

Prescribing Cascades Potentially Associated with Harms Before and After Transition to Long-Term Care: A National Cohort Study

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BACKGROUND

- Prescribing cascades occur when a new medicine is prescribed to treat an adverse drug reaction and are associated with an increased risk of medication-related harms.^{1,2}

1 INITIAL MEDICATION

2 ADVERSE DRUG REACTION OCCURS

3 ADR MISTAKEN FOR NEW CONDITION

4 NEW MEDICATION PRESCRIBED

5 FURTHER ADVERSE DRUG REACTIONS OCCUR

1 Patient is started on a medication

2 The medication causes an adverse drug reaction (ADR).
Examples: dizziness, fatigue, insomnia, confusion, edema, etc.

3 The adverse drug reaction is interpreted as a new symptom or medical condition.
Examples: falls → vertigo, fatigue → depression, edema → heart failure

4 A new medication is prescribed to treat the "new condition."

5 The new medication may cause additional adverse drug reactions.
Examples: drowsiness, confusion, low blood pressure, electrolyte imbalances, bleeding, etc.

CYCLE CONTINUES

More medications → more adverse drug reactions → more misdiagnoses → more medications

While some prescribing cascades may be considered appropriate, many are considered to be inappropriate.

APPROPRIATE

INAPPROPRIATE

- Transition between care settings are associated with an increased risk of medication-related harms, including medication errors and adverse events.³ Little is known about prescribing cascades among older people when they transition to long term care facilities (LTCF).

AIM

- To examine prescribing cascades potentially associated with harms before and after LTCF entry, and to examine the impact of dementia.

METHODS

- A retrospective population-based cohort study of 167,850 individuals aged 65 years or older who entered 2771 LTCFs nationally in Australia between January 2018 and June 2020 was conducted.
- Prescription sequence symmetry analysis⁴ was used to examine 143 previously identified prescribing cascades³ with a 12-month exposure window between the index and marker medicines.
- Analyses were stratified by people living with and without dementia.

1 Identify sequences within the 1-year observation window

Two possible sequences:
Index → Marker
Count patients where the marker starts within 1 year after index start
Marker → Index
Count patients where the index starts within 1 year after marker start

2 Calculate sequence symmetry

Crude Sequence Ratio (cSR)
cSR = (Index → Marker) / (Marker → Index)
cSR > 1 indicates more Index → Marker sequences

Adjust for prescribing trends
Adjusted Sequence Ratio (aSR)
Adjusts for underlying changes in medication use over time and other prescribing patterns.

RESULTS

- Median age at study entry was 86 yrs (IQR 80-90), 60.4% were female and 50.1% had dementia.

Prescribing cascades increase after transition to LTCF

- Before transition to LTCF 16.7% (n = 28,018) had at least one statistically significant prescribing cascade and 25.1% (n = 42,101) after LTCF entry, with little difference in prevalence by dementia status.

Impact of Dementia

- Thirteen cascades unique to those living with dementia were identified following LTCF transition. The most common being:
 - Benzodiazepines leading to high ceiling diuretics (aSR 1.32, 95%CI 1.24-1.40, n = 4147)
 - SSRI/SNRI leading to sedating antidepressants (aSR 1.28, 95%CI 1.16-1.42, n = 1437)
 - Antiepileptics leading to antiemetic (aSR 1.38, 95%CI 1.24-1.53, n = 1434).
- Initiation of non-steroidal anti-inflammatory drugs (NSAIDs) leading to antiemetics for nausea was the only cascade significantly higher among those living with dementia (aSR 1.50, 95%CI 1.36-1.67) compared to those without dementia (aSR 1.12, 95%CI 1.03-1.22).

