Online Supplemental Appendix: Estimating the impact of physician risky-prescribing on the network structure underlying physician shared-patient relationships

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1 Physician network and risky prescribing indexes data pipelines

As described in Section 2 of the main text, distinct data wrangling pipelines are used to construct the physician network and the prescribing indexes for each physician (Figure 1).

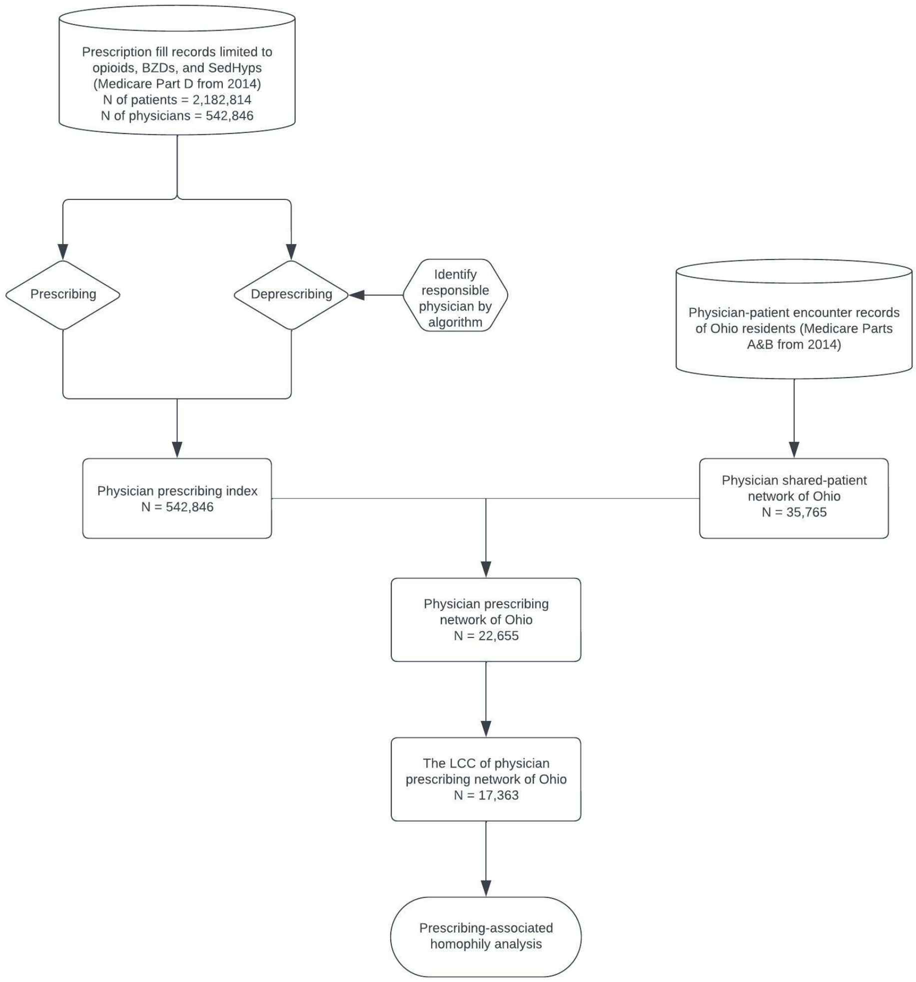

Fig. 1: Study cohort definition and workflow. Note: Beneficiaries were included in the study if they had at least 3 months of continuous coverage of Medicare Parts A, B, and D, and 2 years of continuous parts A and B coverage prior to cohort entry. LCC = largest connected component.

2 Attributing physician responsibility to prescribing and deprescribing events

To facilitate the construction of a physician transition responsibility count matrix (PTRCM) for each physician who prescribed opioids (O), benzodiazepines (B) or sedative-hypnotics (S), we needed to attribute each patient transition between the drug states $\{\text{zero}, O, B, S, OB, OS, BS, OBS\}$ to a responsible physician or physicians. To do so, we first needed to distinguish new prescription fills from refills. In the remainder of this section we describe how we distinguished new fills from refills (Section 2.1) and then review the attribution process when a patient receives a new prescription and two algorithms we developed for identifying deprescribing events and attributing them to one or more physicians.

