

编者按:为深入学习贯彻党的十九届四中全会精神以及习近平总书记关于卫生健康工作系列重要论述和重要指示批示精神,坚决贯彻落实党中央、国务院决策部署,启动实施健康中国行动,深化医改和健康扶贫工作,稳步提升医疗服务水平,振兴中医药发展,我刊特从2020年7月起开设“全民健康助力全面小康”专栏,从我刊实际出发,陆续推出一系列健康中国建设与药学工作结合的相关文章,从而助力提高人民健康水平制度保障、坚持和发展中国特色卫生健康制度。本期专栏文章《老年多重用药研究现状与热点前沿的文献计量学分析》是在全球老龄化的背景下,针对老年患者因基础疾病多、用药情况复杂而出现的多重用药现象,对全球范围内开展该领域研究的热点、重点以及趋势等进行文献计量学分析,为我国加强国内以及国际间在该研究领域的交流与合作、建立和完善适合我国国情的潜在不适当用药筛选标准提供有益的参考。

老年多重用药研究现状与热点前沿的文献计量学分析[△]

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摘要 目的:分析近10年老年多重用药的研究现状与热点前沿,为我国老年多重用药的研究提供参考。方法:检索2010年1月1日—2019年12月31日Web of Science数据库中核心数据库收录的老年多重用药相关的文献,采用CiteSpace 5.6.R5软件对发文量、作者、国家/地区、机构、期刊共被引情况、文献共被引情况进行分析,对关键词进行共现分析、聚类分析及突现(Burst)分析,绘制可视化图谱并分析结果。结果:共纳入文献3 521篇,老年多重用药研究的发文量整体呈上升趋势,高产作者主要以Bell JS和Hilmer SN为代表,均发表36篇,占总发文量的1.02%。美国(929篇,26.3%)和澳大利亚悉尼大学(101篇,2.87%)分别是发表文献最高产的国家 and 机构。*Journal of the American Geriatrics Society*是收录文章最多的期刊(2 202篇)。文献共被引频次最高是Radcliff S等在2015年发表的对Beers标准进行更新以用于减少潜在不适当用药的研究;文献共被引中心度最高是Spinewine A等在2007年发表的如何优化老年人处方的研究;关键词出现次数较多的包括老年人、多重用药、危险因素,中心度排名较高的包括

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生活质量、多重用药、Beers 标准, 目前研究的热点包括危险因素、结局指标以及对多重用药的减少策略; 形成 Breast cancer、Prescription、Disorder、Schizophrenia、Medication adherence、Trial 等 6 个聚类; 研究前沿是并发症、痛苦、老年衰弱、健康相关质量、认知障碍。结论: 近 10 年来老年多重用药的研究日趋受到学者的重视, 美国以及澳大利亚在该领域的贡献较大; 研究主要集中在多重用药对健康结局的影响以及减少多重用药的策略上; 未来可能会更多关注于多重用药对老年心理和认知、衰弱的相关研究。

关键词 老年人; 多重用药; 文献计量学; Web of Science

Bibliometric Analysis of Research Status and Hotspot Frontier of Polypharmacy in the Elderly

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ABSTRACT **OBJECTIVE:** To analyze the research status and hotspot frontier of polypharmacy in the elderly in recent ten years, and to provide reference for polypharmacy study in the elderly in China. **METHODS:** The related literatures about polypharmacy in the elderly were retrieved from Web of Science core database during Jan. 1st, 2010-Dec. 31th, 2019. CiteSpace 5.6.R5 software was used to analyze the quantity of published literatures, authors, country/area, institution, co-citation of journals and literatures. The keywords were taken as nodes for co-occurrence analysis, cluster analysis and Burst analysis, the visual maps were drawn and the results were analyzed. **RESULTS:** A total of 3 521 literatures were included, and the quantity of published literatures about polypharmacy in the elderly was on the rise; high-yield authors mainly were Bell JS and Hilmer SN which were the representative with 36 papers published, accounting for 1.02% of the total. America (929 literatures, 26.3%) and University of Sydney (101 literatures, 2.87%) were the most high-yield country and institution respectively; *Journal of the American Geriatrics Society* was the journal with the most articles (2 202 pieces). The most frequently cited literature was those published by Radcliff S team in 2015 to update Beers standard to reduce potential inappropriate drug use; the research on how to optimize the prescription for the elderly published by Spinewine A team in 2007 had the highest co-citation centrality. The hot keywords were elderly, polypharmacy and risk factor; keywords with high centrality included quality of life, polypharmacy and Beers standard. Research hotspots included risk factor, outcome index and reduction strategy for polypharmacy. Six clusters were formed, including Breast cancer, Prescription, Disorder, Schizophrenia, Medication attachment and Trial; complications, pain, frailty, health-related quality, intellectual disability were at the forefront of research. **CONCLUSIONS:** In the past 10 years, the research on polypharmacy in the elderly has been paid more and more attention by scholars; the United States and Australia have made great contributions in this field; the research mainly focused on the impact of polypharmacy on health outcomes and the strategies for reduce polypharmacy. In the future, more attention will be paid to the related research on psychological, cognitive and debilitating effects of polypharmacy in the elderly.

