

Modeling the association between physician risky-prescribing and the complex network structure of physician shared-patient relationships - Supplemental Online Appendix

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1 Supplemental methods

1.1 Materials and overview of risky prescribing study

In this study, a 40% random sample of Medicare Part D claims (prescription drug events) from 2014 was used to retrieve beneficiaries' prescription fill records and their corresponding prescribers, for three classes of risky drugs: opioids, benzodiazepines, and sedative-hypnotics. The beneficiaries' prescription records including the physicians who prescribed their drugs from Medicare Part D claims were used to trace the trajectories of patients' prescriptions and to construct physicians' prescribing indexes. See the beginning of Section 2 and Figure S1 in for more details on the physician prescribing indexes and the study cohort definition and workflow. Separately, we used a 40% random sample of all Medicare fee-for-service claims from 2014 of beneficiaries residing in the state of Ohio to extract relevant physician-patient encounters for constructing the physician network. Because the complete physician-patient encounter data was only available for patients residing in the state of Ohio, we limited our shared-patient physician network to physicians caring for Ohio residents in 2014.

1.2 Construction of shared-patient physician network

A unipartite physician network is constructed from the ensemble of physician-patient encounters observed in the Medicare fee-for-service claims data. A visit to physician i followed by another visit to physician j by the same patient within a certain time window may provide evidence for a meaningful professional relationship ("patient referral") from physician i to j [8, 2, 1]. A lengthy time window of 365 days is used to allow gaps between physician visits to span months, minimizing the chance that a true directed relationship is missed. However, because a dyad with a bidirectional relationship is most likely to involve

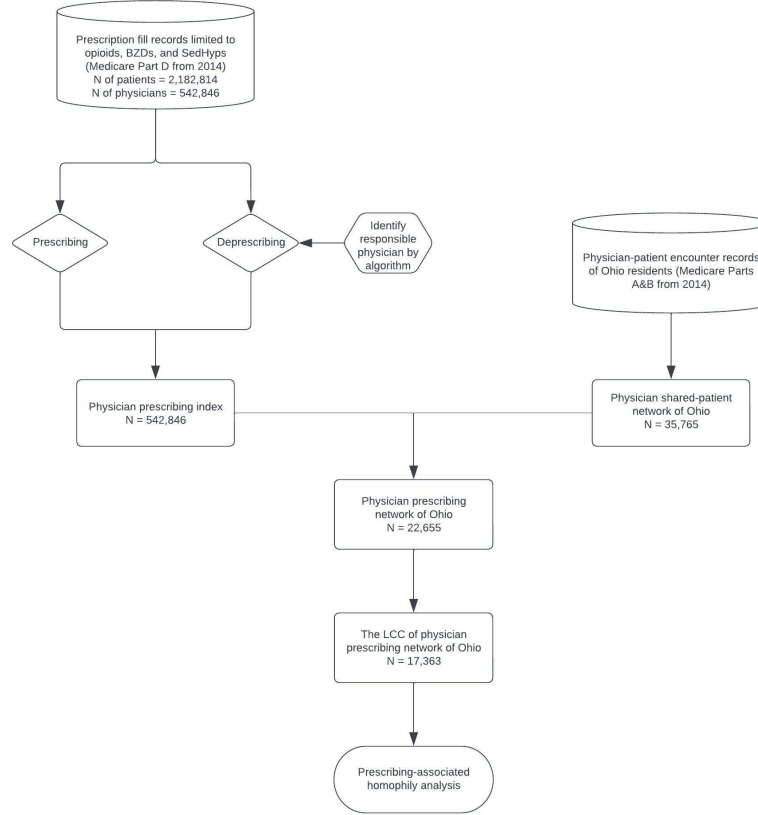


Figure S1: Study cohort definition and workflow

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.

physicians who know each other and who have made a deliberate choice to refer their patients to one another, we restricted the connections between physician pairs to only mutual ties (those dyads with directed edges in both directions). Next, we transformed the network to a binary network using a threshold of 0; thus, sharing at least one patient in each direction constitutes an edge in the network. We limit the network to physicians who had at least prescribed one drug in the drug classes of interest, including opioids, benzodiazepines, or sedative-hypnotics in 2014 according to Medicare Part D data. Finally, we reduce the network to its largest connected component (LCC) to eliminate isolated dyads (pairs of physicians who only shared patients with each other and thus have a

network degree of 1) as such physicians are likely practicing in a part-time or other reduced restricted manner.

