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Figure A1. Flow chart describing the literature search

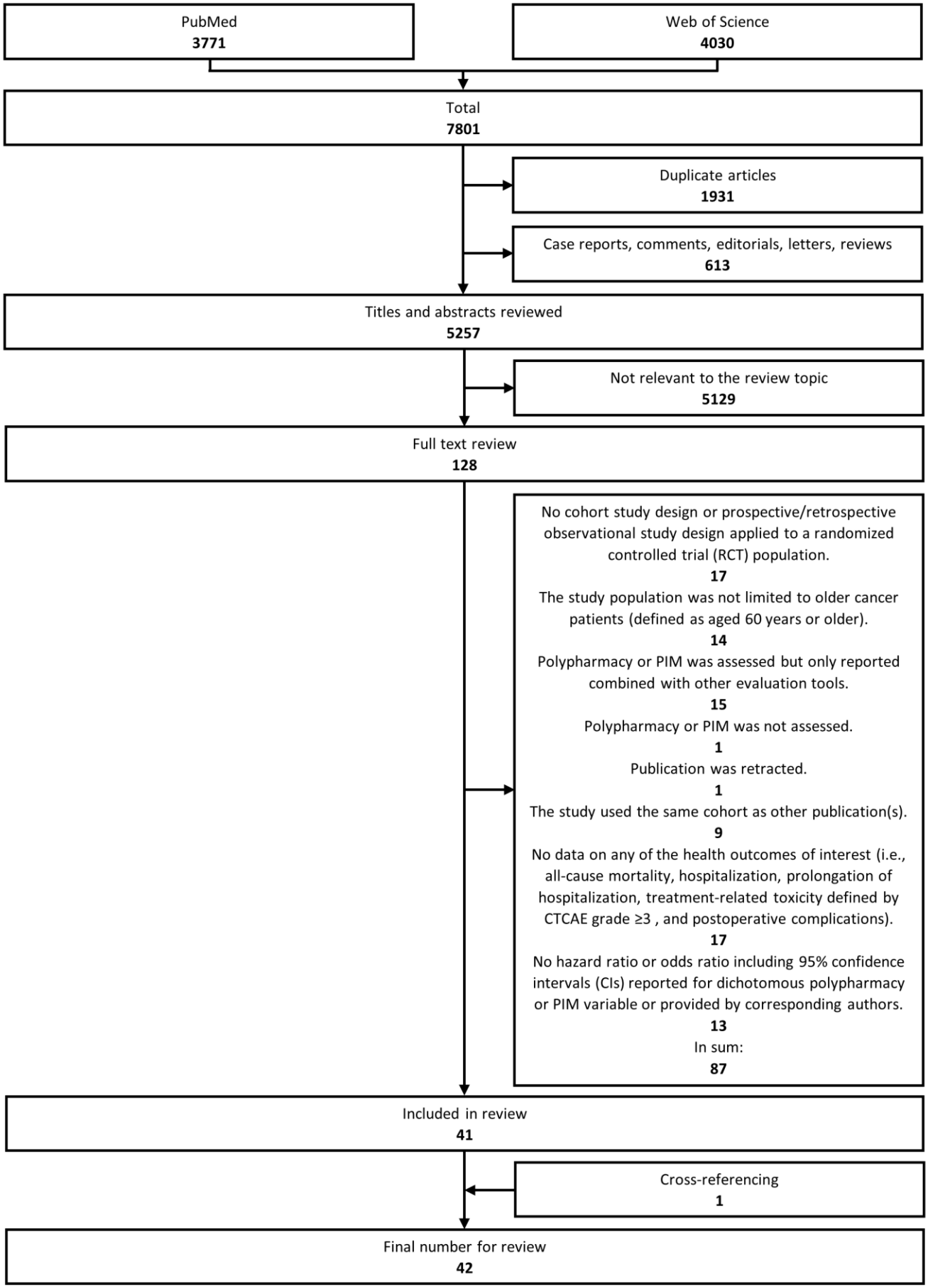
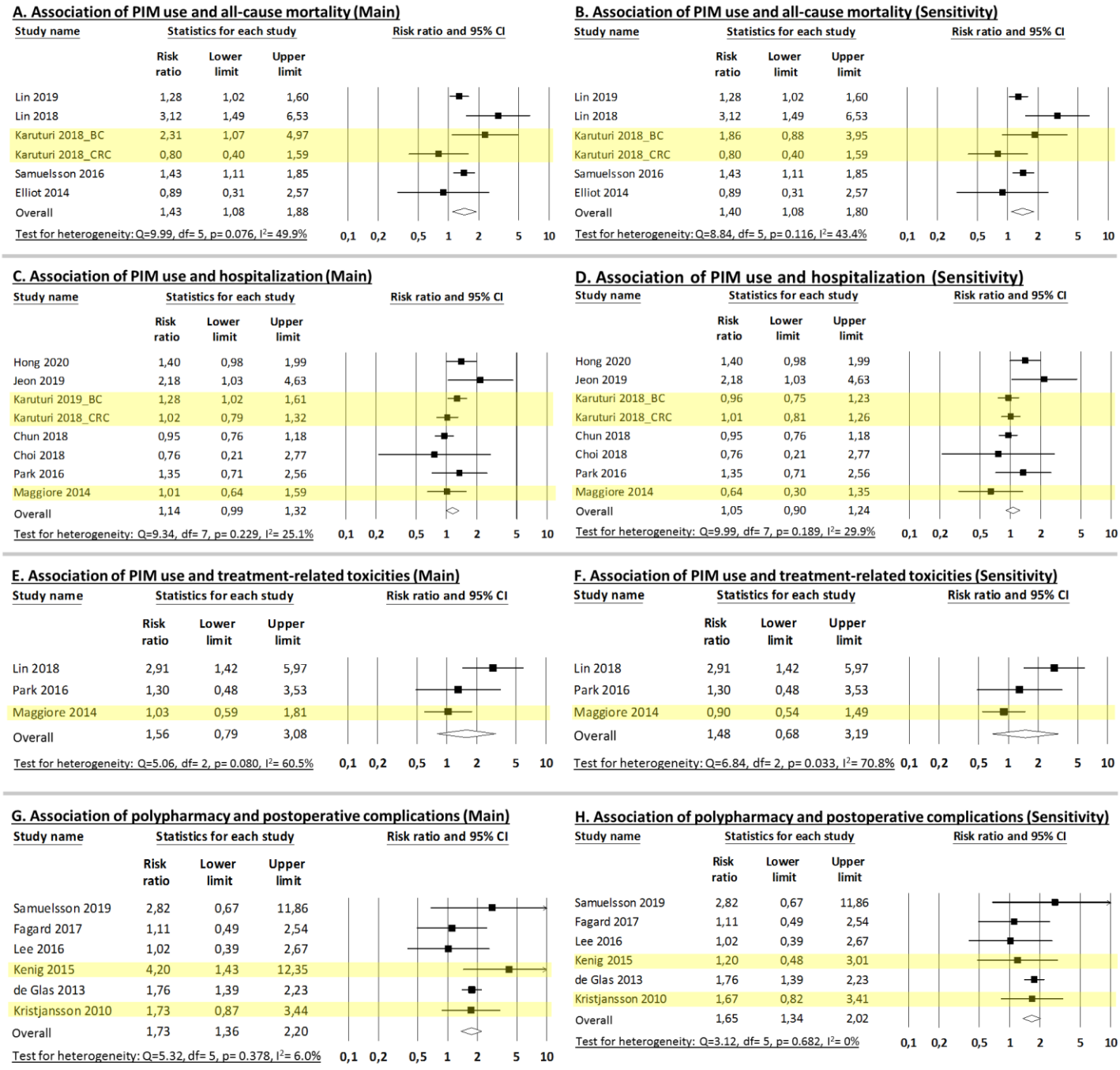