2.1 Distinguishing new prescription fills from refills

Our primary interest is in new prescription fills instead of refills because they represent a definitive step towards increased polypharmacy or risky drug combinations. Therefore, to help distinguish new fills from refills, we implemented an empirical rule of 20% overlapping fill length, where a subsequent prescription fill of the same drug written by the same physician was merged to the preceding fill if they overlapped or the gap in between was less than 20% of the fill length of the preceding prescription. It is also highly likely that a subsequent prescription of the same drug signed by a different physician that overlaps with this 20% buffer zone is still a refill of the preceding prescription. Therefore, subsequent prescription fills satisfying the 20% buffer were joined to the preceding fill and attributed to the initializing physician. Such preprocessing enabled us to reduce false positive discontinuations by distinguishing the discontinuation of a prescription from a temporary stop prior to a refill.

2.2 Attribution of prescribing events

We attributed the physician(s) who initiated the prescription according to Medicare Part D claims data as the responsible physician(s). For example, the physician who prescribed an opioid to a patient who was already taking a benzodiazepine is deemed responsible for the patient's prescription state transition from state B to state OB (or from state 3 to state 5 using the numerical labels).

2.3 Attribution of deprescribing events

Although deprescribing often results from conversations during physician-patient encounters in which the physician(s) review and discuss medications with their patients (Farrell and Mangin, 2019), unlike prescribing it does not trigger an insurance claim. Therefore, we developed two heuristic algorithms to fill this gap by identifying likely instances of deprescribing using claims data alone. The assumption that motivates these algorithms is that a deprescribing conversation took place during the patient's most recent clinical visit if they do not refill a long-term prescription following the encounter (Algorithms 1 and 2).

Algorithms algo:deprescPhys1 and algo:deprescPhys2 combine to attribute physicians to deprescribing prescription events, addressing a current limitation of claims data that the physician responsibility for deprescribing is not documented. In Algorithm 1, each prescription of each patient is initially treated as a target prescription that can potentially be discontinued. We then excluded the prescriptions for acute conditions to obtain a set of prescriptions for which intentional deprescribing by physicians could have occurred by requiring the target prescriptions to be longer than 30 days.

Algorithm 1 Pseudo code: Attributing the physicians responsible for deprescribing prescriptions

Input: A set of n prescriptions patient h receives and their prescribing physicians (a lone physician responsible for deprescribing prescription s is denoted P_{hs}).

Output: The responsible physician P_{hs} for deprescribing the prescription of interest.

for $s = 1, 2, \ldots, n$ **do**
    if length of prescription $s >= 30$ days **then**
        $\Delta \leftarrow$ empty list ▷ difference between two dates
        for $w = s+1, s+2, \ldots, n$ **do**
            $b_w \leftarrow$ begin date of prescription w
            $e_s \leftarrow$ end date of prescription s
            if $e_s - b_w > 0$ and $e_s - b_w <= 30$ **then** ▷ prescription s discontinues within 30 days of encountering a physician
                Add $e_s - b_w$ to Δ
            end if
        end for
        Find the prescription p with minimum Δ and corresponding prescriber P_{hp} ▷ most recent encountered physician
        responsible physician for deprescribing prescription $p \leftarrow$ physician P_{hp}
        if multiple responsible physicians **then**
            contribution weight $\leftarrow$ 1 / number of contributors
        end if
        if no physician is held accountable after applying above criteria **then**
            responsible physician for deprescribing prescription $p \leftarrow$ a pseudo-physician
        end if
    else
        responsible physician for deprescribing prescription $s \leftarrow$ a pseudo-physician
        $s \leftarrow s + 1$
    end if
end for

The start date of a prescription fill is assumed to be the date when the patient visited the physician. The physician that the patient visited most recently before the end of the target prescription is selected as the candidate physician for having deprescribed the target prescription. To be a deprescribing event, the patient has to discontinue filling the prescription within 30 days (inclusive) after visiting the candidate physician. Recall that any subsequent prescriptions are joined with the preceding prescription if they are likely to be refills of that original prescription (see Section 2.1). This data wrangling step is a preprocessing procedure that protects against any temporary suspension of a prescription that a patient may refill later on, which can be a false positive

Algorithm 2 Pseudo code: Determining the deprescribing state transition to attribute to the responsible physicians

Input: (1) The responsible physician P_{hs} for deprescribing at prescription transition s for patient h; (2) a set of n prescriptions patient h receives.

Output: The deprescribing state transition that physician k is responsible for.