To further study homophily in hospital referral regions (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 included in that HRR sub-network.

1.3 Homophily statistics: Isolating their effect and associated identifiability results

Several ERGM terms are available to study the homophily of continuous and categorical attributes. When studying the homophily of an attribute, it is important to adjust for the main effect of the node attribute to ensure that homophily is a relative measure as opposed to being impacted by the prevalence of the attribute across the network. The network statistics associated with these main effects are often named *nodecov* (for continuous attributes) and *nodefactor* (for categorical attributes) in ERGMs. Therefore, homophily can be thought of as a within-dyad interaction between the two nodes comprising the dyad of the given attribute [6, 7]. Table S1 shows the mathematical definitions of the ERGM terms used in this study and their respective interpretation. When estimating the homophily effect while adjusting for the node-level effect of the same attributes, only the effect of uniform homophily (the same effect of having the attribute in common across all levels of the attribute) can be estimated. Otherwise, the coefficients of the network statistics will be unidentifiable due to the linear dependency between the predictors. In the following, we demonstrate the mathematics of such linear dependency when estimating differential homophily while controlling for network density and the main effect of the node attribute. As displayed in Table S1, for a binary node attribute taking a value of 0 or 1, the network statistic added to the model by the *nodefactor* term is equivalent to,

$$\frac{1}{2} \sum_{ij} (x_i + x_j) a_{ij}. \quad (1)$$

The two statistics added by the differential homophily term *nodematch* are,

$$\frac{1}{2} \sum_{ij} x_i x_j a_{ij} \quad (2)$$

for the node attribute taking a value of 1, and

$$\frac{1}{2} \sum_{ij} (1 - x_i)(1 - x_j) a_{ij} = \frac{1}{2} \sum_{ij} (1 - (x_i + x_j) + x_i x_j) a_{ij} \quad (3)$$

for the node attribute taking a value of 0. For a binary node attribute, three predictors in Equations 1, 2, and 3 are linearly dependent and the model is

unidentifiable when including the *edges* term, the *nodefactor* term, and two *nodematch* terms of differential network homophily statistics in an ERGM for an undirected network. The result is observed by the fact that the *nodematch* term (Equation 3) is the sum of the *edges* (Table S1), *nodefactor* (Equation 1), and the 1-level *nodematch* (Equation 2) terms. Therefore, when controlling for the network density with the *edges* term and the main effect of an attribute with the *nodefactor* term, the uniform homophily statistic $\frac{1}{2} \sum_{ij} ((1-x_i)(1-x_j) + x_i x_j) a_{ij}$ (the sum of the two *nodematch* levels) can be identified but its components (the two differential homophily terms) cannot.

Table S1: Definitions of ERGM terms for undirected networks and interpretations

Terms	Math definition	Interpretation
edges	$m = \frac{1}{2} \sum_{ij} a_{ij}$	Number of edges in the network; controls for network density
Node attribute nodefactor	$Z_k = \frac{1}{2} \sum_{ij} (\mathbf{1}(x_i = k) + \mathbf{1}(x_j = k)) a_{ij}$	Number of times a node possessing a categorical attribute of value k appears on an edge in the network
nodecov	$Z = \frac{1}{2} \sum_{ij} (x_i + x_j) a_{ij}$	For continuous attributes, the sum of the attribute across node pairs for all edges present in network
Homophily term		
nodematch	$S = \frac{1}{2} \sum_l \sum_{ij} (\mathbf{1}(x_i = l) \mathbf{1}(x_j = l)) a_{ij}$	Uniform homophily; the number of edges when two nodes have the same categorical attribute
nodematch	$S_l = \frac{1}{2} \sum_{ij} (\mathbf{1}(x_i = l) \mathbf{1}(x_j = l)) a_{ij}$	Differential homophily; the number of edges when two nodes have the same categorical attribute taking a value of l
absdiff	$S = \frac{1}{2} \sum_{ij} x_i - x_j a_{ij}$	For continuous attributes, the sum of absolute difference in the attribute within a dyad across all edges present in the network