Figure A2. Comparison of main meta-analysis using the strongest association if multiple results, eligible to be included in the same meta-analysis, were reported (left column) and sensitivity analysis using the weakest associations (right column)



Notes: Yellow shading highlights studies with multiple results, eligible to be included in the same meta-analysis (e.g., different PIM definitions or different postoperative complications). Only meta-analyses are presented, which included studies with multiple outcomes.

Appendix Table A1. MOOSE Checklist of Current Systematic Review and Meta-Analysis

Item No.	Reporting Criteria	Reference to manuscript.
Reporting of Background		
1	Problem definition	Introduction, 4th paragraph
2	Hypothesis statement (Aim statement)	Introduction, 4th paragraph
3	Description of Study Outcome(s)	Introduction, 4th paragraph
4	Type of exposure or intervention used	Introduction, 4th paragraph
5	Type of study design used	Introduction, 4th paragraph
6	Study Population	Introduction, 4th paragraph
Reporting of Searching Strategy		
7	Qualifications of searchers (eg, librarians and investigators)	Methods, 5th paragraph
8	Search strategy, including time period included in the synthesis and keywords	Methods, 2nd and 3rd paragraph; Appendix Table A2, A3
9	Effort to include all available studies, including contact with authors	Methods, 5th paragraph
10	Databases and registries searched	Methods, 2nd paragraph
11	Search software used, name and version, including special features used (eg, explosion)	Methods, 4th paragraph
12	Use of hand searching (eg, reference lists of obtained articles)	Methods, 4th paragraph
13	List of citations located and those excluded, including justification	Methods, 4th paragraph; Appendix Table A4
14	Method of addressing articles published in languages other than English	Results, 1st paragraph
15	Method of handling abstracts and unpublished studies	Methods, 5th paragraph
16	Description of any contact with authors	Methods, 5th paragraph
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Methods, 2-4th paragraph
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	Methods, 2-5th paragraph
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	Methods, 5th paragraph
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	Methods, 6th paragraph
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	Methods, 6th paragraph
22	Assessment of heterogeneity	Methods, 7th paragraph
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Methods, 7-9th paragraph
24	Provision of appropriate tables and graphics	Tables 1-4, Figure 1
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figure 1
26	Table giving descriptive information for each study included	Tables 1-4
27	Results of sensitivity testing (eg, subgroup analysis)	Results, 15th paragraph
28	Indication of statistical uncertainty of findings	Results, 5-13th paragraph
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	Results, 4th paragraph
30	Justification for exclusion (eg, exclusion of non-English language citations)	Results, 4th paragraph
31	Assessment of quality of included studies	Results, 4th paragraph; Appendix Table A5
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	Conclusions
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	Conclusions
34	Guidelines for future research	Discussion, 17th paragraph
35	Disclosure of funding source	Disclosure of Funding Source