KEYWORDS Elderly; Polypharmacy; Bibliometrics; Web of Science

目前, 全世界老年人口的数量正在增加。随着年龄增长, 老年人所患慢性病的数量也逐渐增加, 多数老年人存在多病共存的状态^[1], 易导致多重用药^[2]。多重用药是指一个人使用多种药物治疗, 一般被定义为使用 5 种及以上的药物^[3], 其是应对老年人复杂健康问题的一种合理治疗方法^[4]。然而, 越来越多的人担心, 老年人多重用药, 尤其是在复杂的药物组合中会使个别药物之间产生相反的效果。研究发现, 多重用药老年患者中, 73.24% 的患者存在药物相关问题, 接近 60% 的药物相关问题与治疗有效性相关, 且 64.81% 的药物相关问题对老年人健康存在潜在不利影响^[5]。因此, 对于老年人多重用药的研究越来越受到人们的重视。

文献计量学是一种定量方法, 用于分析科学领域的文献, 并评估研究活动的长期趋势^[6]。过去的 10 年中,

相当多的学者和学术期刊集中发表了老年多重用药的研究。基于此, 本文采用 CiteSpace 软件等对 2010—2019 年发表的关于老年多重用药的文献进行可视化分析, 并对当前的研究热点以及现状进行总结, 旨在为老年多重用药的研究提供参考。

1 资料与方法

1.1 资料来源及策略

以 Web of Science 数据库为检索平台, 数据库来源为 Web of Science Core Collection, 根据医学主题词和自由词制订检索词与检索策略: (“Older adults” OR “Aged” OR “Elderly”) AND (“Polypharmacy” OR “Polymedication”)。文献类型选择 “Article” OR “Review”, 语种选择 “English”, 时间年限为 2010 年 1 月 1 日—2019 年 12 月 31 日。

1.2 分析方法

将下载至目标文件中的纯文本信息导入 CiteSpace 5.6.R 5 软件中,对导入的文献进行去重处理。利用 Excel 2007 软件分析老年多重用药研究文献的发表年份分布。使用 CiteSpace 5.6.R5 软件分别以文献的作者、国家/地区、机构为节点进行合作网络分析;以期刊、文献为节点进行共被引分析;以关键词为节点进行共现分析后继续对关键词进行聚类分析和突现(Burst)分析;根据所选节点的不同,选取不同的时间分区、阈值设置及裁剪方式,以达到出图清晰、直观的目的^[7]。

2 结果与分析

2.1 发文量趋势

共纳入老年多重用药研究文献 3 521 篇,近 10 年的年均发文量约 352 篇,纳入文献的发表年份分布分析结果见图 1。由图 1 可见,2010—2019 年老年多重用药研究的发文量整体呈上升趋势。

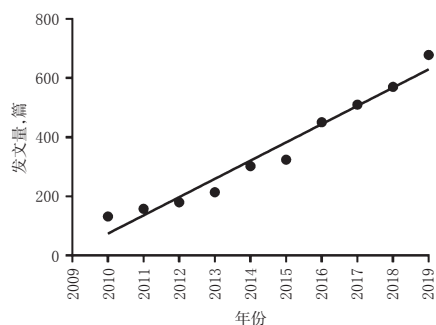


图 1 老年多重用药研究文献的发表年份分布(2010—2019年)

