·临床研究·

老年患者多重用药处方精简干预临床效果的 Meta 分析

李晨[1],林欣[2],陈孟莉[1*]
([1]解放军总医院药学部南楼药房,[2]解放军总医院国家老年疾病临床医学研究中心,北京 100853)

【摘 要】 目的 系统评价处方精简干预对老年多重用药患者临床结局的影响。**方法** 检索数据库公开发表有关老年多重用药患者处方精简干预及相关结局的文献。根据纳入排除标准进行筛选,采用 Review Manager 5.3 软件,利用 I^2 衡量文献研究内容的异质性,运用固定效应模型或随机效应模型合并分析处方精简干预对老年多重用药患者临床结局的影响。**结果** 本研究最终纳入 18 篇随机对照研究(RCT),文献总体质量较好。Meta 分析显示,处方精简干预不能降低老年多重用药患者全因死亡率[*OR*=0.86, 95%*CI*(0.67~1.09)]。不同干预方式比较:特异性处方精简干预在一定程度上降低全因死亡率[*OR*=0.68, 95%*CI*(0.51~0.92);*P*<0.05]。随访时间长短比较:随访时间较长(>6 个月)相较于随访时间较短(≤6 个月)的处方精简干预在降低全因死亡率方面具有一定优势[*OR*=0.58, 95%*CI*(0.39~0.86) *vs* *OR*=1.02, 95%*CI*(0.76~1.36); *P*<0.05]。不同年龄段比较:对不同年龄段患者进行精简干预,全因死亡率没有变化[*OR*=0.63, 95%*CI*(0.40~1.02) *vs* *OR*=0.95, 95%*CI*(0.72~1.25);*P*>0.05]。认知状态比较:对不同认知状态患者进行精简干预,全因死亡率不发生改变[*OR*=0.63, 95%*CI*(0.37~1.07) *vs* *OR*=0.93, 95%*CI* (0.71~1.22);*P*>0.05]。处方精简干预不能减少跌倒患者的数量[*OR*=0.98, 95%*CI*(0.74~1.27)],但可以显著降低年人均跌倒次数[*MD*=-0.11, 95%*CI*(-0.21~-0.02)],缩短患者住院时长[*MD*=-0.49, 95%*CI*(-0.76~-0.22)]。**结论** 现有数据分析表明,处方精简干预不能降低老年多重用药患者的全因死亡率,特异性或长时间随访的处方精简干预在降低患者全因死亡率方面有一定优势;处方精简干预不能减少跌倒患者人数但可以减少患者跌倒次数;处方精简干预有缩短住院时长的趋势。特异性处方精简干预在减少不适当的多重用药方面是安全可行的。

【关键词】 老年人;多重用药;处方精简;Meta 分析
【中图分类号】 R969.3 **【文献标志码】** A **【DOI】** 10.11915/j.issn.1671-5403.2019.03.032

Impact of deprescribing interventions on clinical outcomes in the elderly patients: a Meta-analysis

LI Chen[1], LIN Xin[2], CHEN Meng-Li[1*]
([1]South Building Pharmacy, Department of Pharmacy, [2]National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing 100853, China)

【Abstract】 Objective To perform a systematic review to evaluate the impact of deprescribing interventions on the clinical outcomes in the elderly patients with polypharmacy. **Methods** A thorough search was made in the databases of the literature related to deprescribing interventions in the elderly patients with polypharmacy. The studies were screened according to the inclusion and the exclusion criteria. I^2 test for heterogeneity among studies was performed using Review Manager 5.3. Fixed effect model or random effect model was employed to analyze the impact of deprescribing interventions in the elderly patients with polypharmacy. **Results** A total of 18 studies were selected for the final randomized controlled trials (RCT), with overall quality of the literature being good. Meta-analysis showed that deprescribing interventions were not able to decrease all-cause mortality among elderly patients with polypharmacy [*OR*=0.86, 95%*CI* (0.67-1.09)]. The comparison between different intervention methods showed that patient-specific interventions decreased all-cause mortality [*OR*=0.68, 95%*CI* (0.51-0.92)]. The comparison of the follow-up length showed that long follow-up (>6 months) outperformed shorter follow-up (≤6 months) in decreasing all-cause mortality [*OR*=0.58, 95%*CI* (0.39-0.86) *vs* *OR*=1.02, 95%*CI* (0.76-1.36); *P*<0.05]. The comparison between different age groups showed no change in all-cause mortality [*OR*=0.63, 95% *CI* (0.40-1.02) *vs* *OR*=0.95, 95%*CI* (0.72-1.25); *P*>0.05]. The comparison of cognitive status showed that deprescribing interventions in the groups of different cognitive statuses did not alter all-cause mortality [*OR*=0.63, 95%*CI* (0.37-1.07) *vs* *OR*=0.93, 95%*CI* (0.71-1.22); *P*>0.05]. Deprescribing interventions did not decrease the number of patients with falls [*OR*=0.98, 95%*CI* (0.74-1.27)] but were able to significantly decrease the average falls they experienced [*MD*=-0.11,

收稿日期:2018-12-05;**接受日期**:2019-01-28
基金项目:军队保健课题面上项目(16BJZ20)
通信作者:陈孟莉,E-mail:hellolily301cn@126.com

95%*CI* (−0.21−−0.02)] and the length of hospital stay [*MD*=−0.49, 95%*CI* (−0.76−−0.22)]. **Conclusion** The analysis of data available suggested that deprescribing interventions did not decrease all-cause mortality in elderly patients with polypharmacy, but patient-specific or long-term follow-up seemed to have an advantage in decreasing it; that deprescribing interventions did not decrease the number of patients with falls but reduced the number of falls they experienced and the length of hospital stay. Patient-specific deprescribing interventions seem to be safe and feasible in decreasing inappropriate polypharmacy.