$D_b \leftarrow$ empty list ▷ List of drugs patient h is taking before discontinuation of prescription s
$D_a \leftarrow$ empty list ▷ List of drugs patient h is taking after discontinuation of prescription s
for $w = 1, 2, \ldots, n$ **do**
  $b_w \leftarrow$ begin date of prescription w
  $e_w \leftarrow$ end date of prescription w
  $e_s \leftarrow$ end date of prescription s
  if $e_s - 0.1 > s_w$ and $e_s - 0.1 < e_w$ **then**
    Add w to D_b
  end if
  if $e_s + 0.1 > s_w$ and $e_s + 0.1 < e_w$ **then**
    Add w to D_a
  end if
end for
determine prescription state u based on D_b
determine prescription state v based on D_a
physician k is responsible for patient h's deprescribing state transition from u to v

deprescribing event by the identified physician. Finally, if multiple responsible physicians were identified, the patient prescription state transition associated with such termination was attributed to the identified physicians with a contribution weight.

After attributing each prescribing and deprescribing event to one or more physicians, we were able to form a matrix reflecting the transitions in patient drug states each physician was deemed responsible for (described in Section 4.3 of the main text) and then multiple physician prescribing indexes (defined and derived in Section 4.4 of the main text).

3 Visualization of physician network and homophily patterns

Figure 2 shows the homophily patterns in terms of prescribing and deprescribing in the egocentric networks of 5 of the most connected physicians (those with the greatest number of connections to other physicians or, in other words, those with the highest degree). These may each be thought of as a magnification of one small part of the entire Ohio prescribing physician network and its LCC. An important observation is that central physicians with higher patient volume and higher node degrees have lower risky prescribing intensity than peripheral physicians. In addition, there are closely positioned clusters of physicians with similar prescribing intensity and behavior.

4 Goodness-of-fit analysis

To assess the appropriateness of the ERGM models and confirm that nothing untoward occurred in estimating them, we performed a goodness-of-fit analysis for all models in Table 3 using the ergm.gof function in the StatNet package in R. The ergm.gof function simulates networks under a fitted model and compares the distribution of the network statistics in the simulated networks to the observed frequency of the statistic's values in the observed network. The fit of the models was assessed with respect to actor degree, edge-wise shared partners and minimum geodesic distances. The results revealed that the simulated networks recovered the observed network statistic with no indication of major lack-of-fit (the means of the simulated values were in the proximity of the observed value and the distributions of the simulated values largely encompassed the corresponding observed values). For illustration, in Figure 3, the plots of the simulated and observed distributions of these network statistics are presented for Model 1 in Table 3 of the main text. We have added Figure R1 and the associated comments to the Supplemental Appendix. We have also noted that due to the inclusion of only dyadic independence terms as network statistics in each of the ERGMs, there are no concerns of model degeneracy and so we have near to 100% assurance that the estimators for each model properly converged.

5 Heterogeneity in Homophily Across Geographic Regions

Previous studies have documented geographic variation in patient healthcare utilization and outcomes in relation to network characteristics (Landon et al, 2012; Fisher et al, 2003a,b; Wennberg, 2010; Pollack et al, 2012) in the United States. By comparing physician homophily associated with prescribing within states and hospital referral regions (HRRs) within the United States (US), we investigate whether physician prescribing intensity clusters within and varies across geographic regions, yielding the cautionary insight that one intervention may not work universally and that in contrast, region-specific regions might be needed.

To study variation in homophily across HRRs and the possible variation of risky-prescribing-associated homophily across different HRRs, we divided the LCC of the physician prescribing network into HRR sub-networks according to where the majority of their patients reside based on their Medicare fee-for-service claims in 2014. Both physicians must belong to the same HRR in order for the edge between them to be in that HRR sub-network.

For the HRR sub-network analyses, only the 12 HRR sub-networks with at least 100 physicians, a network size for which prescribing behavior could be measured stably for all physicians in the network, were retained. We find that 6 out of 12 HRRs show significant homophily in terms of the index I_{OBS} of riskiest prescribing, and 10 of them show significant homophily in terms of the index quantifying the intensity of the

Table 1: ERGM adjusted homophily effects in HRR shared-patient sub-networks in 2014.