Fig 1 Distribution of research literature on polypharmacy in the elderly(2010-2019)

2.2 作者合作网络分析

作者的合作网络分析可以得出具有影响力的作者,这些信息可以帮助研究人员识别潜在的合作者^[8]。使用 CiteSpace 5.6.R5 软件对作者的合作网络进行分析,结果见图 2。图中每一个节点代表 1 位作者,节点的大小代表该作者发文量的多少,节点间的连线表示连线两端的作者在同一篇文章中出现,即两位作者之间存在合作关系;节点年轮最外圈的颜色越深则表明该节点具有越高的中介中心性(中介中心性的高低代表该节点在联系整个网络中发挥的作用大小,以中心度来表示^[9])。由图 2 可知,Bell JS 团队和 Hilmer SN 团队均发表了 36 篇论文,占总发文量的 1.02%,发文数排名并列第 1 位;其次是 Nobili A 团队(31 篇,0.88%)、Gnjidic D 团队(30 篇,0.85%)和 Johnell K 团队(28 篇,0.80%)。在中心度方面,Ballestrero A 团队(0.20)和 Marra A 团队(0.20)是中

心度最高的作者,其次是 Reeve E 团队(0.16)和 Mannucci PM 团队(0.14)。



图 2 作者合作网络关系图谱

Fig 2 Graph of author cooperation network

根据作者的文献数量以及中心度的综合分析,Nobili A 团队、Marengoni A 团队、Onder G 团队、Mannucci PM 团队和 Reeve E 团队在老年多重用药领域是影响力较高的作者。Nobili A 团队和 Mannucci PM 团队有一定的合作,他们认为多重用药与多病有关,且可以导致不良结局的发生,如住院时间延长、院内死亡^[10-12]。Marengoni A 团队认为研究者应该关注老年人多重用药的状况,并对有药物相关风险的患者进行早期干预^[13]。Onder G 团队认为减少服药数量是有必要的,并积极寻找解决策略^[14-15]。Reeve E 团队认为应该关注不同病种的老年人停药的态度,以及停药后产生的影响^[16-17]。

2.3 国家/地区合作网络分析

使用 CiteSpace 5.6.R5 软件对国家/地区的合作网络进行分析,结果见图 3。图中每一个节点代表 1 个国家/地区,节点的大小代表该国家/地区发文量的多少,节点间的连线表示两个国家/地区存在合作关系;节点年轮最外圈的颜色深度则表明该节点具有较高的中介中心性。由图 3 可知,发文量排名前 5 位的国家依次是美国 929 篇(26.3%)、澳大利亚 334 篇(9.5%)、英国 286 篇(8.1%)、意大利 283 篇(8.0%)、西班牙 221 篇(6.2%),这 5 个国家的发文量占据总发文量的 58.3%;从文献的中心度看,排名前 5 位的国家或地区依次是美国(0.22)、苏格兰(0.20)、瑞典(0.12)、中国(0.12)、意大利(0.10)。与发展中国家相比,发达国家在老年多重用药领域研究较

表2 共被引频次排名前10位的文献

Tab 2 Top 10 literatures in the list of co-citation frequency

序号	作者	发表年份	题目	被引频次
1	Radcliff S等	2015	American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults	301
2	Fick D等	2012	American geriatrics society updated beers criteria for potentially inappropriate medication use in older adults	290
3	O'Mahony D等	2015	STOPP/START criteria for potentially inappropriate prescribing in older people; version 2	267
4	Gnjidic D等	2012	Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes	249
5	Maher RL等	2014	Clinical consequences of polypharmacy in elderly	221
6	Scott IA等	2015	Reducing inappropriate polypharmacy: the process of deprescribing	186
7	Gallagher P等	2008	STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria	161
8	Fried TR等	2014	Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review	124
9	Garfinkel D等	2010	Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy	119
10	Daniel SB等	2011	Emergency hospitalizations for adverse drug events in older Americans	107