From: Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA.* 2000; 283(15):2008-12.[1]

Appendix Table A2. PubMed Search (01.01.1991 - 23.03.2020)

Step	Step combination	Search Term(s)	Results
1		**Potentially Inappropriate Medication List[MeSH]**	421
2		PIM List*[tw]	31
3		Inappropriate Medication*[tw]	1,631
4		Inappropriate Medicine*[tw]	118
5		Inappropriate Prescrib*[tw]	3,948
6		Inappropriate Prescription*[tw]	682
7		Inappropriate Drug*[tw]	619
8		Suboptimal Medication*[tw]	90
9		Suboptimal Medicine[tw]	1,734
10		Suboptimal Medicines[tw]	215
11		Suboptimal Prescrib*[tw]	84
12		Suboptimal Prescription*[tw]	15
13		Suboptimal Drug Use[tw]	12
14		Suboptimal Drugs[tw]	2,386
15		Incorrect Medication*[tw]	80
16		Incorrect Prescribing[tw]	22
17		Incorrect Prescription*[tw]	45
18		Incorrect Drug*[tw]	87
19		Potentially inappropriate prescrib*[tw]	315
20		Potentially inappropriate prescription*[tw]	223
21		Potentially inappropriate medication*[tw]	1157
22		Potentially inappropriate medicine*[tw]	70
23		Potentially inappropriate drug*[tw]	127
24		Beers Criteria[tw]	636
25		STOPP[tw]	425
26		Screening Tool of Older Person's Potentially Inappropriate Prescriptions[tw]	16
27		Medication Appropriateness Index[tw]	125
28	OR 1 - 27		10,084
29		**Polypharmacy[MeSH]**	5,010
30		Polypharmacy[tw]	9,508
31		Polymedication*[tw]	221
32		Polymedicine[tw]	12
33		Polyprescription*[tw]	2
34		Polydrug*[tw]	1,532
35		Multiple Prescription*[tw]	135
36		Multiple Prescrib*[tw]	104
37		Multiple Medication*[tw]	1,643
38		Multiple Medicine[tw]	9
39		Multiple Medicines[tw]	75
40		Multiple Drug*[tw]	7,917
41		Multiple Drug Use[tw]	254
42		Geriatric assessment[tw]	28,491
43		Geriatric assessments[tw]	245
44		Geriatric review[tw]	4
45		Geriatric reviews[tw]	1,585
46	OR 29 – 45		49,526
47		**Neoplasms[MeSH Terms]**	3,297,252
48		Neoplasms[tw]	2,641,421
49		Neoplasm[tw]	709,792
50		Neoplasia[tw]	60,136
51		Neoplasias[tw]	5,705
52		Tumors[tw]	603,992
53		Tumor[tw]	1,641,379
54		Cancer[tw]	1,692,423

55		Cancers[tw]	254,370
56		Malignancy[tw]	140,247
57		Malignancies[tw]	115,634
58		Malignant Neoplasms[tw]	9,493
59		Malignant Neoplasm[tw]	4,677
60		Neoplasm, Malignant[tw]	1
61		Neoplasms, Malignant[tw]	1
62		Benign Neoplasms[tw]	1,871
63		Neoplasms, Benign[tw]	5
64		Benign Neoplasm[tw]	1,760
65		Neoplasm, Benign[tw]	1
66		Carcinoma[tw]	815,373
67		Carcinomas[tw]	118,794
68		Metastasis[tw]	352,672
69		Metastases[tw]	159,856
70		Lymphoma[tw]	232,981
71		Lymphomas[tw]	41,912
72		Lymphoid malignancy[tw]	702
73		Lymphoid malignancies[tw]	2,591
74		Lymphoid[tw]	109,900
75		Leukemia[tw]	307,885
76		Leukemias[tw]	16,224
77		Myeloma[tw]	60,076
78		Myelomas[tw]	1,123
79		Adenoma[tw]	88,095
80		Adenomas[tw]	34,905
81		Oncology[tw]	115,839
82		Oncological[tw]	22,357
83		Hematology[tw]	21,443
84		Hematological[tw]	44,745
85		Carcinogenesis[tw]	85,912
86		Carcinogeneses[tw]	13
87		Adenocarcinoma[tw]	229,681
88		Adenocarcinomas[tw]	27,274
89	OR 47 - 88		4,509,385
90	28 OR 46	Polypharmacy or PIM	58,161
91	89 AND 90	(Polypharmacy or PIM) and Neoplasm	6,054
92	NOT	"Editorial" [Publication Type] "Comment" [Publication Type] "Review" [Publication Type] "Review Literature as Topic"[Mesh] "Letter" [Publication Type] "Correspondence as Topic"[Mesh] "Case Reports" [Publication Type]	-2,011
93	91 NOT 92	((Polypharmacy or PIM) and Neoplasm) NOT 92	4,043
94		Since 1991	3,771

Appendix Table A3. Web of Science Search (01.01.1991 - 23.03.2019)