【Key words】 aged; polypharmacy; deprescribing; meta-analysis

This work was supported by General Program of Military Health Care (16BJZ20).

Corresponding author: CHEN Meng-Li, E-mail: hellolily301cn@126.com

老年患者多病共存现象较为普遍,≥65 岁老年患者中约一半有≥3 种疾病共存,1/5 的患者存在≥5 种疾病,这意味着大多数老年患者每天用药数目远远≥3 种。适当的多重用药[1]可以改善患者症状,延缓疾病进展,而不适当的多重用药常会引起药物间相互作用、不良事件发生,据统计有约 17%老年患者入院是由药物不良反应导致的[2]。

“处方精简”一词于 2003 年被澳大利亚的 Woodward 首次提及[3],并定义为:在医疗保健人员或团队的监督下,重新评估使用该药物的原因及有效性,逐渐减少、撤回或停止可能导致患者损害或患者不再受益的药物,以期减少不适当的多重用药、降低药物不良事件的过程[4]。2013 年英国国家卫生服务体系(National Health Service, NHS)发布第一部多重用药指南,在 2015 年进行更新并提出[4]:通过对目标药物进行处方精简干预获得用药优化是管理慢性疾病、避免或减少不良反应和改善结局的重要部分。2017 年加拿大发表有关处方精简的指南主要涉及质子泵抑制剂药物、苯二氮䓬类药物、抗精神病药物和降血糖药物[5]。

Cooper 等[7]对老年患者使用特定类别药物进行处方精简的研究进行系统综述,概括总结目前处方精简具体的目标药物类别; 2018 年 Thillainadesan 等[8]分析处方精简干预对老年住院患者用药及临床结局的影响,结局指标主要涉及潜在不适当用药数目及用药相关问题分析。目前相关研究均未从临床较为直观的结局指标如全因死亡率、不良反应事件发生率等方面表明处方精简干预措施的临床可行性及益处。笔者将通过荟萃分析方法评价处方精简干预对老年多重用药患者临床结局的影响。

1 对象与方法

1.1 检索策略

本次文献检索范围为建库(1990 年)至 2018 年 2 月,收集已发表的处方精简干预对老年多重用药患者临床结局的中英文文献。通过在 Pubmed、Web of Science(SCI)、Embase、The Cochrane Library、中国知网(CNKI)、万方(WanFang)数据库中使用主题词检索文献。检索主题词包括:(1)“elderly” or “aged” or “the aged” or “geriatric” or “older” or “aging” or “veteran” or “older adult”;(2)“polypharmacy” or “≥3 种药物” or “drug” or “medication” or “prescri*”;(3)“deprescrib*” or “reduc*” or “stop*” or“withdraw*” or “cessation” or “ceas*” or “discontinu*”;(4)文章类型选择 Clinical Trial, Controlled Clinical Trial, Multicenter Study, Pragmatic Clinical Trial, Randomized Controlled Trial (RCT); (5) 1 and 2 and 3 and 4。由 2 位研究者独立对检索文献的标题和摘要进行审查,按照纳入排除标准进行筛选,并排除重复数据和文献,如有分歧,进行讨论。纳入标准:(1)研究对象年龄≥65 岁,用药种类数≥3 种,如果纳入人群绝大多数用药种类中位数≥3 种,该研究也包含在内;(2)干预措施包括特异性处方精简及以教育为主处方精简,对照组干预为日常照护;(3)结局指标涉及全因死亡率、跌倒,住院时长、急诊访问率等其他临床指标;(4)研究类型为公开发表的随机对照实验。排除标准:(1)非 RCT 研究;(2)有关健康结局或生活质量相关指标未使用标准化量表进行描述;(3)除中文和英文外其他语种的相关文章。

1.2 数据提取

仔细阅读文献标题、摘要进行筛选,根据纳入排除标准阅读全文,确定文献是否入选,并对文章质量进行评价,最后进行资料提取。资料提取内容包括:标题、第一作者、文章类型、国家、干预类型、使用辅助工具、干预地点、随访时间、纳入人数、平均年龄、结局指标、具体见表 1。

1.3 文献质量评估方法

RCT 研究根据 Cochrane 协作网偏倚风险评价工具进行偏倚评估,主要包括 6 个方面,即随机分配方法、分配方案隐藏、盲法、结果数据的完整性、选择性报告研究结果、其他偏倚来源,具体见图 1。

1.4 统计学处理

采用 Review Manager 5.3 软件进行 Meta 分析。

表1 老年多重用药患者处方精简干预纳入随机对照试验基本特征

Table 1 Characteristics of included randomized controlled trials about deprescribing polypharmacy (≥ 3 drugs or drug classes)