表3 共被引中心度排名前10位的文献

Tab 3 Top 10 literatures in the list of co-citation centrality

序号	作者	发表年份	题目	中心度
1	Spinevine A等	2007	Appropriate prescribing in elderly people: how well can it be measured and optimised?	0.14
2	Gnjidic D等	2012	Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes	0.11
3	Scott IA等	2015	Reducing inappropriate polypharmacy: the process of deprescribing	0.11
4	Gallagher P等	2008	STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria	0.11
5	Garfinkel D等	2010	Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy	0.11
6	O'Mahony D等	2015	STOPP/START criteria for potentially inappropriate prescribing in older people; version 2	0.10
7	Gnjidic D等	2012	High-risk prescribing and incidence of frailty among older community-dwelling men	0.10
8	Hilmer SN等	2009	The effects of polypharmacy in older adults	0.10
9	Barnett K等	2012	Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study	0.09
10	Gallagher PF等	2011	Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria	0.09

通过对热门关键词进行分析,可以推测老年多重用药的危险因素、健康结局(包括衰弱、住院、死亡)以及对多重用药的减少策略是目前研究的热点^[25-29]。

2.7.2 聚类分析 利用CiteSpace 5.6.R5软件对关键词

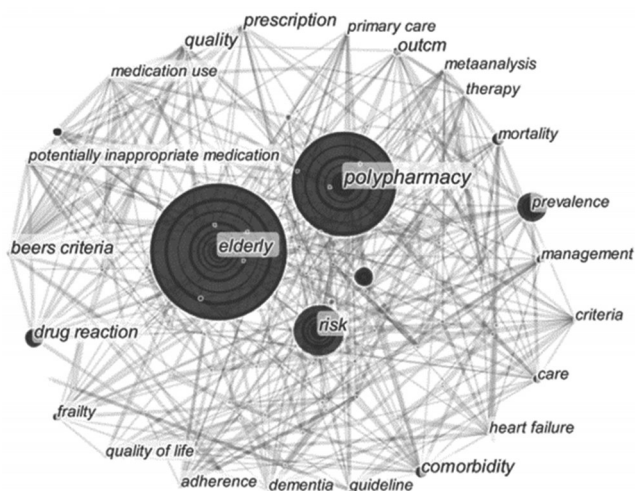


图5 关键词共现网络关系图谱

Fig 5 Relation graph of keywords co-occurrence network

进行聚类分析,通过对数拟然率算法(LLR)聚类方式命名,生成聚类图谱,详见图6。图谱中Modularity Q表示网络的模块度(Q值),取值范围为0~1(取值越接近1,即聚类间的联系越紧密,聚类结果越好;Q>0.3表明网络聚类结构是显著的^[9]);图谱中Silhouette表示轮廓值(S值),是衡量网络同质性的指标,取值范围为-1~1(取值越接近1,表示聚类内节点间的联系越紧密,同质性相对越好,聚类结果可信度越高;S>0.7表明聚类效果是令人信服的^[7])。结果得到6个关键词聚类群标签,聚类的Q=0.375 7>0.3, S=0.699 2>0.5,说明网络模块结构较为显著,聚类效果良好,同质性较好^[7-9]。对每一聚类的关键词按频次从高到低排序,其聚类及包含的关键词见表4。

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 June 16, 2020 3:19:07 PM CST
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 Timespan: 2010-2019 (Slice Length=1)
 Selection Criteria: Top 50 per slice, LRF=3.0, LBY=8, e=2.0
 Network: N=114, E=435 (Density=0.0675)
 Largest CC: 114 (100%)
 Nodes Labeled: 1.0%
 Pruning: Pathfinder
 Modularity Q=0.3757
 Mean Silhouette=0.6992