Step	Step combination	Search Set	Results
1	PIM	TS=("Potentially Inappropriate Medication List" OR "PIM List*" OR "Inappropriate Medication*" OR "Inappropriate Medicine*" OR "Inappropriate Prescrib*" OR "Inappropriate Prescription*" OR "Inappropriate Drug*" OR "Suboptimal Medication*" OR "Suboptimal Medicine" OR "Suboptimal Medicines" OR "Suboptimal Prescrib*" OR "Suboptimal Prescription*" OR "Suboptimal Drug Use" OR "Suboptimal Drugs" OR "Incorrect Medication*" OR "Incorrect Prescribing" OR "Incorrect Prescription*" OR "Incorrect Drug*" OR "potentially inappropriate prescrib*" OR "potentially inappropriate prescription*" OR "potentially inappropriate medication*" OR "potentially inappropriate medicine*" OR "potentially inappropriate drug*" OR "Beers Criteria" OR STOPP OR "Screening Tool of Older Person's Potentially Inappropriate Prescriptions" OR "Medication Appropriateness Index") *Indexes=SCI-EXPANDED Timespan=All years*	4,509
2	Polypharmacy	TS=("Polypharmacy" OR "Polymedication*" OR "Polymedicine" OR "Polyprescription*" OR "Polydrug*" OR "Multiple Prescription*" OR "Multiple Prescrib*" OR "Multiple Medication*" OR "Multiple Medicine" OR "Multiple Medicines" OR "Multiple Drug*" OR "Multiple Drug Use" OR "Geriatric assessment" OR "Geriatric assessments" OR "Geriatric review" OR "Geriatric reviews") *Indexes=SCI-EXPANDED Timespan=All years*	23,216
3	Neoplasms	TS=("Neoplasms" OR "Neoplasm" OR "Neoplasia" OR "Neoplasias" OR "Tumors" OR "Tumor" OR "Cancer" OR "Cancers" OR "Malignancy" OR "Malignancies" OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Neoplasm, Malignant" OR "Neoplasms, Malignant" OR "Benign Neoplasms" OR "Neoplasms, Benign" OR "Benign Neoplasm" OR "Neoplasm, Benign" OR "Carcinoma" OR "Carcinomas" OR "Metastasis" OR "Metastases" OR "Lymphoma" OR "Lymphomas" OR "Lymphoid malignancy" OR "Lymphoid malignancies" OR "Lymphoid" OR "Leukemia" OR "Leukemias" OR "Myeloma" OR "Myelomas" OR "Adenoma" OR "Adenomas" OR "Oncology" OR "Oncological" OR "Hematology" OR "Hematological" OR "Carcinogenesis" OR "Carcinogeneses" OR "Adenocarcinoma" OR "Adenocarcinomas") *Indexes=SCI-EXPANDED Timespan=All years*	4,083,743
4	PIM OR PP	#1 OR #2 *Indexes=SCI-EXPANDED Timespan=All years*	26,546
5	(PIM OR PP) AND Neoplasms	#3 AND #4 *Indexes=SCI-EXPANDED Timespan=All years*	4,891
6	Unwanted study design	TS=("Editorial" OR "Comment" OR "Review" OR "Review Literature as Topic" OR "Letter" OR "Correspondence as Topic" OR "Case Reports") *Indexes=SCI-EXPANDED Timespan=All years*	1,979,970
7		#5 NOT #6	4,097
8	Since 1991		4,030