Reference	Intervention type	Tool to identify targets	Country	Setting
Hanlon 1996[9]	Pharmacist led (patient-specific)	MAI	USA	Community
Tabloski 1998[10]	Doctor led(patient-specific)	Pre-specified list of target medications	USA	Community
Campbell 1999[11]	Doctor led (patient-specific)	Benzodiazepine, hypnotic or antidepressant	New Zealand	Community
Allard 2001[12]	Multidisciplinary (patient-specific)	List of potentially inappropriate medications	Canada	Community
Weber 2008[13]	Multidisciplinary (patient-specific)	No identification method tool specified	USA	Community
Gnjidic 2010[14]	Multidisciplinary (patient-specific)	DBI	Australia	Community
Beer 2011[15]	Doctor led (patient-specific)	Pre-specified list of target medications	Australia	Residential care
Gallagher 2011[16]	Doctor led(patient-specific)	STOPP	Ireland	Hospital
Dalleur 2014[17]	Multidisciplinary (patient-specific)	STOPP	Belgium	Hospital
Gollarte 2014[18]	Education to nursing home physicians	STOPP	Spain	Residential care
Pitkala 2014[19]	Education to nursing home physicians	Beer	Finland	Residential care
Tannenbaum 2014[20]	Education to community	Benzodiazepine use	Canada	Community
Potter 2016[21]	Doctor led (patient-specific)	Modified Good Palliation-Good Practice tool	Australia	Residential care
Wehling 2016[22]	Doctor led(patient-specific)	FORTA-guided treatment	Germany	Hospital
Boyé 2017[23]	Doctor led(patient-specific)	Pre-specified list of target medications (complete list of FRIDs)	Netherlands	Community
Polinder 2016[24]	Doctor led(patient-specific)	Pre-specified list of target medications (complete list of FRIDs)	Netherlands	Community
Wouters 2017[25]	Nurse led (patient-specific)	START, Beer	Netherlands	Residential care
Pazan 2018[26]	Doctor led(patient-specific)	FORTA-guided treatment	Germany	Hospital

Reference	Follow-up duration (months)	Number of participants enrolled	Mean age (years)	Dementia	Outcome
Hanlon 1996[9]	12	207	≥65	No	MAI, SF-36, ADR, all-cause mortality
Tabloski 1998[10]	1.25	20	77.5	No	Sleep complaints, time in bed (min), sleep latency (min), total sleep time (min), sleep period (min), sleep efficiency (score)
Campbell 1999[11]	10	93	74.6	No	Falls
Allard 2001[12]	12	503	80.4	No	Total number of PIM per person, mortality, change in the medications pre-intervention and post-intervention
Weber 2008[13]	15	620	76.9	Yes	Medication use, falls, percentage of participants who reported at least one fall, mortality
Gnjidic 2010[14]	3	115	80.4	No	DBI, prescribing change, mortality
Beer 2011[15]	3	44	81	Unclear	SF-36, EQ-5D, Sleep quality, MMSE, medication adherence, mortality
Gallagher 2011[16]	6	400	≥65	Yes	MAI, PIM, DBI, falls, hospital readmission, general practitioner visits, all cause mortality
Dalleur 2014[17]	12	158	≥65	Unclear	Proportion of PIM ceased between admission and discharge, mortality
Gollarte 2014[18]	6	1 018	81.4	Yes	Falls, delirium, number of episodes, mortality, physician visits, ED visits
Pitkala 2014[19]	6	227	82.9	Yes	Number of hospitalizations, ambulatory service utilization, EQ-15D, mortality
Tannenbaum 2014[20]	6	303	75	No	Complete cessation of benzodiazepine use
Potter 2016[21]	6	95	84.3	Yes	Median number of regular medicine, cognitive function, IADL, falls, sleep quality, quality of life, mortality
Wehling 2016[22]	Unclear	409	84	Yes	ADR, falls, ADL
Boyé 2017[23]	12	612	76.4	No	Mortality, time to the first and second self-reported fall
Polinder 2016[24]	12	612	76.4	No	Fall-related healthcare costs, EQ-5D, SF-12, mortality
Wouters 2017[25]	4	46	83.2	Yes	Proportion of successfully discontinued after 4 months of follow-up, DBI, number of falls, visits to outpatient clinics, mortality, EQ-5D-3L, SIB-S, MMSE
Pazan 2018[26]	Unclear	409	83	Yes	Disease-related over- and under-treatments

MAI: medication appropriateness index; DBI: drug burden index; STOPP: screening tool of older person's prescriptions; FORTA: fit for the aged; FRIDs: fall-risk-increasing drugs; START: screening tool to alert right treatment; SF-36: short-form 36; ADR: adverse drug reactions; PIM: potentially inappropriate medication; EQ-5D: the Euro Qol-5D instrument; MMSE: mini-mental state examination; ED: Emergency Department; IADL: instrumental activity of daily living; ADL: activity of daily living; SIB-S: short form of severe impairment battery.