Note: $\mathbf{A} = [a_{ij}]$ is the adjacency matrix of the binary-undirected network in this study, and $a_{ij} = 1$ if physician i and j shared patients during 2014. The variables x_i and x_j are the node attributes of physician i and j , and k and l denote the values of a categorical attribute held by the two actors comprising a dyad.

We focus on the homophily of prescribing behaviors and homophily of physician specialty in the risky-prescribing-specific network while adjusting for network density and the above-mentioned network statistics. To avoid collinearity between different prescribing measures, the uniform homophily terms involving them were added one at a time in the model, adjusting in each model for network density, the differential effect of physician specialty on network density (i.e., the physician specialty *nodefactor* term), and the uniform homophily of physician specialty. The R package statnet was used to implement the ERGM

containing the associated network statistics as predictors [6, 5].

2 Supplemental application to study of physician homophily in prescribing and deprescribing

2.1 Data preprocessing

To quantify physicians’ prescribing behaviors, our primary interest is new prescription fills instead of refills because they represent a definitive step towards increased polypharmacy or risky drug combinations. 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 is 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, as described in the following sections.

2.2 Modeling patient prescription states

For each of the patients, their prescription fills of the three-drug classes of interest were divided into discrete time intervals, capturing the initialization and discontinuation of a prescription, with each time interval reflecting the number and class of drugs they were exposed to. Based on the number and the class of drugs a patient was taking during each of the discrete time intervals, we assigned the patient to the $2^3 = 8$ combinations of prescription states. Figure S2 shows the workflow of modeling patient prescription states. Every initialization or discontinuation of a drug will lead to the changing of a patient’s prescription state. State *zero* is a state of taking no drugs in the three-drug classes of interest. States $\{O, B, S\}$ correspond to taking at least one drug in precisely one of the opioids, benzodiazepines, or sedative hypnotics drug classes. States $\{OB, OS, BS\}$ correspond to taking at least two drugs concurrently involving two different drug classes. State *OBS* is to take at least three drugs of three different classes at the same time. Numbers from 1 to 8 were respectively assigned to these eight prescription states for the ease of mathematical notation in the following sections. A sequence of prescription states was thereby obtained for each patient, including both prescribing and deprescribing events.

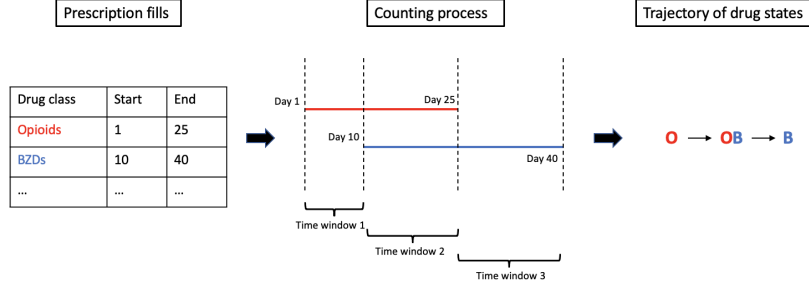


Figure S2: Workflow of modeling patient prescription states.