Appendix Table A4. Excluded studies and reasons

1. No cohort study design or prospective/retrospective observational study design applied to randomized controlled trial (RCT) population. **(n=17)**	1. Williams GR, Deal AM, Pergolotti M, Muss HB, Sanoff HK, Lund JL. Association of comorbidity and polypharmacy with skeletal muscle measures in older adults with cancer. J Clin Oncol 2018;36. 2. Wildes TM, Maggiore RJ, Tew WP, et al. Factors associated with falls in older adults with cancer: a validated model from the Cancer and Aging Research Group. Support Care Cancer 2018;26:3563-70 3. Russo C, Terret C, Cropet C, Albrand G. Geriatric assessment in oncology: Moving the concept forward. The 20 years of experience of the Centre Leon Berard geriatric oncology program. J Geriatr Oncol 2018;9:673-8. 4. Turner JP, Tervonen HE, Shakib S, Singhal N, Prowse R, Bell JS. Factors associated with use of falls risk-increasing drugs among patients of a geriatric oncology outpatient clinic in Australia: a cross-sectional study. J Eval Clin Pract 2017;23:361-8. 5. Pamoukdjian F, Aparicio T, Zelek L, et al. Impaired mobility, depressed mood, cognitive impairment and polypharmacy are independently associated with disability in older cancer outpatients: The prospective Physical Frailty in Elderly Cancer patients (PF-EC) cohort study. J Geriatr Oncol 2017;8:190-5. 6. Tan T, Ong WS, Rajasekaran T, et al. Identification of Comprehensive Geriatric Assessment Based Risk Factors for Malnutrition in Elderly Asian Cancer Patients. PLoS One 2016;11:e0156008. 7. Rajasekaran T, Tan T, Ong WS, et al. Comprehensive Geriatric Assessment (CGA) based risk factors for increased caregiver burden among elderly Asian patients with cancer. J Geriatr Oncol 2016;7:211-8 8. Canoui-Poitrine F, Reinald N, Laurent M, et al. Geriatric assessment findings independently associated with clinical depression in 1092 older patients with cancer: the ELCAPA Cohort Study. Psychooncology 2016;25:104-11. 9. Williams GR, Deal AM, Nyrop KA, et al. Geriatric assessment as an aide to understanding falls in older adults with cancer. Support Care Cancer 2015;23:2273-80. 10. Tournigand C, Canoui-Poitrine F, Reinald N, et al. Association between geriatric assessment findings and clinical depression in 1092 older patients with cancer: The ELCAPA Cohort study. J Clin Oncol 2015;33. 11. Yeoh TT, Tay XY, Si P, Chew L. Drug-related problems in elderly patients with cancer receiving outpatient chemotherapy. J Geriatr Oncol 2015;6:280-7. 12. Turner JP, Shakib S, Singhal N, et al. Prevalence and factors associated with polypharmacy in older people with cancer. Support Care Cancer 2014;22:1727-34. 13. Prithviraj GK, Koroukian S, Margevicius S, Berger NA, Bagai R, Owusu C. Patient Characteristics Associated with Polypharmacy and Inappropriate Prescribing of Medications among Older Adults with Cancer. J Geriatr Oncol 2012;3:228-37. 14. Parks RM, Hall L, Tang S, et al. Evaluation of a cancer-specific comprehensive geriatric assessment (CGA) tool in older women with newly diagnosed primary breast cancer. J Clin Oncol 2011;29. 15. Prithviraj GK, Bagai R, Koroukian SM, Berger NA, Owusu C. Polypharmacy and functional status in older patients with breast, colon, and lung cancers. J Clin Oncol 2010;28. 16. Beltran BE, Motta R, Gamarra MP, Araujo R, Castillo JJ. Comprehensive Geriatric Assessment in Elderly Patients with Aggressive Non-Hodgkin Lymphoma in Peru. Blood 2018;132:3 17. Mir N, MacLennan P, Al-Obaidi M, et al. Patient-reported cognitive complaints in older adults with gastrointestinal malignancies at diagnosis- Results from the Cancer & Aging Resilience Evaluation (CARE) study. J Geriatr Oncol 2020 [epub ahead of print]..
2. Study population was not limited to older cancer patients (defined as aged 60 years or older). **(n=14)**	18. Hoemme A, Barth H, Haschke M, et al. Prognostic impact of polypharmacy and drug interactions in patients with advanced cancer. Cancer Chemother Pharmacol 2019;83(4):773-774. 19. Laurent M, Guetz GD, Bastuji-Garin S, et al. Chronological Age and Risk of Chemotherapy Nonfeasibility: A Real-Life Cohort Study of 153 Stage II or III Colorectal Cancer Patients Given Adjuvant-modified FOLFOX6. AM J CLIN ONCOL-CANC 2018;41:73-80. 20. Senel G, Uysal N, Oguz G, et al. Delirium Frequency and Risk Factors Among Patients With Cancer in Palliative Care Unit. Am J Hosp Palliat Care 2017;34:282-6