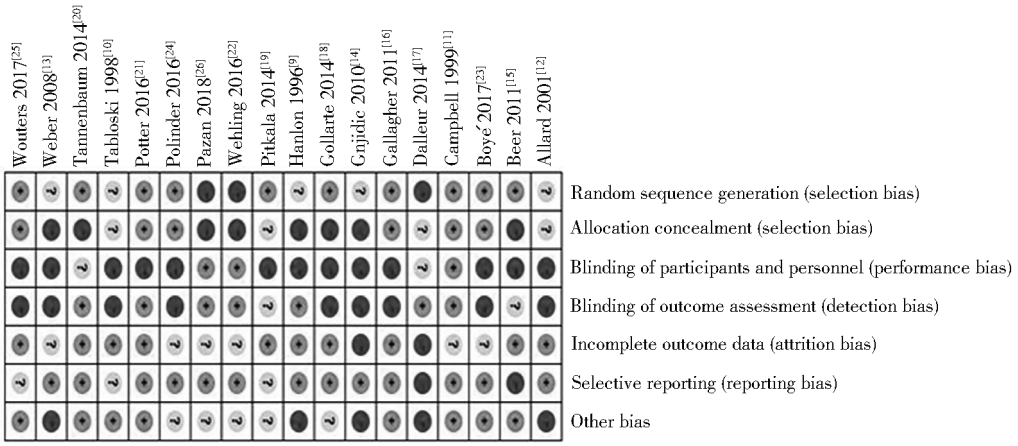

图 1 纳入随机对照研究偏倚分布

Figure 1 Bias assessment of enrolled studies

通过 I^2 来评估纳入研究的异质性;若研究之间具有较好的同质性,即 I^2<50%,采用固定效应模型进行合并分析;反之,采用随机效应模型进行合并分析。计算合并统计量 *OR* 值及 95%置信区间(95%*CI*)。

2 结 果

2.1 文献检索结果

本研究共检索得到文献 1 185 篇(PubMed 455 篇;Embase 509 篇;Cocharne 21 篇;SCI 200 篇;CNKI 0 篇;万方 0 篇),自动及手动去重后共 870 篇,通过阅读筛选最终纳入 18 篇 RCT 文献。

2.2 Meta 分析结果

2.2.1 全因死亡率 在已纳入的 18 篇 RCT 研究中,13 篇文章中研究结局包含全因死亡率[9,12-19,23-25],随访时间在 1.25~15 个月不等。在 13 篇文章中有 2 篇报道同一研究的不同临床结局[23,24]。2014 年 Pitkala 等[19]研究中是对病房进行随机分组而非单个患者进行随机分组,研究人群选择年老体弱患者导致流失较多,尚未进行干预,随机组和对照组死亡人数已有差异,在全因死亡率的分析中对结果造成显著差异,对该研究进行敏感性分析,发现剔除该研究后异质性降低较多,故将此研究从全因死亡率分析中剔除,偏倚见图 2。

对纳入的 11 篇文章进行异质性检验,I^2=18%,采用固定效应模型进行 meta 分析,共涉及 3 961 名患者(干预组,*n*=2 108),为减少结局偏倚,全因死亡率采用意向性分析(Intention-To-Treat,ITT),基于目前纳入数据表明:处方精简不能改善多重用药老年患者的全因死亡率[*OR*=0.86(0.67,1.09)]。

2.2.1.1 随访时间不同全因死亡率比较 根据随访时间不同汇总 11 篇 RCT 研究中全因死亡率,对

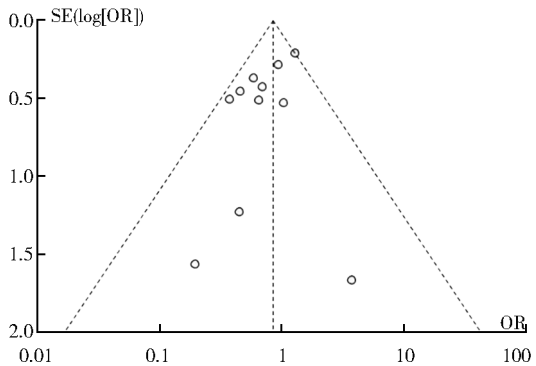

图 2 全因死亡率的漏斗图

Figure 2 Funnel plot of all-cause mortality

随访时间较长(>6 个月)、随访时间较短(≤6 个月)全因死亡率异质性分析显示 I^2 值分别为 0%和 10%,故选用固定效应模型分析全因死亡率,结果发现随访时间较长(>6 个月)的处方精简干预对降低患者全因死亡率有一定优势[*OR*=0.58,95%*CI*(0.39~0.86);6 篇 RCT,*n*=1 959],而随访时间较短(≤6 个月)的处方精简过程并未改变患者全因死亡率[*OR*=1.02,95%*CI*(0.76~1.36);6 篇 RCT,*n*=2 097]。图 3 为不同随访时间处方精简干预全因死亡率的森林图。

2.2.1.2 特异性干预全因死亡率分析 仅有一篇 RCT 研究采用教育干预方式,其余 10 篇均为特异性干预。汇总特异性干预全因死亡率相关数据,异质性分析显示 I^2=0%,故选用固定效应模型。结果显示特异性处方精简干预方式可以降低患者全因死亡率[*OR*=0.68,95%*CI*(0.51~0.92);10 篇 RCT,*n*=2 997],图 4 为特异性精简干预对全因死亡率的森林图。

