.55 for thresholds from 1 to 9; the clustering coefficient ranged from 0.33 to 0.45 for thresholds from 1 to 9." (page 11, line 191-194)

4. The authors should justify using logistic regression instead of using ERGM, that may be more appropriate

Thank you for your comment. We agree that ERGM is an effective tool for exploring the formation and dynamics of social networks, especially for identifying the factors associating with the connecting

establishment[1,2]. However, our study primarily focused on assessing the strength and persistence of the physicians' relationships already identified, rather than examining how network was formed or how individuals in the network interact with others. Therefore, after careful consideration, we believe that ERGM may not be the most suitable method for this study; nevertheless, it could serve as a valid approach for further investigations of structure and interaction of physician networks in China. We would take this into account when designing any future studies addressing similar topics.

Considering your comments, we added the explanation in the **Statistical Analysis** section of **Methods** part:

"We conducted logistic regression to analyze factors associating with the persistence of patient-sharing relationships, with the 95% confidence interval (CI) and P-value reported for each odds ratio (OR).[46] We applied logistic regression rather exponential random graph models (ERGM) as we primarily focused on assessing the strength and persistence of the physicians' relationships already identified, rather than examining the formation of the network." (page 9, line 158-162)

5. The one – year time frame for the patient sharing relationship may be rather long, so I suggest that the authors also test shorter time frames.

Thank you for your suggestion. Although the one-year time frame is widely used for identifying relationship in studies on similar topics,[3,4] and some research has observed that shorter time frames do not significantly affect the results,[5] we totally agree that different time frames may lead to variations in network structure in our study setting. Unfortunately, due to restrictions on the availability of data, we were unable to test physician networks under shorter time frames for sensitivity analysis. In response, we added that in the **Limitation** part:

"Third, we only constructing network using the one-year time frame to identifying physicians' relationship. Though there was study observing that shorter time frames do not significantly affect the results,[60] it is possible that the results could be different if we change the time frames in our setting. Future research should consider constructing networks over different time frames as data permit." (page 15, line 282-286)

6. The persistency of the patient sharing relationship may dependent on the length of stay or the number of different episodes of the patient. Did the authors take into account the severity of the hypertension or potential co-morbidities? Similarly, how many of the patients had episodes in multiple years and thus would increase the persistence?

Thank you for your comment. In response,

a) As mentioned in the previous comment, given that we constructed the network over a relatively long time frame, we believe that a one-year time frame effectively captures the most of potential patient-sharing relationships, and thus patient-level characteristics such as the length of stay or the number of episodes are unlikely to significantly affect the persistence of these relationships in the physician-level.

b) Additionally, in our study area Yinzhou, Ningbo, all hypertension patients receive quarterly follow-up visits after their diagnosis of hypertension.[6] The patients included in our study are expected to occur at least one outpatient visit per year. Thus, we believe that patients' episodes in multiple years would not affect our current analysis of relationship persistence.

c) Despite considering the explanation above, we acknowledge that, to some extent, patient-level characteristics may still be associated with the persistence of physician relationships. However, as our analysis was conducted in the physician-level, it is challenging to include the patient-level characteristics. We have elaborated that in the **Limitation** part:

"Second, we limited the disease area to hypertension to represent the characteristics of the patient-sharing network of physicians managing NCDs. However, physician networks may be affected by differences in chronic diseases, such as patient characteristics, which were unable to incorporate in this study. For instance, the differences in severity of the disease or co-morbidities may lead to distinct patient visiting pattern, thus our results should be interpreted within the specific context." (page 15, line 278-282)

8. It would be interesting to see in the future studies whether the persistence of the patient sharing relationships would be associated with patient outcomes.

Thank you for your comment. We fully agree that studies exploring the association between the persistence of physician relationships and patient outcomes are of greater clinical and policy significance. As the first study of physician networks conducted in China, the primary objectives of this study were to test the feasibility of network methods within database in Chinese healthcare settings and to explore the strength and persistence of physician relationships. The association between the persistence of physician relationships, continuity of care, and patient clinical outcomes will be examined in a separate study as the next step to this work.

In response, we also added that in the **Limitation** part:

"Last, we have not examined the relationship between the persistence of physician relationships and patient health outcomes, which holds greater clinical and policy relevance. Future research should focus on this topic to offer novel insights for healthcare policy and practice, especially on leveraging physicians' social networks to improve healthcare delivery." (page 15, line 291-294)

Reviewer #2

Introduction

1. Specificity of the research question: While the objectives are stated, the research question could be articulated more explicitly. For example, what specific factors do they hypothesize will influence the persistence of patient-sharing networks?