Note: Panel (A) shows a made-up example of a patient’s sequence of prescription fills with their corresponding drug class, the start and the end of the fill. Panel (B) shows the counting process to split the sequence of prescription fills into discrete exposure time intervals which reflect the initialization and the discontinuation of a prescription fill. The red line indicates the prescription fill length of the opioid in panel (A), and the blue line indicates the benzodiazepine fill length. Panel (C) shows the corresponding prescription state during each time interval in panel (B) and the transition between them, forming a trajectory of prescription states across time. “O” stands for filling an opioid, “B” stands for filling a benzodiazepine, and “OB” stands for filling an opioid and a benzodiazepine concurrently. BZDs = benzodiazepines

2.3 Attributing physician responsibility to prescribing and deprescribing prescriptions

The physician who initiated the prescription was attributed as the responsible physician. For example, the physician who prescribed an opioid to a patient who was already taking a benzodiazepine is the one responsible for the patient’s prescription state transition from state *B* to state *OB* (or from state 3 to state 5 using numerical notation). Deprescribing often takes place in conversations during physician-patient encounters where the physician reviews and discusses medications with their patients [4]. A decision to terminate a prescription triggers no insurance claims. Therefore, there is no record of a responsible deprescribing physician in the Medicare data. However, when a patient no longer refills a long-term prescription following a physician-patient encounter, we assume that a deprescribing conversation took place during the patient’s most recent clinical visit in developing our deprescribing algorithm (Algorithms 1 and 2). Each prescription of each patient is initially treated as a target prescription that can potentially be discontinued. We first sought to exclude the prescriptions for acute conditions and thereby 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. 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 deprescribing the target prescription. 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 refilled as described in Section 2.1. This preprocessing step protects against any temporary suspension of a prescription that a patient may refill later on, which can be a false positive deprescribing event by the identified physician. Finally, the patient prescription state transition associated with such termination was attributed to this identified physician with a contribution weight if multiple responsible physicians were identified. In this way, we obtained relatively balanced information regarding each physician’s prescribing and deprescribing activities.

Algorithm 1 Pseudo code: Crediting physicians for the deprescribing

Input: A set of n prescriptions patient h receives and their prescribing physicians.

Output: The responsible physician for deprescribing the prescription of interest.

```
1: for  $i = 1, 2, \dots, n$  do
2:   if length of prescription  $i \geq 30$  days then
3:      $\Delta_t \leftarrow$  empty list  $\triangleright$  difference between two dates
4:     for  $j = 1, 2, \dots, n$  and  $j \neq i$  do
5:        $s_j \leftarrow$  start date of prescription  $j$ 
6:        $e_i \leftarrow$  end date of prescription  $i$ 
7:       if  $e_i - s_j > 0$  and  $e_i - s_j \leq 30$  then  $\triangleright$  prescription  $i$ 
         discontinues within 30 days of encountering a physician
8:         Add  $e_i - s_j$  to  $\Delta_t$ 
9:       end if
10:    end for
11:    Find the prescription  $p$  with minimum  $\Delta_t$  and corresponding prescriber  $k$   $\triangleright$  most recent encountered physician
12:    responsible physician for deprescribing prescription  $i \leftarrow$  physician  $k$ 
13:    if multiple responsible physicians then
14:      contribution weight  $\leftarrow 1 / \text{number of contributors}$ 
15:    end if
16:    if no physician is held accountable after applying above criteria then
17:      responsible physician for deprescribing prescription  $i \leftarrow$  a pseudo-physician
18:    end if
19:  else
20:    responsible physician for deprescribing prescription  $i \leftarrow$  a pseudo-physician
21:     $i \leftarrow i + 1$ 
22:  end if
23: end for
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Algorithm 2 Pseudo code: Determining the deprescribing state transition a physician is responsible for

Input: (1) The responsible physician k for deprescribing target prescription i for patient h ; (2) a set of n prescriptions patient h receives.

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