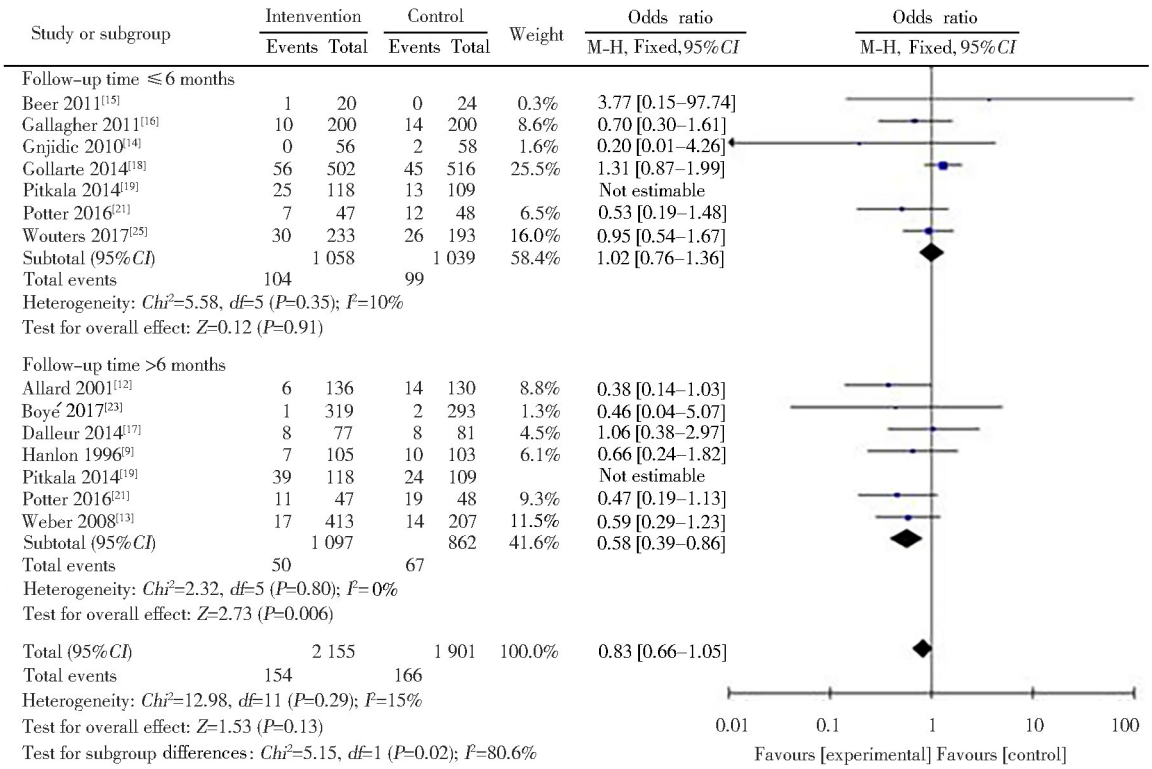

图3 基于随访时间进行处方精简干预对多重用药老年患者死亡率的亚组分析(随机对照研究)

Figure 3 Mortality associated with deprescribing interventions to reduce polypharmacy for subgroup analysis based on following-up time (randomized controlled trials)

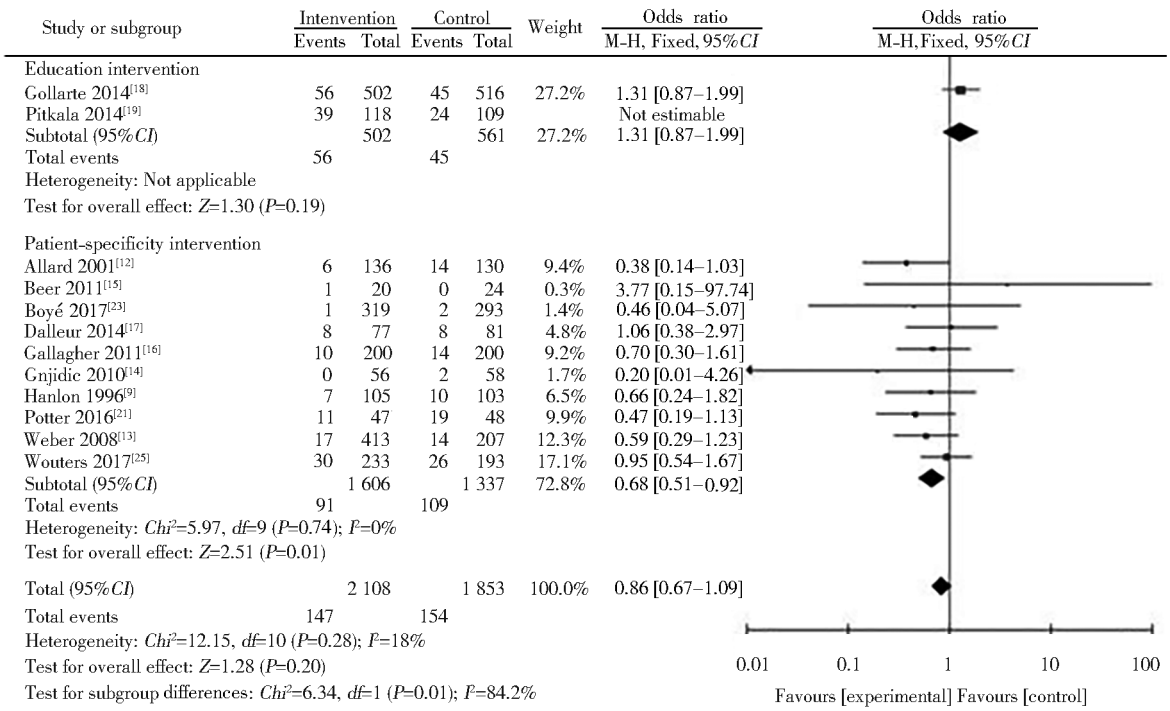

图4 基于干预方式不同进行处方精简干预对多重用药老年患者死亡率的亚组分析(随机对照研究)

Figure 4 Mortality associated with deprescribing interventions to reduce polypharmacy for subgroup analysis based on intervention method (randomized controlled trials)