Thank you for your suggestion. We have revised the **Abstract** and **Introduction** part to explicitly state the hypothesis underlying our research:

Abstract- Objective:

"To explore the robustness of the patient-sharing network ~~method~~ and validate ~~possible influencing factors~~ the association between strength and persistence of physicians' relationship in China." (page 2, line 5-6)

Introduction:

"... we conducted a social network analysis to describe the persistence of patient-sharing relationships of physicians managing patients with hypertension and ~~identify factors influencing the network~~ measure the association between strength and persistence of physicians' relationship in China ..." (page 6, line 92-94)

2. Theoretical framework: While the introduction mentions the importance of persistence and strength of relationships, it could benefit from explicitly stating a theoretical framework or model guiding the analysis. This would strengthen the study's conceptual foundation.

Thank you for your suggestion. We have carefully reviewed the related theoretical framework and add the *diffusion of innovation* as the guiding framework of our analysis.

a) We applied the theoretical framework to illustrate the importance of persistence of relationships:

"Persistent patient-sharing relationships could enable physicians to foster trusting relationship with one another and help to create new referral loops and are thus facilitative to information exchange and coordinating care, which has been interpreted through theories of diffusion of innovation or social contagion.[23, 26, 27]" (page 5, line 73-76)

b) We applied the theoretical framework to help identify potential factors:

"We included the tie characteristics, physician specialty, strength of the relationship, and when such relationships occurred as covariates in our analysis, based on previous literature, theoretical framework of diffusion, and data availability." (page 9, line 146-149)

3. Justification for focusing on hypertension: While the introduction provides statistics on hypertension prevalence, it could elaborate on why hypertension was chosen as the focus of this study. Are there specific characteristics of hypertension management that make it particularly relevant to study through the lens of patient-sharing networks?

Thank you for your comment. In China, hypertension is the most prevalent chronic disease, which requires collaborative across different healthcare level to achieve disease control. Previous studies have shown that the closer physician relationships can improve the care coordination and promote the control of hypertension. Considering there is limited evidence of physicians' relationships in Chinese healthcare settings, we chose the hypertension as target disease, use the patient-sharing network methods measure the relationship among

physicians, in order to provide knowledge for better care coordination and disease control. We have revised the last paragraph of the **Introduction** part accordingly:

"In China, hypertension is one of the most prevalent NCD, with a high prevalence of 44.7% among adults aged 35-75 years and generally poorly managed.[32] The management and control of hypertension typically requires collaborative across different healthcare institutional and healthcare providers, especially between various healthcare levels.[33, 34] Improved hypertension control have been reported in the well-connected physician professional environment,[35-38] underscoring the significant of promoting the physician's relationship in hypertension management. The patient-sharing network models were widely applied and validate methods to depict and measure these relationships among physicians in prior research.[39,40] Given the knowledge gap in structure and persistence of physicians' relationships in China, we conducted a social network analysis to describe the persistence of patient-sharing relationships of physicians managing patients with hypertension and measure the association between persistence and strength of physicians' relationship in China, for providing insights for achieving better hypertension care coordination and disease control."
(page 6, line 85-96)

4. Clarity on "persistence": While the introduction defines persistence as stability, it could benefit from further clarifying how "persistence" will be measured and analyzed in the study.

Thank you for your comment. We added more explanation in the **Introduction** and **Method** for clarity:

Introduction:

"...The persistence (also known as stability, referring to the continuation of relationships from the previous year into the next) and strength (the number of shared patients between two physicians) of the patient-sharing relationships have been identified as important metrics in network-based interventions ..." (page 5, line 71-73)

Method - Outcome Measures:

"The main outcome of the analysis was the persistence of the physician-physician connections in the patient-sharing network, defined as the physician relationship in a given year continued to exist in the following year.[23] We used the persistence ratio, which refers to the proportion of remained relationships, to measure the degree of persistence. For instance, if ten pairs of patient-sharing relationships were observed in 2008 and eight of them persisted to 2009, the one-year persistence ratio would be 80% ..." (page 8, line 139-143)

Methods:

5. Ethical considerations: While the authors mention data de-identification, they could elaborate on the ethical approvals obtained for this study. This is crucial when dealing with patient data.

Thank you for your comment. We have elaborated the related information in the **Method** part and added the ethical approval information:

"All information stored in the system has been de-identified to safeguard patient privacy, thus the requirement of informed consent was exempted according to the national legislation and the institutional

requirements. Ethical approval was obtained from the Peking University Institution Review Board (IRB00001052-22052)." (page 7, line 113-116)

6. Justification for threshold selection: The authors mention using a threshold to identify stable relationships. -However, they could provide more justification for the specific threshold values used in the analysis. How did they determine the optimal threshold to balance inclusivity and identifying meaningful relationships?