Descriptive Stats			Homophily effects of indexes							
			absdiff(I_{OBS})		absdiff($I_{presc2mr}$)		absdiff($I_{depresc2mr}$)		$I_{everOBS}$	
HRR	N	Density	Coef.	SE	Coef.	SE	Coef.	SE	Coef.	SE
180	129	0.116	-3.998	3.662	0.004	1.623	1.052	1.898	0.026	0.133
357	193	0.106	0.810	2.707	-1.541*	0.714	0.467	0.775	-0.268	0.149
331	256	0.128	-5.156	2.675	-1.792*	0.697	-0.325	0.773	0.047	0.117
332	415	0.048	-1.765*	0.745	-0.863***	0.250	0.299	2.410	0.056	0.079
335	550	0.060	-1.887*	0.920	-0.881**	0.305	-0.545	0.416	0.063	0.070
326	648	0.050	-1.281	0.795	-1.066***	0.306	44.210	280.321	-0.080	0.056
325	750	0.030	-0.469	0.814	-0.917**	0.279	0.496	0.699	0.0002	0.089
334	1039	0.029	-0.532	0.416	-1.190***	0.226	-0.301	0.209	0.018	0.045
330	1164	0.024	-1.205**	0.419	-0.339	0.196	-0.071	0.319	0.0002	0.037
327	1760	0.015	-1.711**	0.584	-0.783***	0.179	-0.362*	0.171	0.120**	0.044
328	2623	0.010	-1.603***	0.370	-0.897***	0.142	-0.193	0.227	0.060	0.034
329	3101	0.008	-1.181***	0.234	-0.754***	0.109	-0.327*	0.157	-0.018	0.025

Note: The HRR sub-networks were partitioned from the largest connected component of the Ohio 2014 shared-patient physician prescribing network. These sub-networks were not restricted to their respective largest connected components; thus, they may not be fully connected. Significance levels: $***p < 0.001$; $**p < 0.01$; $*p < 0.05$.

addition of drugs in two of the three drug classes, $I_{presc2mr}$ (Table 1). Clearly, the level of homophily varies across HRRs. The signs of the estimated coefficients were almost exclusively negative, implying that the more similar the measure the more likely a tie is to be present (positive homophily). For other prescribing or deprescribing indexes, we do not see as significant nor prevalent homophily compared to the LCC of the entire Ohio prescribing physician network, which is consistent with these transitions being less common and thus having less information to estimate their coefficients. The discrepancy of prescribing-associated homophily between the state and HRRs, especially the homophily found at the state-level but not in some of the HRRs, may indicate that some prescribing groups at the state-level rely on cross-HRR physician patient-sharing.

The substantial variation in prescribing-associated homophily across HRRs revealed by the HRR-stratified models in Table 1 reinforces previous literature on the geographic variability in physician patient-sharing network characteristics (Landon et al, 2012) but does so from a unique physician network perspective.

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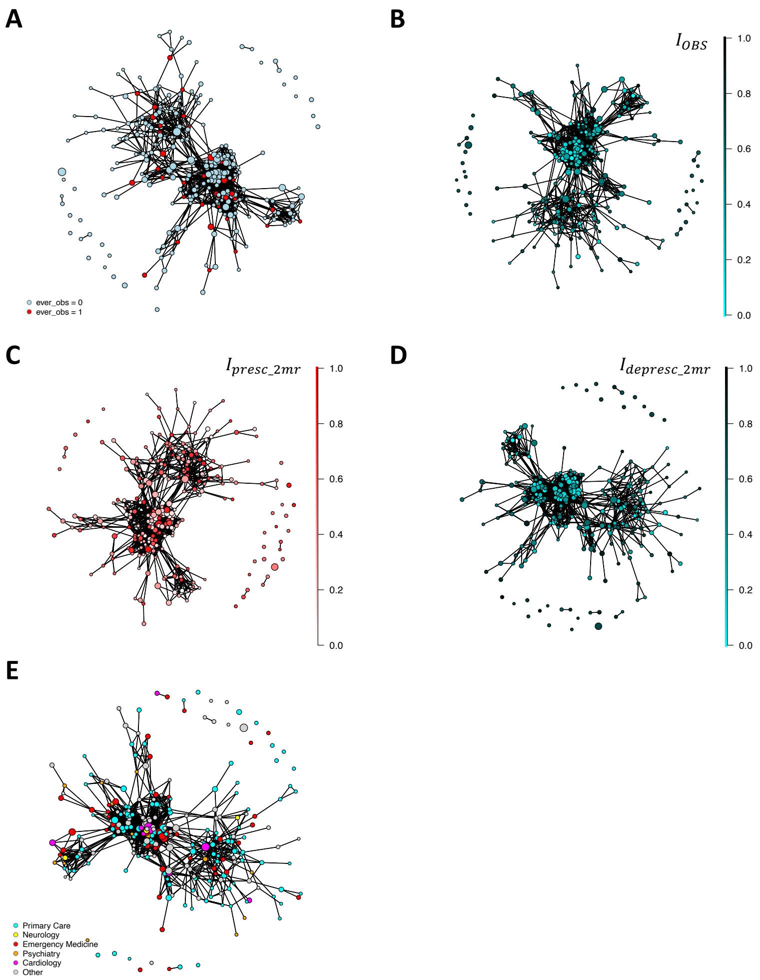