	21. Calip GS, Xing S, Jun DH, Lee WJ, Hoskins KF, Ko NY. Polypharmacy and Adherence to Adjuvant Endocrine Therapy for Breast Cancer. J Oncol Pract 2017;13:e451-e62. 22. Pujara D, Mansfield P, Ajani J, et al. Comprehensive geriatric assessment in patients with gastric and gastroesophageal adenocarcinoma undergoing gastrectomy. J Surg Oncol 2015;112:883-7. 23. Fisch MJ, Zhao F, Manola J, Miller AH, Pirl WF, Wagner LI. Patterns and predictors of antidepressant use in ambulatory cancer patients with common solid tumors. Psychooncology 2015;24:523-32. 24. Sasaki T, Fujita K, Sunakawa Y, et al. Concomitant polypharmacy is associated with irinotecan-related adverse drug reactions in patients with cancer. Int J Clin Oncol 2013;18:735-42. 25. Chou WC, Chang PH, Chen PT, et al. Clinical Significance of Vulnerability Assessment in Patients with Primary Head and Neck Cancer Undergoing Definitive Concurrent Chemoradiation Therapy. Int J Radiat Oncol Biol Phys 2020 [epub ahead of print]. 26. de Vries J, Heirman AN, Bras L, et al. Geriatric assessment of patients treated for cutaneous head and neck malignancies in a tertiary referral center: Predictors of postoperative complications. Eur J Surg Oncol 2020;46:123-30. 27. Jeppesen SS, Matzen LE, Brink C, et al. Impact of comprehensive geriatric assessment on quality of life, overall survival, and unplanned admission in patients with non-small cell lung cancer treated with stereotactic body radiotherapy. J Geriatr Oncol 2018;9:575-82 28. Jorgensen TL, Herrstedt J. The influence of polypharmacy, potentially inappropriate medications, and drug interactions on treatment completion and prognosis in older patients with ovarian cancer. J Geriatr Oncol 2019;S1879-4068(19)30293-0. 29. van Abbema D, van Vuuren A, van den Berkmortel F, et al. Functional status decline in older patients with breast and colorectal cancer after cancer treatment: A prospective cohort study. J Geriatr Oncol 2017;8:176-84. 30. Oldak S, Ioannou S, Kamath P, et al. Polypharmacy in Patients with Ovarian Cancer. Oncologist 2019;24:1201-8. 31. Sanchez-Barroso L, Apellaniz-Ruiz M, Gutierrez-Gutierrez G, et al. Concomitant Medications and Risk of Chemotherapy-Induced Peripheral Neuropathy. Oncologist 2019;24:E784-E92.
3. Polypharmacy or PIM was assessed but only reported combined with other assessments. **(n=15)**	32. Kirkhus L, Saltyte Benth J, Rostoft S, et al. Geriatric assessment is superior to oncologists' clinical judgement in identifying frailty. Br J Cancer 2017;117:470-7. 33. Antonio M, Saldana J, Carmona-Bayonas A, et al. Geriatric Assessment Predicts Survival and Competing Mortality in Elderly Patients with Early Colorectal Cancer: Can It Help in Adjuvant Therapy Decision-Making? Oncologist 2017;22:934-43 34. Patel D, Turner J, Athreya V, Barry F, Singhal N. Outcomes of Geriatric Assessment for Metastatic Colorectal Cancer Patients from a Dedicated Geriatric Oncology Program. Asia Pac J Clin Oncol 2015;11:62. 35. Patel D, Mah A, Turner J, Barry F, Singhal N. Outcomes of geriatric assessment for advance non-small cell lung carcinoma (NSCLCA) patients from a dedicated geriatric oncology program. Ann. Oncol. 2015;26:131. 36. Kristjansson SR, Ronning B, Hurria A, et al. A comparison of two pre-operative frailty measures in older surgical cancer patients. J Geriatr Oncol 2012;3:1-7. 37. Caparrotti F, O'Sullivan B, Bratman SV, et al. Exploring the Impact of Human Papillomavirus Status, Comorbidity, Polypharmacy, and Treatment Intensity on Outcome of Elderly Oropharyngeal Cancer Patients Treated With Radiation Therapy With or Without Chemotherapy. Int J Radiat Oncol Biol Phys 2017;98:858-67. 38. Gavriatopoulou M, Fotiou D, Koloventzou U, et al. Vulnerability variables among octogenerian myeloma patients: a single-center analysis of 110 patients. Leuk Lymphoma 2019;60:619-28. 39. Kenig J, Mastalerz K, Mitus J, Kapelanczyk A. The Surgical Apgar score combined with Comprehensive Geriatric Assessment improves short- but not long-term outcome prediction in older patients undergoing abdominal cancer surgery. J Geriatr Oncol 2018;9:642-8. 40. Kotzerke D, Moritz F, Mantovani L, et al. The performance of three oncogeriatric screening tools - G8, optimised G8 and CARG - in predicting chemotherapy-related toxicity in older patients with cancer. A prospective clinical study. J Geriatr Oncol 2019;10:937-43. 41. Moth EB, Kiely BE, Stefanic N, et al. Predicting chemotherapy toxicity in older adults: Comparing the predictive value of the CARG Toxicity Score with oncologists' estimates of toxicity based on clinical judgement. J Geriatr Oncol 2019;10:202-9.