Thank you for your question. In response:

a) A key study reported that when two physicians shared nine or more patients, the likelihood that they had a recognized professional relationship exceeds 80%.[7] Consequently, in subsequent research, the "threshold = 9" has been widely applied to constructed patient-sharing network. Based on those works, to avoid arbitrariness in threshold decision, we did not apply a specific threshold in the analysis; instead, we tested network characteristics under thresholds ranging from 1 to 9, as we explained in the **Methods** part:

"In the analysis, we did not apply a fixed threshold; instead, we tested multiple thresholds from 1 to 9 (range was determined based on previous report and validation) to identify stable patient-sharing relationships and reduce the impact of incidental connections that have a lower probability of knowledge exchange.[27, 39]"
(page 8, line 134-137)

b) Determining the optimal threshold was not the primary objective of this study. However, by describing network properties under different thresholds, we observed that the pattern of persistence of network relationship when threshold = 1 was distinctly different from that at other thresholds, as detailed in our results section:

"When threshold equaled 1, relationships seemed random and displayed trends vastly different from those shown when other thresholds were applied. …. Patient-sharing relationships showed similar patterns when the threshold was set at 3, 5, 7, or 9, with at least 80% of the relationships persisting after one year…" (page 11, line 197-201)

Similarly, when examining network characteristics, including network density and clustering coefficient, the disparity was found between threshold = 1 and other thresholds (**Supplementary Materials**, **eTable 1**). Thus, we consider the "threshold = 3" to be a reasonable threshold, balancing inclusivity and identifying meaningful relationships, in our study setting.

7. Potential limitations of YHIS data: While YHIS seems comprehensive, the authors could acknowledge any potential limitations, such as missing data or potential biases in data collection.

Thank you for your comment. Due to the exploratory feature of the study and limitation in data availability, we only included a small set of physician characteristics in the analysis, with no missing data. However, we acknowledge some following potential limitations in YHIS database:

a) The YHIS database was restricted to a single district in China, and since network characteristics may vary across different regions, the generalizability of this study will be limited. We have added that in the **Limitation** part:

"First, we established the social network of physicians based on a database from a single district in China, thus our result may not be generalized to other areas in China with different physician network structures." (page 14, line 273-275)

b) We were unable to observe the patient flow and the direction of physician relationships, which makes it challenging to capture the dynamic process of knowledge and behavior diffusion among physicians. We have elaborated that in the **Limitation** part:

"... Additionally, we were unable to observe the actual patient flow and the dynamics of these relationships from the retrospective data. A fuller landscape of the impact of knowledge diffusion through these relationships on physicians' prescribing behaviors may only be gained through conducting qualitative studies in the future." (page 14, line 275-278)

c) Our findings are subject to potential bias due to unmeasured confounding. As we responded in **Comment #1-6**, we were unable to include more patient-level or physician-level characteristics, which could be related to the persistence of physician relationship. Thus, the association between persistence and strength of relationship could be overstate. We will further discuss the impact of unmeasured confounding in our responses to **Comments #2-9**.

8. Explanation of variable selection: While Table 1 likely provides details, the methods section could briefly explain the rationale behind selecting the specific variables in the logistic regression model.

Thank you for your question. We included specific variables primarily considering the data availability, theoretical meaning, and whether the variables have been reported associating with the relationship persistence in prior studies. We have mentioned related information in the **Introduction** part:

"Studies have found that many factors might affect the persistence ratio of patient-sharing relationships, including tie characteristics, physician specialty, strength, and when such relationships occurred.[18, 24, 28]" (page 5, line 76-78)

Considering your comments, we also added the explanation in the **Measurements and Covariates** section for clarify:

"Many factors have been reported the association with persistence of patient-sharing relationships.[24, 29] We included the tie characteristics, physician specialty, strength of the relationship, and when such relationships occurred as covariates in our analysis, based on previous literature, theoretical framework of diffusion, and data availability." (page 9, line 146-149)

9. Addressing potential confounding factors: The authors could discuss potential confounding factors that might influence the persistence of relationships and how they plan to address them in the analysis.