2.2.1.3 不同年龄段全因死亡率比较 对≥80 岁及< 80 岁 2 个年龄段全因死亡率的异质性分析发现，I^2 值分别为 39%和 0%，选用固定效应模型分析死亡率，结果表明对不同年龄段患者进行处方精简干预不影响全因死亡率[*OR* = 0.63, 95% *CI* (0.40~1.02) *vs* *OR*=0.95, 95%*CI*(0.72~1.25)]。

2.2.1.4 不同认知状态全因死亡率比较 汇总不同认知状态对全因死亡率影响数据，对认知完好及认知障碍患者全因死亡率异质性分析显示 I^2 分别为 0%和 42%，差异无统计学意义(P>0.05)，选用固定效应模型，结果显示处方精简干预对不同认知状态患者的全因死亡率无显著性影响[*OR* = 0.63, 95% *CI* (0.37~1.07) *vs* *OR*=0.93, 95%*CI* (0.71~1.22)]。

2.2.2 跌倒 汇总有关处方精简干预后跌倒人数及年人均跌倒次数的数据，异质性分析显示 I^2 分别为 0%和 8%，采用固定效应模型分析显示处方精简不能减少跌倒人数(*OR*=0.98, 95%*CI* (0.74~1.27)；4 篇 RCT；n = 1 614)，但可以降低年人均跌倒次数(mean difference, MD)[*MD* = −0.11, 95% *CI* (−0.21~−0.02)，3 篇 RCT，n=844]。森林图见图 5。

2.2.3 住院时长 在 18 篇 RCT 中有 3 篇以住院时长作为结局指标，异质性分析显示 I^2 = 65%，有较高异质性，采用随机效应模型分析。结果显示处方精简干预可以缩短老年多重用药患者住院时长[*MD*=−0.49, 95%*CI*(−0.76~−0.22)，n = 1 325]，森林图见图 6。

3 讨 论

处方精简作为一种新兴药学服务尚未被国内医务人员所熟悉[27]。2016 年 NHS 向医疗保健工作者推行“PrescQIPP 多重用药和处方优化”程序并进行调查，结果显示医护人员对多重用药定期评估产生的获益表示认同，但只有 41%的医疗保健人员对处方精简干预行为进行积极回应，主要是因为该干预对医护人员或团队要求较高，且临床支持证据不充分[4]。本文是国内首次系统描述处方精简干预对老年多重用药患者临床结局的影响。

目前纳入研究尚未显示精简干预降低全因死亡率这一临床优势，但在亚组分析中发现，特异性或长时间随访的精简干预在降低死亡率方面有一定优势，提示处方精简可能需要较长的随访时间或处方精简是个长久获益的过程。另一方面，随访时间的长短可能与患者依从性相关，尤其是对苯二氮䓬类或其他抗精神病药物进行精简干预时，随访时间较长，患者依从性较好。在进行特殊类别药物精简时应注意随访时间长短的重要性。根据干预方式不同进行亚组分析时，教育干预涉及 RCT 较少，尚不能表明特异性处方精简干预较教育干预在降低死亡率方面有优势，需更多 RCT 进行验证。以上证据均表明处方精简是一种安全可行的干预措施，这与之前有关处方精简干预的临床研究得到结论相似[8]。

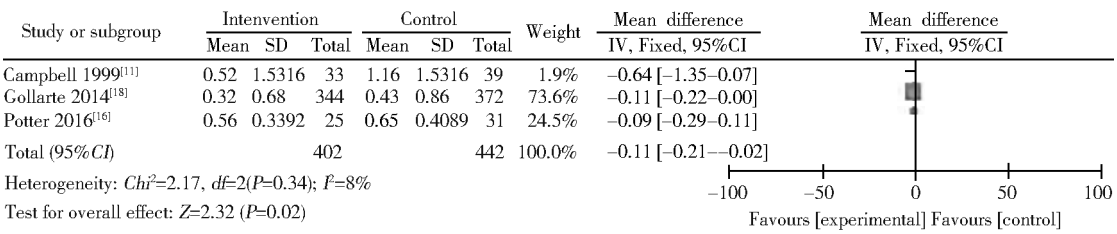

图 5 处方精简干预对多重用药老年患者人均年跌倒次数的影响(随机对照研究)

Figure 5 Impact on frequency of falls with deprescribing interventions to reduce polypharmacy (randomized controlled trial)

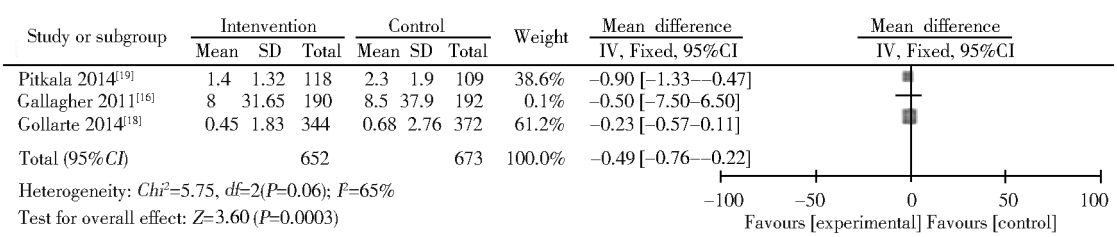

图 6 处方精简干预对多重用药老年患者住院时长的影响(随机对照研究)

Figure 6 Impact on length of hospital stay with deprescribing interventions to reduce polypharmacy (randomized controlled trial)