	42. Orum M, Gregersen M, Jensen K, Meldgaard P, Damsgaard EMS. Frailty status but not age predicts complications in elderly cancer patients: a follow-up study. Acta Oncol 2018;57:1458-66. 43. Owusu C, Schluchter M, Koroukian SM, Schmitz KH, Berger NA. Black-white disparity in physical performance among older women with newly diagnosed non-metastatic breast cancer: Exploring the role of inflammation and physical activity. J Geriatr Oncol 2018;9:613-9. 44. Sbrana A, Antognoli R, Pasqualetti G, et al. Effectiveness of Multi-Prognostic Index in older patients with advanced malignancies treated with immunotherapy. J Geriatr Oncol 2020;11(3):503-507. . 45. Shahrokni A, Vishnevsky BM, Jang B, et al. Geriatric Assessment, Not ASA Physical Status, Is Associated With 6-Month Postoperative Survival in Patients With Cancer Aged >/=75 Years. J Natl Compr Canc Netw 2019;17:687-94. 46. Souwer ETD, Verweij NM, van den Bos F, et al. Risk stratification for surgical outcomes in older colorectal cancer patients using ISAR-HP and G8 screening tools. J Geriatr Oncol 2018;9:110-4.
4. Polypharmacy or PIM was not assessed **(n=1)**	47. Jones SM, Rosenberg D, Ludman E, Arterburn D. Medical comorbidity and psychotropic medication fills in older adults with breast or prostate cancer. Support Care Cancer 2015;23:3005-9 (antidepressant and sedative fills)
5. Publication was retracted **(n=1)**	48. Rocco N, Rispoli C, Pagano G, et al. RETRACTED: Breast cancer surgery in elderly patients: postoperative complications and survival (Retracted article. See vol. 15, pg. 2, 2015). BMC Surgery 2013;13
6. Study used the same cohort as in other publication(s) **(n=9)**	49. Jeong YM, Lee KE, Lee ES, et al. Preoperative medication use and its association with postoperative length of hospital stay in surgical oncology patients receiving comprehensive geriatric assessment. Geriatr Gerontol Int 2018;18:12-9. 50. Jeong YM, Lee E, Kim KI, et al. Association of pre-operative medication use with post-operative delirium in surgical oncology patients receiving comprehensive geriatric assessment. BMC Geriatr 2016;16:134. 51. Lin RJ, Ma H, Guo R, Troxel A, Diefenbach CS. Potentially Inappropriate Medication Use in Elderly Patients with Diffuse Large B-Cell Lymphoma Predicts Inferior Survival and Treatment-Related Toxicities. Blood 2017;130. 52. Lin RJ, Ma H, Guo R, Grossbard ML, Troxel AB, Diefenbach CSM. Polypharmacy and potentially inappropriate medication use in older patients with aggressive non-Hodgkin lymphoma (NHL) leads to inferior survival and increased treatment-related toxicities. J Clin Oncol 2017;35. 53. Lin RJ, Guo R, Becker DJ, Grossbard ML, Diefenbach CSM. Adverse impact of polypharmacy and potentially inappropriate medication use in newly diagnosed, elderly lymphoma patients. J Clin Oncol 2016;34 54. Lin RJ, Guo R, Becker DJ, Grossbard ML, Diefenbach CSM. Contribution of polypharmacy and potentially inappropriate medication use to inferior survival in older patients with aggressive lymphoma. J Clin Oncol 2016;34. 55. Kwon M, Kim SA, Roh JL, et al. An Introduction to a Head and Neck Cancer-Specific Frailty Index and Its Clinical Implications in Elderly Patients: A Prospective Observational Study Focusing on Respiratory and Swallowing Functions. Oncologist 2016;21:1091-8. 56. Vande Walle N, Kenis C, Heeren P, et al. Fall predictors in older cancer patients: a multicenter prospective study. BMC Geriatr 2014;14:135. 57. Baitar A, Kenis C, Decoster L, et al. The prognostic value of 3 commonly measured blood parameters and geriatric assessment to predict overall survival in addition to clinical information in older patients with cancer. Cancer 2018;124:3764-75.
7. No data on any of the adverse health outcomes of interest (i.e., all-cause mortality, inpatient hospitalization, prolongation of existing hospitalization, treatment-related toxicity defined by CTCAE grade ≥3, and postoperative complications). **(n=17)**	58. Losada B, Guerra JA, Malon D, Jara C, Rodriguez L, Del Barco S. Pretreatment neutrophil/lymphocyte, platelet/lymphocyte, lymphocyte/monocyte, and neutrophil/monocyte ratios and outcome in elderly breast cancer patients. Clin Transl Oncol 2018. 59. Inci G, Woopen H, Richter R, Chekerov R, Muallem MZ, Sehouli J. The impact of polypharmacy and comorbidities on surgical morbidity and mortality in patients with gynecological malignancies: Results of a prospective study in 237 patients. J Clin Oncol 2017;35. 60. Parks RM, Hall L, Tang SW, et al. The potential value of comprehensive geriatric assessment in evaluating older women with primary operable breast cancer undergoing surgery or non-operative treatment--a pilot study. J Geriatr Oncol 2015;6:46-51. 61. Luciani A, Biganzoli L, Colloca G, et al. Estimating the risk of chemotherapy toxicity in older patients with cancer: The role of the Vulnerable Elders Survey-13 (VES-13). J Geriatr Oncol 2015;6:272-9. 62. Korc-Grodzicki B, Sun SW, Zhou Q, et al. Geriatric Assessment as a Predictor of Delirium and Other Outcomes in Elderly Patients With Cancer. Ann Surg 2015;261:1085-90.

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8. No hazard ratio or odds ratio reported for dichotomous polypharmacy or PIM variable or, if reported, 95 % confidence intervals (CI) are missing. **(n=13)**	75. Nieder C, Mannsaker B, Pawinski A, Haukland E. Polypharmacy in Older Patients ≥ 70 Years Receiving Palliative Radiotherapy. Anticancer Res 2017;37:795-9. 76. Lima JTO, Bergmann A, Mello MJG, et al. A practical clinical score to predict early death after a comprehensive geriatric assessment (CGA) in elderly cancer patients: A prospective cohort study with 608 patients. J Clin Oncol 2017;35 77. Decoster L, Kenis C, Schallier D, et al. Geriatric Assessment and Functional Decline in Older Patients with Lung Cancer. Lung 2017;195:619-26 78. Sendur MA, Silay K, Aksoy S, Ozbek S, Ozdemir N, Altundag K. Effect of polypharmacy on treatment preferences and outcome in older breast cancer patients. Ann. Oncol. 2016;27. 79. Brunello A, Fontana A, Zafferri V, et al. Development of an oncological-multidimensional prognostic index (Onco-MPI) for mortality prediction in older cancer patients. J Cancer Res Clin Oncol 2016;142:1069-77. 80. Jolly TA, Mariano CJ, Deal AM, et al. The association of Geriatric Assessment (GA) identified deficits and 30-day re-admission in hospitalized older cancer patients. J Clin Oncol 2015;33. 81. Kim JW, Kim YJ, Lee KW, et al. The early discontinuation of palliative chemotherapy in older patients with cancer. Support Care Cancer 2014;22:773-81. 82. Li DN, Korc-Grodzicki B, Zhou Q, et al. Preoperative geriatric assessment (GA) and surgical outcomes in older women with gynecological (gyn) cancer. J Clin Oncol 2012;30. 83. Honecker FU, Wedding U, Rettig K, Huschens S, Bokemeyer C. Use of the Comprehensive Geriatric Assessment (CGA) in elderly patients (pts) with solid tumors to predict mortality. J Clin Oncol 2009;27.