```

1:  $D_b \leftarrow$  empty list  $\triangleright$  List of drugs patient  $h$  is taking before discontinuation
   of prescription  $i$ 
2:  $D_a \leftarrow$  empty list  $\triangleright$  List of drugs patient  $h$  is taking after discontinuation of
   prescription  $i$ 
3: for  $j = 1, 2, \dots, n$  do
4:    $s_j \leftarrow$  start date of prescription  $j$ 
5:    $e_j \leftarrow$  end date of prescription  $j$ 
6:    $e_i \leftarrow$  end date of prescription  $i$ 
7:   if  $e_i - 0.1 > s_j$  and  $e_i - 0.1 < e_j$  then
8:     Add  $j$  to  $D_b$ 
9:   end if
10:  if  $e_i + 0.1 > s_j$  and  $e_i + 0.1 < e_j$  then
11:    Add  $j$  to  $D_a$ 
12:  end if
13: end for
14: determine prescription state  $m$  based on  $D_b$ 
15: determine prescription state  $n$  based on  $D_a$ 
16: physician  $k$  is responsible for patient  $h$ 's deprescribing state transition from
     $m$  to  $n$ 

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2.4 Physician transition responsibility matrix

Given the eight different prescription states patients can take, and the sequence of their prescription states, an 8 by 8 transition responsibility matrix was established for every physician to capture their contribution to prescribing and deprescribing across all of their patients' prescription state transitions.

The physician transition responsibility count matrix ($PTRCM$) is constructed for each physician by summarizing across all the patients to whom they've prescribed and deprescribed. The rows in the matrix $PTRCM$ correspond to patients' prescription states in the preceding prescription exposure time intervals, while the columns correspond to patients' prescription states in the subsequent time intervals. For a given physician k , the ij 'th cell in the $PTRCM$ is the total number of patient prescription state transitions from state i to state j to which the physician contributed. It is mathematically defined as,

$$PTRCM^{(k)} = \begin{bmatrix} C_{1,1}^{(k)} & C_{1,2}^{(k)} & \dots & C_{1,j}^{(k)} & \dots & C_{1,8}^{(k)} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ C_{i,1}^{(k)} & C_{i,2}^{(k)} & \dots & C_{i,j}^{(k)} & \dots & C_{i,8}^{(k)} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ C_{8,1}^{(k)} & C_{8,2}^{(k)} & \dots & C_{8,j}^{(k)} & \dots & C_{8,8}^{(k)} \end{bmatrix}. \quad (4)$$

Let h denote a patient and t the prescription exposure time interval. Then D_{ht} denotes patient h 's prescription state during time intervals t and P_{ht} denotes the corresponding responsible physician for patient h 's prescription state transition between time interval t and $t+1$. In addition, i and j are prescription states. Let $\mathbf{1}(event) = 1$ if $event$ is true and 0 otherwise. Then cell (i, j) in the $PTRCM$ for physician k is given by,

$$C_{i,j}^{(k)} = \sum_h \sum_t \mathbf{1}(D_{ht} = i, D_{h(t+1)} = j) \mathbf{1}(P_{ht} = k). \quad (5)$$

To account for the scenario when multiple physicians are responsible for a prescription state transition from i to j , suppose the total number of responsible physicians for patient h at time t is N_{ht} . Then compute $C_{i,j}^{(k)}$ as

$$C_{i,j}^{(k)} = \sum_h \sum_t \mathbf{1}(D_{ht} = i, D_{h(t+1)} = j) \frac{\sum_r \mathbf{1}(P_{ht} = r)}{N_{ht}}. \quad (6)$$

2.5 Quantitative measures of physician prescribing behavior

2.5.1 Difference between prescribing and deprescribing

Given the $PTRCM$, we compute different prescribing indexes corresponding to various aspects of decision-making during physicians' prescribing practice. First, we compute the relative difference between the number of prescribing and deprescribing events. Notice that the cells above the diagonal of the $PTRCM$ are the prescribing transitions while cells below the diagonal are contributions to deprescribing transitions. By construction, there was no transition between the same prescription states (these were subsumed by the continuation of the prior fill event as described in the Materials section). The resulting measure for physician k is given mathematically as,

$$I_{base}^{(k)} = \frac{\sum_j \sum_{i < j} C_{i,j}^{(k)} - \sum_i \sum_{i > j} C_{i,j}^{(k)}}{\sum_j \sum_{i < j} C_{i,j}^{(k)} + \sum_i \sum_{i > j} C_{i,j}^{(k)}}. \quad (7)$$