Fig. 2: Egocentric network of the physician with maximum node degree (N = 276) in the LCC of the prescribing network. The ego physician was removed from the plot for the clarity of presentation. The ties shown in the plots are among the peers of the ego physician. The nodes are sized by physician annual volume (the number of distinct patients treated throughout the year). The colors of nodes correspond to their prescribing behavior or specialties. A) The connections among physicians are distinguished by whether they have ever contributed to bringing patients to the riskiest prescription state (the OBS state). B) The connections among physicians where the node color represents the value of I_{OBS}, the proportion of times they bring their patients to prescription state OBS. C) The connections among physicians where the node color represents I_{presc_2mr}, the proportion of prescribing events when two or more drugs are prescribed at once to the patients. D) The connections among physicians where the node color represents $I_{depresc_2mr}$, the proportion of deprescribing events at which two or more drugs are deprescribed at once to the patients. E) The connections among physicians are colored by their specialties.

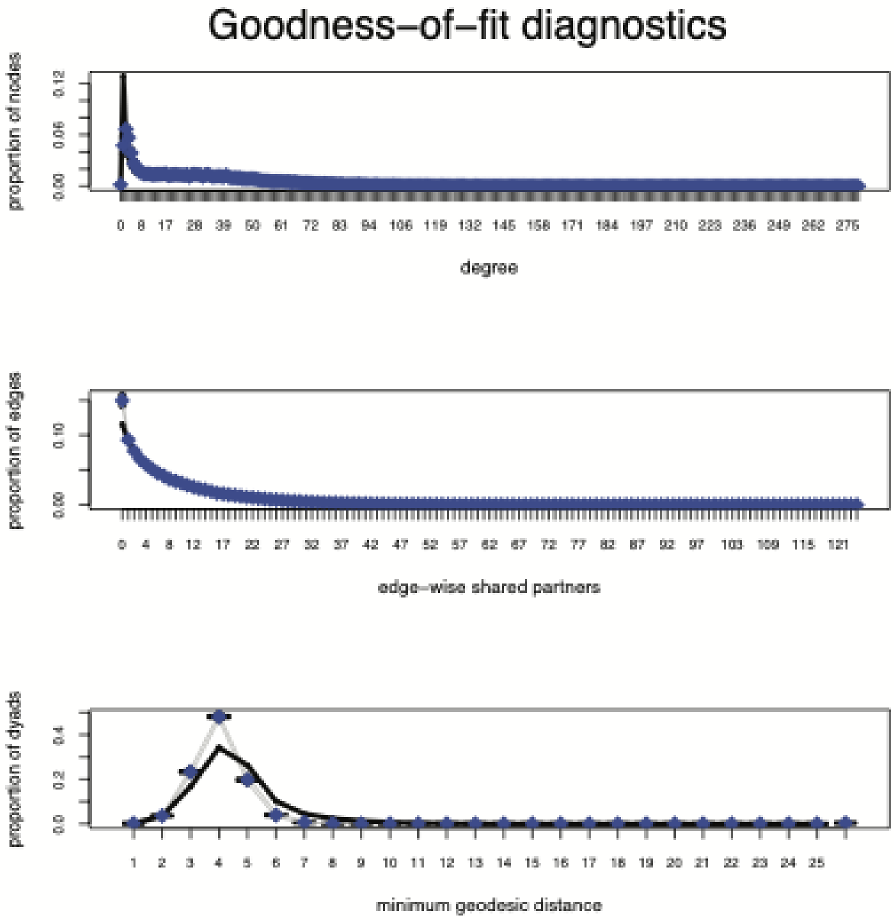

Fig. 3: GOF analysis of Model 1 in Table 3 of the main text