Thank you for your comment. In response:

a) We totally agree the unmeasured confounding could influence the association between network characteristics and relationship persistence. However, the other our key finding that the physician network relationships in our sample area demonstrate strong strength and great persistence, would not be impaired by unmeasured potential confounding factors. Thus, although the relationship between network persistence and network characteristics may require further investigation, our results indicate that physician networks can serve as a stable and viable channel for promoting knowledge diffusion and care coordination.

b) We have added the issues of potential confounding factors in the **Limitation** part:

"However, physician networks may be affected by differences in chronic diseases, such as patient characteristics, which were unable to incorporate in this study. For instance, the differences in severity of the disease or co-morbidities may lead to distinct patient visiting pattern, thus our results should be interpreted within the specific context." (page 15, line 279-282)

"Forth, our association analysis may subject to unmeasured confounding bias since we failed to include additional physician factors potentially associating with the persistence. For instance, factors such as physicians' practicing department, years in practice, or professional title were not included, whereas it is possible that physicians may be more likely to establish connections with others who shared similar characteristics.[61] Future research should consider incorporating relevant factors more comprehensively or applied methods such as instrumental variables to effectively control for potential confounding." (page 15, line 286-291)

10. Interpretation of threshold analysis: While the authors describe the persistence patterns across different thresholds, they could further elaborate on the implications of these findings. How do these patterns inform our understanding of knowledge diffusion in the network?

Thank you for your comment. We have elaborated the significance of persistence patterns under different network thresholds in the second paragraph of **Discussion** part:

"We observed that physician relationships were more persistent as the relationship threshold increased, which aligned with observations from previous studies.[23, 39] This suggests that physicians with more shared patients may be more likely to form a more stable professional relationship and demonstrate a great relationship persistence, thereby exerting profound influence on knowledge diffusion within the network.[24] Enhanced knowledge diffusion and information exchange strengthen the quality and coordination of healthcare services, as evidenced by reduced emergency room visits and lower medical costs for patients treated by physicians persistent connection.[29, 48] This effect may also expend across physicians from different hospitals, to produce desirable patient outcomes, including lowered odds of readmissions and adverse events.[39, 49-51] Therefore, it is feasible to improve the relationship strength and improve healthcare quality by fostering physicians' professional network and promoting regular physician communication among providers." (page 12, line 229-238)

11. Further exploration of specialty effects: The analysis shows differences in persistence based on physician specialty. The authors could explore these differences further and offer potential explanations.

Thank you for your comment. In response:

a) We have elaborated the difference in the persistence of different physician specialty, and provide a potential explanation, attributing the disparity to the less cohesive care coordination across different level of facilities in Chinese healthcare system:

"Our study confirmed that physicians both from primary care facilities were more likely to form and keep patient-sharing relationships, a result similar to a previous study.[52] The finding implied the less cohesive care coordination across different level of facilities in Chinese healthcare system,[53] may lead to suboptimal care continuity and disease control.[54]" (page 13, line 248-251)

b) We further placed this disparity within the context of Chinese hierarchical medical system policy, and explored the impact of the policy on the formation and persistence of physician relationship. By citing our another study, we demonstrate that the hierarchical medical system policy promoted the centrality of primary care physicians, thereby strengthening the persistence of physician relationship across different healthcare levels:

"The Chinese government has launched a hierarchical medical system policy in 2014, aiming to alter patients' healthcare-seeking behaviors … This redirection of patient flow to primary care facilities may cause PCPs to share patients more frequently, and thus more physicians could have more possibility to form more strength patient-sharing relationships.[54] … Our another study has confirmed in the increased persistence of patient-sharing relationships cross different healthcare levels since 2015, when the hierarchical medical system policy was implemented in China. which attributed to the policy's promotion of primary care physician's centrality in disease management.[54]" (page 14, line 260-272)

12. Discussion of physician characteristics: The authors acknowledge the limitation of not analyzing physician characteristics. They could expand on this point by discussing which factors might be relevant and how they could be incorporated in future research.

Thank you for your suggestion. As we responded in **Comment #2-9**, we have elaborated the **Limitation** section to add potential factors might be relevant and how they could be address in the future works:

"Forth, our association analysis may subject to unmeasured confounding bias since we failed to include additional physician factors potentially associating with the persistence. For instance, factors such as physicians' practicing department, years in practice, or professional title were not included, whereas it is possible that physicians may be more likely to establish connections with others who shared similar characteristics.[61] Future research should consider incorporating relevant factors more comprehensively or applied methods such as instrumental variables to effectively control for potential confounding." (page 15, line 286-291)

VERSION 2 - REVIEW

Reviewer	1
Name	Elovainio, Marko
Affiliation	university of helsinki, psychology
Date	28-Feb-2025
COI	

The authors have been responsive and I have no further comments.