A second family of measures is instead based on the total number of drugs changed (not the number of transitions) to which the physician contributed, obtained by multiplying the count of transitions with the number of drug changes

involved. For example, a transition from state B (or state 3) to state OBS (or state 8) involves a change of two drugs, as does the transition in the opposite direction. Let $\mathbf{1}_{num}(\omega)$ quantify the number of drugs a patient is taking under the prescription state ω , given by,

$$\mathbf{1}_{num}(\omega) = \begin{cases} 0, & \omega = 1, \\ 1, & \omega \in \{2, 3, 4\}, \\ 2, & \omega \in \{5, 6, 7\}, \\ 3, & \omega = 8. \end{cases} \quad (8)$$

The resulting risky drug index of physician k is defined as,

$$I_{\alpha}^{(k)} = \frac{\sum_j \sum_{i < j} C_{i,j}^{(k)} |\mathbf{1}_{num}(i) - \mathbf{1}_{num}(j)|^{\alpha} - \sum_i \sum_{i > j} C_{i,j}^{(k)} |\mathbf{1}_{num}(i) - \mathbf{1}_{num}(j)|^{\alpha}}{\sum_j \sum_{i < j} C_{i,j}^{(k)} |\mathbf{1}_{num}(i) - \mathbf{1}_{num}(j)|^{\alpha} + \sum_i \sum_{i > j} C_{i,j}^{(k)} |\mathbf{1}_{num}(i) - \mathbf{1}_{num}(j)|^{\alpha}}. \quad (9)$$

Here α takes the value of 0 or 1 to define two measures distinguished by whether to account for the number of drug changes involved in the prescription state transition from state i to j . The index $I_{\alpha}^{(k)}$ is bounded between -1 (exclusive) and 1 (inclusive). The index I_{base} defined in Equation 7 can be obtained from Equation 9 when $\alpha = 0$.

2.5.2 Prescribing involving risky prescription state

Our next measure quantifies the extent of physicians' involvement in the riskiest form of prescribing, state OBS (or state 8), given mathematically as,

$$I_{OBS}^{(k)} = \frac{\sum_j \sum_{i < 8} C_{i,8}^{(k)}}{\sum_j \sum_{i < j} C_{i,j}^{(k)} + \sum_i \sum_{i > j} C_{i,j}^{(k)}} \quad (10)$$

where $C_{i,8}^{(k)}$ is the number of transitions physician k contributed to for which patients transitioned from state i to state 8 (state OBS). We also binarized the numerator to obtain a binary indicator of whether physician k has ever contributed to bringing a patient into state OBS , given by,

$$I_{everOBS}^{(k)} = \mathbf{1}(\sum_{i < 8} C_{i,8}^{(k)} > 0). \quad (11)$$

2.5.3 Quantifying extent of prescribing and deprescribing

We also developed several measures to quantify the intensities of physicians' prescribing and deprescribing. First, we quantified the percentage of patients' prescription state transitions a physician contributed to that involved two or more drug changes. For example, a transition from state $zero$ to state OBS , and a transition from state OBS to state B involves three and two drug changes respectively, the former by prescribing and the latter by deprescribing. For

physician k , the proportion of physician's prescribing that contributes two or more drug changes is,

$$I_{presc2mr}^{(k)} = \frac{\sum_j \sum_{i < j} C_{i,j}^{(k)} \mathbf{1}(|\mathbf{1}_{num}(i) - \mathbf{1}_{num}(j)| \geq 2)}{\sum_j \sum_{i < j} C_{i,j}^{(k)}}. \quad (12)$$