目前已有流行病学和动物学证据表明多重用药与高龄状态较差的健康结局相关[28,29]，但从目前纳入研究的荟萃分析结果表明，高龄老年患者药物精简未能改变全因死亡率。若仅从 *OR* 值分析，<80岁老年患者相较高龄患者精简干预降低全因死亡率的趋势更明显，可能表明处方精简敏感性受年龄周期的限制；认知完好较认知障碍患者在降低全因死亡率方面似乎更有优势，以上两方面均需进一步研究。选择适宜年龄段及认知状态的老年患者，采用特异性干预方式、适宜的随访时间等均可能是精简干预取得临床获益的因素。

处方精简干预要求每次只精简一种药物，且精简的目标药物不影响治疗用药临床结局，这也是处方精简干预临床获益不明确的重要原因。例如对高龄患者使用的预防用药进行精简，患者的健康结局尤其是全因死亡率几乎不受影响，这与之前对特定类别药物进行处方精简的系统分析结果一致，所以仅从临床结局分析，可能会削弱处方精简干预的优势。

在纳入的18篇RCT中有6篇是对易致跌倒药物进行精简研究[11,13,16,18,21-23]，荟萃分析结果表明处方精简不能减少跌倒人数，但可降低老年患者年人均跌倒次数，这和Iyer等研究得到的结论是一致的，对中枢神经系统药物如镇静药物、抗抑郁药、胆碱酯酶抑制剂和抗精神病药物等进行干预并长期随访，结果显示抗精神病药物干预在降低老年患者跌倒次数、提高认知功能方面具有一定优势[30]。处方精简干预RCT研究中有3篇结局涉及患者的住院时长，分析结果表明处方精简干预可以缩短患者住院时长，但文章间的异质性较大，需谨慎解读[16,18,19]。

处方精简一词广泛使用较迟，因此在检索时需要扩大检索范围。本文纳入的研究中，较多研究旨在评估处方精简干预的可行性而不是对健康相关结局指标或临床结局的影响，导致结局指标较多且散，难以进行定量分析。患者的健康状况、干预地点、随访时间的不确定性均会对结局产生偏倚影响，因此得到的荟萃分析结果需谨慎解读。从检索结果可以看到近年有关处方精简的RCT研究越来越多，大家越来越关注处方精简这一药学干预手段，但上述局限性很难在目前的研究中得到获得最佳临床受益的目标人群，仍需更高质量、更严谨的RCT进行验证。

综上，目前证据表明特异性处方精简干预或较长随访时间的处方精简干预过程可能会延长患者寿命。有限的证据表明，处方精简干预不能减少跌倒患者人数，但可以减少患者年跌倒次数，缩短住院时长。尽管仍需要更多的RCT研究，但目前证据表明通过处方精简干预减少不适当的多重用药是安全可行的。

【参考文献】

[1] Mangin D, Heath I, Jamoulle M, *et al*. Beyond diagnosis: rising to the multimorbidity challenge[J]. BMJ, 2012, 344: e3526. DOI: 10.1136/bmj.e3526.

[2] Tangiisuran B, Wright J, Van der Cammen T, *et al*. Adverse drug reactions in elderly: challenges in identification and improving preventative strategies[J]. Age Ageing, 2009, 38(4): 358-359. DOI: 10.1093/ageing/afp050.

[3] Woodward M. Deprescribing: achieving better health outcomes for older people through reducing medications[J]. J Pharm Pract Res, 2003, 33(4): 323-328. DOI:10.1002/jppr2003334323.

[4] The PrescQIPP Polypharmacy and Deprescribing webkit. 2016, PrescQIPP. https://www.prescqipp.info/projects/polypharmacy-and-deprescribing.

[5] Farrell B. Deprescribing Guidelines and Algorithms[EB]. [2016-10-23], http://deprescribing.org/resource/deprescribing-guidelines and algorithms.

[6] Rodríguez-Pérez A, Alfaro-Lara ER, Albiñana-Perez S, *et al*. Novel tool for deprescribing in chronic patients with multimorbidity: List of Evidence-Based Deprescribing for Chronic Patients criteria[J]. Geriatr Gerontol Int, 2017, 17(11): 2200-2207. DOI: 10.1111/ggi.13062.

[7] Cooper JA, Cadogan CA, Patterson SM, *et al*. Interventions to improve the appropriate use of polypharmacy for older people: a cochrane systematic review[J]. Br Med J, 2015, 5(12): e009235. DOI: 10.1136/bmjopen-2015-009235.

[8] Thillainadesan J, Gnjidic D, Green S, *et al*. Impact of deprescribing interventions in older hospitalised patients on prescribing and clinical outcomes: a systematic review of randomised trials[J]. Drugs Aging, 2018, 35(4): 303-319. DOI: 10.1007/s40266-018-0536-4.

[9] Hanlon JT, Weinberger M, Samsa GP, *et al*. A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy[J]. Am J Med, 1996, 100(4): 429-437. DOI: 10.1016/S0002-9343(97)89519-8.

[10] Tabloski PA, Cooke KM, Thoman EB, *et al*. A procedure for withdrawal of sleep medication in elderly women who have been long-term users[J]. J Gerontol Nurs, 1998, 24(9): 20-28.

[11] Campbell AJ, Robertson MC, Gardner MM, *et al*. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized controlled trial[J]. J Am Geriatr Soc, 1999, 47(7): 850-853. DOI: 10.1111/j.1532-5415.1999.tb03843.x.