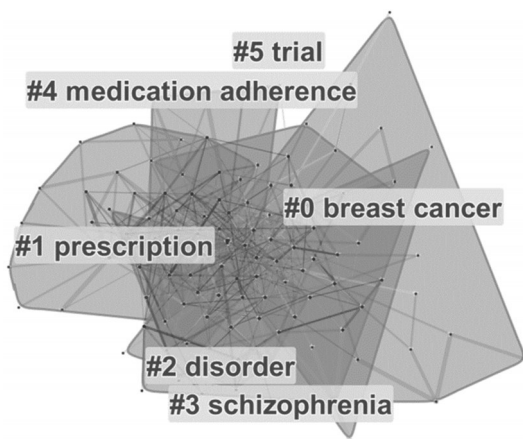


图6 关键词聚类图谱

Fig 6 Clustering graph of keywords

表4 关键词聚类及其包含关键词

Tab 4 Keyword clustering and its keywords

聚类序号	S	聚类名称	关键词
0	0.754	Breast cancer	Risk, Mortality, Management, Health, Frailty, Fall, Quality of life, Association, Meta Analysis, Older等
1	0.61	Prescription	Drug reaction, Prescription, Beers criteria, Potentially, Inappropriate medication, Quality, Hospitalization, Medicine, Event, Inappropriate Prescribing, Screening tool等
2	0.824	Disorder	Elderly, Polypharmacy, Prevalence, Comorbidity, Care, Population, Dementia, Medication use, Impact, Disease等
3	0.666	Schizophrenia	Double blind, Drug use, Alzheimers disease, Geriatrics schizophrenia, Safety, Efficacy, Antipsychotics, Nursing home, Pattern等
4	0.586	Medication adherence	Outcome, Therapy, Adherence, Drug interaction, Validation, Predictor, Cohort, HIV, Medication adherence, Cost等
5	0.755	Trail	Primary care, Criteria, Intervention, Randomized Controlled trial, Guideline, Pharmacist, Pharmacokinetics, Trial, Morbidity等

本研究共得到6个聚类群,分别为Breast cancer、Prescription、Disorder、Schizophrenia、Medication adherence、Trial对其推测分析后认为,目前,多重用药的发病率较高,由于药物间的相互作用以及潜在不适当用药等,加之患者服药依从性较低,导致住院时间长、跌倒、再入院等不良事件的发生,影响了患者的生活质量;药师参与干预的方法主要是通过Beers标准以及STOPP/START标准减少潜在不适当用药。

2.7.3 Burst分析 对关键词出现的时间分布和动态变化性的特点分析可反映老年多重用药的研究前沿和发展趋势^[25]。采用CiteSpace 5.6.R5对近10年老年多重用药研究的关键词进行Burst分析,根据突现时间进行排序,结果显示,该领域研究前沿是并发症、痛苦、老年衰弱、健康相关质量、认知障碍。近10年关键词Burst时间排序见图7。

由图7可以推测,未来该领域可能会集中探讨如多重用药对老年患者心理、疾病并发症、认知功能的影响,对老年多重用药患者与衰弱以及生活质量的相关性研究等。

3 讨论

本文运用CiteSpace 5.6.R5软件对老年多重用药领域近10年的研究文献进行计量学可视化分析,可以比较直观地看出老年多重用药的研究现状、热点及趋势。近10年老年多重用药的研究数量逐年增加,研究热度持续上升。美国以及澳大利亚在该领域的贡献巨大,美国的发文量最多、中心度最高,澳大利亚的多个机构的发文量处于前10位。老年多重用药的研究主要集中在多重用药对健康结局的影响以及减少多重用药的策略上;未来可能会更多地关注于老年多重用药对心理、认知、衰弱的相关研究。

Keywords	Year	Strength	Begin	End	2010 - 2019
adverse drug reaction	2010	6.677	2010	2013	=====
event	2010	4.5871	2010	2014	=====
schizophrenia	2010	6.8132	2010	2012	=====
inappropriate medication use	2010	10.4037	2010	2012	=====
nursing home resident	2010	5.8201	2010	2012	=====
older person	2010	4.7628	2010	2016	=====
geriatric medicine society	2010	4.4619	2010	2014	=====
j geriatr pharmacother	2010	7.6	2010	2012	=====
stopp screening tool	2010	7.1868	2010	2014	=====
beers criteria	2010	8.7363	2010	2012	=====
hospitalized patient	2010	5.5345	2010	2014	=====
consensus panel	2010	8.4261	2010	2014	=====
europa union	2010	3.743	2010	2014	=====
admission	2010	6.3288	2010	2012	=====
double blind	2010	4.8022	2010	2014	=====
disorder	2010	6.6281	2010	2013	=====
cost	2010	5.7334	2010	2013	=====
women	2010	6.1677	2010	2014	=====
depression	2010	5.4771	2010	2012	=====
nursing home	2010	4.134	2010	2013	=====
antipsychotic medication	2010	4.0796	2010	2012	=====
elderly individual	2010	5.3228	2011	2014	=====
high number	2010	4.3926	2011	2015	=====
elderly people	2010	6.0498	2011	2013	=====
coronary heart disease	2010	4.7157	2011	2014	=====
explicit criteria	2010	7.5437	2011	2014	=====
osteoporosis	2010	4.6649	2012	2014	=====
efficacy	2010	3.6943	2012	2014	=====
physical function	2010	3.709	2012	2015	=====
anticholinergic drug	2010	6.5251	2012	2015	=====
risperidone	2010	5.1834	2012	2014	=====
independent predictor	2010	5.3477	2013	2017	=====
elderly person	2010	6.1617	2013	2015	=====
injury	2010	5.9561	2013	2015	=====
medical condition	2010	4.5105	2013	2016	=====
physician	2010	4.8192	2014	2017	=====
social support	2010	4.1882	2014	2016	=====
advanced age	2010	4.3898	2014	2016	=====
stopp criterion	2010	3.8798	2014	2017	=====
anticholinergic burden	2010	3.8606	2015	2017	=====
complication	2010	3.7787	2015	2019	=====
validity	2010	4.8263	2015	2017	=====
oncology	2010	6.1142	2015	2017	=====
pain	2010	3.9242	2015	2019	=====
medication list	2010	5.4702	2015	2017	=====
surgery	2010	5.4702	2015	2017	=====
frail elderly	2010	5.72	2016	2019	=====
health-related quality	2010	4.3463	2016	2019	=====
intellectual disability	2010	3.6596	2016	2019	=====