Likewise, the proportion of physician's deprescribing that involves changing the status of two or more drug classes is,

$$I_{depresc2mr}^{(k)} = \begin{cases} \frac{\sum_i \sum_{i > j} C_{i,j}^{(k)} \mathbf{1}(|\mathbf{1}_{num}(i) - \mathbf{1}_{num}(j)| \geq 2)}{\sum_i \sum_{i > j} C_{i,j}^{(k)}} & , \sum_i \sum_{i > j} C_{i,j}^{(k)} \neq 0, \\ 0 & , \sum_i \sum_{i > j} C_{i,j}^{(k)} = 0. \end{cases} \quad (13)$$

The above measures may enter an ERGM as categorical or continuous node attributes to study the respective homophily effects in the network.

3 Supplemental results

3.1 Prescribing and deprescribing measures

In the LCC of Ohio physician prescribing network, the distribution of indexes based on the difference between prescribing and deprescribing, i.e., I_0 and I_1 , is skewed to the left (Table ??). On average, among all the patient prescription state transitions a physician contributed to, around 0.9% of them involve bringing patients to the riskiest state *OBS*. Around 8.9% of physicians have ever contributed to patients' risky transition to state *OBS*. Among all the contributed transitions associated with prescribing, around 2.9% of them involved adding two or more drugs. Likewise, among all the contributed transitions associated with deprescribing, on average around 1.6% involved a reduction of two or more drugs.

In Figure S3, different prescribing indexes are displayed by physician specialty group for the LCC of the shared-patient prescribing physician network of Ohio in 2014; each physician was assigned to either the primary care physicians, medical specialist, and surgeon specialist group based on their lookup information in the National Plan and Provider Enumeration System (NPPES) [3]. In terms of overall prescribing and deprescribing reflected by I_0 , there was no substantial difference across specialties, although surgeons and medical specialists appeared to have slightly higher prescribing index I_0 than other specialties. Other prescribing measures reflected physicians' prescribing behavior with more granularity. Primary care physicians and physicians of hospital-based services have a higher likelihood of bringing patients to state *OBS*, prescribing two or more drugs, and deprescribing two or more drugs, compared to medical specialists and surgeons.

Figure S4 shows the homophily patterns in terms of prescribing and deprescribing in the ego network. 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 clusters of physicians with similar prescribing intensity and behavior.