[12] Allard J, Hébert R, Rioux M, *et al*. Efficacy of a clinical medication review on the number of potentially inappropriate prescriptions prescribed for community-dwelling elderly people[J]. CMAJ, 2001, 164(9): 1291-1296.

[13] Weber V, White A, McIlvried R, *et al*. An electronic medical record (EMR)-based intervention to reduce polypharmacy and

falls in an ambulatory rural elderly population[J]. J Gen Intern Med, 2008, 23(4): 399-404. DOI: 10.1007/s11 606-007-0482-z.

[14] Gnjidic D, Le Couteur DG, Abernethy DR, *et al*. A pilot randomized clinical trial utilizing the drug burden index to reduce exposure to anticholinergic and sedative medications in older people[J]. Ann Pharmacother, 2010, 44(11): 1725-1732. DOI: 10.1345/aph.1P310.

[15] Beer C, Loh PK, Peng YG, *et al*. A pilot randomized controlled trial of deprescribing[J]. Ther Adv Drug Saf, 2011, 2(2): 37-43. DOI: 10.1177/2042098611400332.

[16] Gallagher PF, O'Connor MN, O'Mahony D, *et al*. Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria[J]. Clin Pharmacol Ther, 2011, 89(6): 845-854. DOI: 10.1038/clpt.2011.44.

[17] Dalleur O, Boland B, Losseau C, *et al*. Reduction of potentially inappropriate medications using the STOPP criteria in frail older inpatients: a randomised controlled study[J]. Drugs Aging, 2014, 31(4): 291-298. DOI: 10.1007/s40266-014-0157-5.

[18] Gollarte FG, Júlvez JB, López IF, *et al*. An educational intervention on drug use in nursing homes improves health outcomes resource utilization and reduces inappropriate drug prescription[J]. J Am Med Dir Assoc, 2014, 15(12): 885-891. DOI: 10.1016/j.jamda.2014.04.010.

[19] Pitkala KH, Juola AL, Kautiainen H, *et al*. Education to reduce potentially harmful medication use among residents of assisted living facilities: a randomized controlled trial[J]. J Am Med Dir Assoc, 2014, 15(12): 892-898. DOI: 10.1016/j.jamda.2014.04.002.

[20] Tannenbaum C, Martin P, Tamblyn R, *et al*. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial[J]. JAMA Int Med, 2014, 174(6): 890-898. DOI: 10.1001/jamainternmed.2014.949.

[21] Potter K, Flicker L, Page A, *et al*. Deprescribing in frail older people: a randomised controlled trial[J]. PLoS One, 2016, 11(3): e0149984. DOI: 10.1371/journal.pone.0149984.

[22] Wehling M, Burkhardt H, Kuhn-Thiel A, *et al*. VALFORTA: a randomised trial to validate the FORTA (Fit fOR The Aged) classification[J]. Age Ageing, 2016, 45(2): 262-267. DOI: 10.109 3/ageing/afv200.

[23] Boyé ND, van der Velde N, de Vries OJ, *et al*. Effectiveness of medication withdrawal in older fallers: results from the Improving Medication Prescribing to reduce Risk Of FALLs (IMPROveFALL) trial[J]. Age Ageing, 2017, 46(1): 142-146. DOI: 10.1093/ageing/afw161.

[24] Polinder S, BoyéNicole D, Mattace-Raso FU, *et al*. Cost-utility of medication withdrawal in older fallers: results from the improving medication prescribing to reduce risk of FALLs (IMPROveFALL) trial[J]. BMC Geriatr, 2016, 16(1): 179-189. DOI: 10.1186/s12877-016-0354-7.

[25] Wouters H, Scheper J, Koning H, *et al*. Discontinuing inappropriate medication use in nursing home residents: a cluster randomized controlled trial[J]. Ann Intern Med, 2017, 167(9): 609-617. DOI: 10.7326/M16-2729.

[26] Pazan F, Burkhardt H, Frohnhofen H, *et al*. Changes in prescription patterns in older hospitalized patients: the impact of FORTA on disease-related over- and under-treatments[J]. Eur J Clin Pharmacol, 2018, 74(3): 339-347. DOI: 10.1007/s00228-017-2383-3.

[27] 曾英彤, 杨敏, 伍俊妍, 等. 药学服务新模式——处方精简(Deprescribing)[J]. 今日药学, 2017, 27(6): 390-393. DOI: 10.12048/j.issn.1674-229X.2017.06.008.
Zeng YT, Yang M, Wu JY, *et al*. A new model of pharmaceutical services — Deprescribing[J]. Pharmacy Today, 2017, 27(6): 339-347. DOI: 10.1007/s00228-017-2383-3.

[28] Turner JP, Jamsen KM, Shakib S, *et al*. Polypharmacy cut-points in older people with cancer: how many medications are too many[J]. Support Care Cancer, 2016, 24(4): 1831-1840. DOI: 10.1007/s00520-015-2970-8.

[29] Huizer-Pajkos A, Kane AE, Howlett SE, *et al*. Adverse geriatric outcomes secondary to polypharmacy in a mouse model: the influence of aging[J]. J Gerontol A Biol Sci Med Sci, 2016, 71(5): 5771-5777. DOI: 10.1093/gerona/glv046.

[30] Iyer S, Naganathan V, McLachlan AJ, *et al*. Medication withdrawal trials in people aged 65 years and older[J]. Drugs Aging, 2008, 25(12): 1021-1031. DOI: 10.2165/0002512-200825120-00004.

(编辑: 门可)