Index Drug	Marker Drug	Index Users (I-M-M-I)	aSR (95% CI)
Proton pump inhibitors	Intestinal anti-infectives	89 [64/25]	3.40 (2.14, 5.40)
HMG CoA reductase inhibitors	Antibiotic	4318 [3320/998]	3.20 (2.98, 3.44)
ACE-inhibitors	Antitussive	66 [47/19]	3.02 (1.77, 5.15)
HMG CoA reductase inhibitors	Antipsychotics	1383 [1032/351]	2.93 (2.59, 3.31)
Digoxin	Antiemetic	2050 [1513/537]	2.81 (2.54, 3.10)
Antihypertensives	Antiemetic	4963 [3628/1335]	2.68 (2.52, 2.86)
HMG CoA reductase inhibitors	Anti-inflammatory	581 [426/155]	2.59 (2.16, 3.11)
Cholinesterase inhibitor	Prochlorperazine	116 [78/38]	2.44 (1.85, 3.59)
HMG CoA reductase inhibitors	Antidepressants	1433 [1001/432]	2.29 (2.05, 2.56)
Amiodarone	Levothyroxine	91 [59/32]	2.26 (1.47, 3.48)
HMG CoA reductase inhibitors	Antirhythmics	63 [43/20]	2.19 (1.29, 3.72)
Metformin	Antidiarrheal	163 [110/53]	2.14 (1.54, 2.97)
Cholinesterase inhibitor	Antiemetic	786 [539/247]	2.14 (1.84, 2.49)
HMG CoA reductase inhibitors	Antithrombotic	535 [357/178]	2.12 (1.77, 2.54)
HMG CoA reductase inhibitors	Hypnotics and sedatives	1164 [789/375]	2.08 (1.84, 2.36)
Dihydropyridines	High-ceiling diuretics	1945 [1298/647]	1.94 (1.76, 2.13)
HMG CoA reductase inhibitors	Anti-dementia	183 [121/62]	1.85 (1.36, 2.52)
Selective CCB (cardiac effects)	TCA SSRI Other Antidepressant	163 [104/59]	1.83 (1.33, 2.51)
Beta blocking agents	TCA SSRI Other Antidepressant	2343 [1534/809]	1.82 (1.67, 1.98)
Antihypertensives	Prochlorperazine	720 [463/257]	1.79 (1.54, 2.08)
ACE-inhibitors	Antibacterials (cough)	2573 [1642/931]	1.72 (1.59, 1.86)
Cholinesterase inhibitor	Antidiarrheal	76 [48/28]	1.66 (1.04, 2.65)
Opioids	Antiemetic	18944 [11816/7128]	1.66 (1.61, 1.71)
Benzodiazepine derivatives	Antipsychotics	10724 [6490/4234]	1.53 (1.47, 1.59)
ACE-inhibitors	Anti-inflammatory	695 [417/278]	1.51 (1.30, 1.76)
HMG CoA reductase inhibitors	Oxybutynin	141 [82/59]	1.44 (1.03, 2.01)
Proton pump inhibitors	Antibiotic	10103 [5983/4120]	1.43 (1.38, 1.49)
ACE-inhibitors	Antidepressants	1722 [1011/711]	1.40 (1.27, 1.54)
Antiepileptics (other)	Antibacterials (UTI)	1302 [772/530]	1.40 (1.25, 1.56)
Dihydropyridines	Antidepressants	1551 [906/645]	1.39 (1.25, 1.53)
Laxative	Antidiarrheal	1604 [948/656]	1.39 (1.25, 1.53)
Benzodiazepine derivatives	Prochlorperazine	1589 [922/667]	1.36 (1.23, 1.51)
Proton pump inhibitors	Denosumab	1889 [1077/812]	1.27 (1.16, 1.40)
Anti-inflammatory	Antiemetic	3500 [1950/1550]	1.27 (1.19, 1.35)
Direct anticoagulants	Antidepressants	1524 [838/686]	1.23 (1.11, 1.36)
Antiepileptics	Corticosteroid	2097 [1162/935]	1.21 (1.11, 1.32)
Benzodiazepine derivatives	Anti-dementia	1224 [668/556]	1.20 (1.07, 1.34)
Antidepressants	Anti-Parkinson drugs	621 [331/290]	1.19 (1.02, 1.40)
SSRI/SNRI	Antidepressant (sedating)	2908 [1556/1352]	1.17 (1.09, 1.26)
Calcium channel blockers (CCB)	Laxative	3156 [1703/1453]	1.16 (1.08, 1.25)
Antiepileptics	Antiemetic	2747 [1458/1289]	1.14 (1.05, 1.22)
ACE-inhibitors	Adrenergics/inhalants	1668 [888/780]	1.13 (1.03, 1.25)
Benzodiazepine derivatives	High-ceiling diuretics	8302 [4341/3961]	1.09 (1.05, 1.14)

Individual prescribing cascades (n=43) identified after LTCF transition

CONCLUSION

- This population-based study highlights prescribing cascades associated with harms during a vulnerable care transition period for older people and provides targets for deprescribing to reduce potential medication-related harms.

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