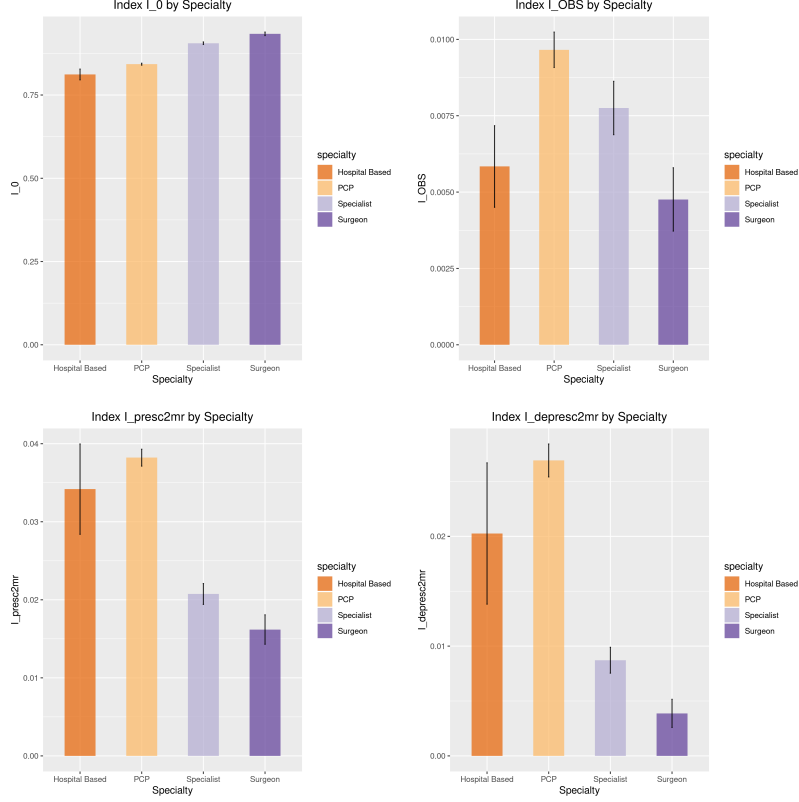


Figure S3: Prescribing measures by specialty of physicians in the largest connected component of the shared-patient prescribing physician Ohio network in 2014. Prescribing measures by specialty of physicians in the largest connected component of the shared-patient prescribing physician Ohio network in 2014. Specialists are medical specialists other than surgeons. Hospital-based services include anesthesiology, radiology, and pathology. PCP denotes primary care physicians. I_{OBS} is the prescribing index based on a physician's contribution to bringing patients to prescription state OBS , $I_{presc2mr}$ is the prescribing index based on a physician's contribution to prescribing two or more drug types to patients, and $I_{depresc2mr}$ is the deprescribing index based on a physician's contribution to deprescribing two or more drug types for patients. Error bars show the standard errors of the respective measures.

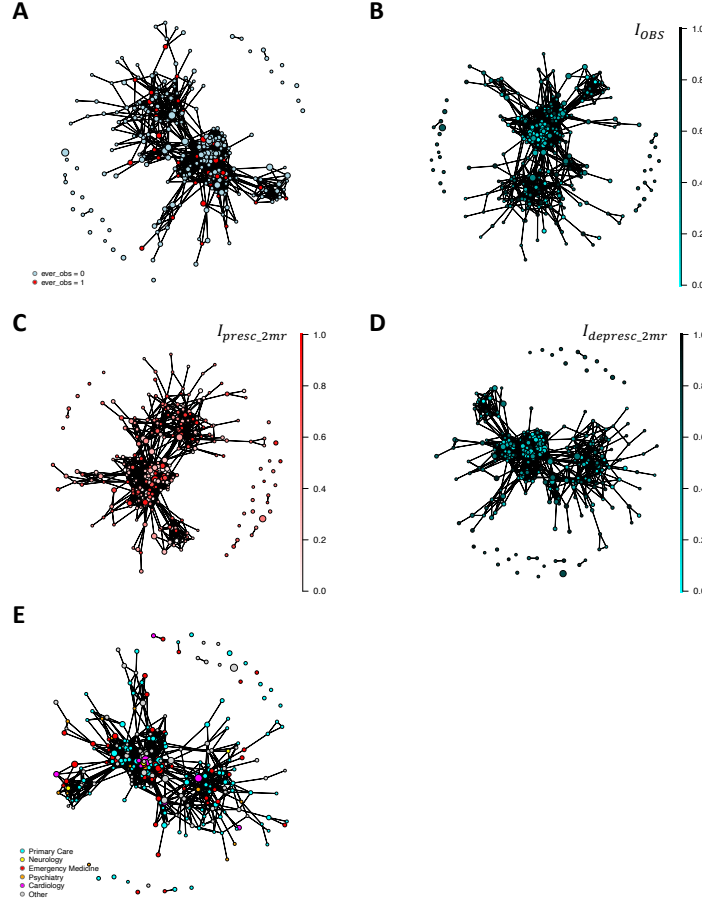


Figure S4: Egocentric network of the physician with maximum node degree (N = 276). The egocentric network of the physician with the highest node degree in the LCC of the prescribing network. The ego physician was removed from the plot for the clarity of presentation. The ties shown in the plots are among 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) It shows the connections among physicians distinguished by whether they have ever contributed to bringing patients to the riskiest prescription state (the *OBS* state). B) It shows 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) It shows 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) It shows the connections among physicians where the node color represents $I_{depresc_2mr}$, the proportion of contribution to deprescribing events at which two or more drugs are deprescribed at once to the patients. E) It shows the connections among physicians colored by their specialties.

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