图7 近10年关键词Burst时间排序

Fig 7 Ranking of keywords Burst time in recent 10 years

既往研究显示,老年多重用药的发生率在10%~90%之间^[26],老年人健康状况不佳是多重用药的主要原因^[27],所有的慢性疾病和阻塞性肺部疾病、抑郁、哮喘、疼痛与多重用药密切相关^[28-29],多重用药还会引起不良的健康结局,如衰弱、跌倒、住院和死亡^[26]。为了改善多重用药的现状,出现了相应的评估工具,主要用于检测老年人不适当用药,包括药物适宜性指数(MAI)、Beers标准、STOPP/START标准^[30]。美国老年医学会(AGS)制定的Beers标准在1991年发布了首版,然后分别于2003、2012、2015年进行更新;爱尔兰的STOPP/START标准于2008年发布首版,于2014年更新至第2版,其中包括PIMs(STOPP标准)和PPOs(START标准)。这些

评估工具对于一般或者身患疾病/综合症的老年人的不适当药物应用起到了监督作用,同时降低了不良事件的发生率^[31]。

相对于国外,我国对于老年多重用药的研究起步较晚。我国学者多采用Beers标准或者STOPP/START标准或者两种方式相结合的方法对潜在不适当用药进行筛选,但这两个标准是基于欧美医药市场、西方患者的用药特点提出,其中许多药物在我国应用很少,不完全适于中国人群^[32]。针对我国国情研发的《中国老年人潜在不适当用药判断标准》虽然涵盖的药物比较广泛,但未涉及药物相互作用警示,没有给出具体的防范措施或替代治疗方案,临床应用可操作性稍欠佳,且未提及国内处方量巨大的中成药的潜在不适当使用^[32]。因此,我国学者需要加强国内以及国际间的交流与合作,更深入地研究与探讨本国老年多重用药领域的发展及目标,探讨出较为完善的适合我国国情的筛选老年多重用药时潜在不适当用药的标准。

本文的亮点包括:(1)本研究是第一次基于2010—2019年发表的文献并通过文献计量学方法评估老年多重用药趋势的报道;(2)选用Web of Science数据库,该数据库文献质量较高,分析的文献涵盖了老年多重用药领域高质量的研究,因此分析结果较为可靠,能为老年多重用药领域学者如何开展下一步的研究提供可靠的依据。但本文仅纳入了英文文献,未对国内相关文献进行系统检索,缺乏对国内外相关研究进展的对比。

综上所述,近10年来,老年多重用药的研究日趋受到学者的重视,美国以及澳大利亚在该领域的贡献较大,老年多重用药的研究主要集中在多重用药对健康结局的影响以及减少多重用药的策略上;未来可能会更多地关注于老年多重用药对心理、认知、衰弱的相关研究。我国学者应加强国内以及国际间的交流与合作,探讨出较为完善的适合我国国情老年多重用药的筛选潜在不适当用药的标准。

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