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Appendix Table A5. Results of the Risk of Bias Evaluation with a Modified Newcastle-Ottawa-Scale (Counting of the Study Quality Score is explained in the table legend)

First Author	Selection				Comparability	Outcome			Study Quality Score (up to 9P) (a)
	Representa-tiveness of the exposed cohort (up to 1P)	Selection of the non-exposed cohort (up to 1P)	Ascertainment of exposure (up to 1P)	Demonstration that outcome of interest was not present at start of study (up to 1P)	Comparability of cohorts on the basis of the design or analysis (up to 2P)	Assessment of outcome (up to 1P)	Was follow-up long enough for outcomes to occur (up to 1P)	Adequacy of follow up of cohorts (up to 1P)	
Dhakal et al.[2]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P	B → 1P	A → 1P	A → 1P	9
Hong et al.[3]	A → 1P	A → 1P	B → 1P	A → 1P	A → 2P[a] C → 0P[b]	A → 1P	A → 1P	A → 1P	9[a] 7[b]
Klepin et al.[4]	A → 1P	A → 1P	C → 0P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	6
Lu-Yao et al.[5]	A → 1P	A → 1P	A → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
Hakozaki et al.[6]	A → 1P	A → 1P	A → 1P	A → 1P	B → 1P[c] C → 0P[d]	B → 1P	A → 1P	A → 1P	8[c] 7[d]
Ku et al.[7]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
Reed et al.[8]	A → 1P	A → 1P	A → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
Sales et al.[9]	A → 1P	A → 1P	B → 1P	A → 1P	A → 2P	B → 1P	A → 1P	A → 1P	9
Samuelsson et al.[10]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	B → 1P	A → 1P	B → 1P	7
Williams et al.[11]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P	B → 1P	A → 1P	A → 1P	9
Nishijima et al.[12]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
Ommundsen et al.[13]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	A or B → 1P	A → 1P	A → 1P	7
Jeon et al.[14]	A → 1P	A → 1P	B → 1P	A → 1P	A → 2P	B → 1P	A → 1P	A → 1P	9
Lin et al.[15]	A → 1P	A → 1P	A → 1P	A → 1P	C → 0P	A or B → 1P	A → 1P	A → 1P	7
Westley et al.[16]	A → 1P	A → 1P	A → 1P	A → 1P	B → 1P	B → 1P	A → 1P	A → 1P	8
Lin et al.[17]	A → 1P	A → 1P	A → 1P	A → 1P	B → 1P[e] C → 0P[f]	A → 1P	A → 1P	A → 1P	8[e] 7[f]
Kenis et al.[18]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Karuturi et al.[19]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P	B → 1P	A → 1P	A → 1P	9
Karuturi et al.[20]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P[g] C → 0P[h]	B → 1P	A → 1P	A → 1P	9[g] 7[h]
Chun et al.[21]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P	B → 1P	A → 1P	A → 1P	9
Choi et al.[22]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Antonio et al.[23]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Fagard et al.[24]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P	A → 1P	A → 1P	A → 1P	9
Woopen et al.[25]	A → 1P	A → 1P	B → 1P	A → 1P	B → 1P	A → 1P	A → 1P	A → 1P	8
Samuelsson et al.[26]	A → 1P	A → 1P	A → 1P	A → 1P	B → 1P	B → 1P	A → 1P	A → 1P	8
Park et al.[27]	A → 1P	A → 1P	A → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Lee et al.[28]	A → 1P	A → 1P	A → 1P	B → 0P	A → 2P	A → 1P	A → 1P	A → 1P	8

First Author	Selection				Comparability	Outcome			Study Quality Score (up to 9P) (a)
	Representa-tiveness of the exposed cohort (up to 1P)	Selection of the non-exposed cohort (up to 1P)	Ascertainment of exposure (up to 1P)	Demonstration that outcome of interest was not present at start of study (up to 1P)	Comparability of cohorts on the basis of the design or analysis (up to 2P)	Assessment of outcome (up to 1P)	Was follow-up long enough for outcomes to occur (up to 1P)	Adequacy of follow up of cohorts (up to 1P)	
Jonna et al.[29]	A → 1P	A → 1P	A → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Bourdel-Marchasson et al.[30]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Sud et al.[31]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P	A → 1P	A → 1P	A → 1P	9
Kenig et al.[32]	A → 1P	A → 1P	B → 1P	A → 1P	B → 1P	A → 1P	A → 1P	A → 1P	8
Chiang et al.[33]	A → 1P	A → 1P	A → 1P	A → 1P	B → 1P	A → 1P	A → 1P	A → 1P	8
Ommundsen et al.[34]	A → 1P	A → 1P	A or B → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
Maggiore et al.[35]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P[i] C → 0P[j]	A → 1P	A → 1P	A → 1P	9[i] 7[j]
Hamaker et al.[36]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Hamaker et al.[37]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
de Glas et al.[38]	A → 1P	A → 1P	A → 1P	B → 0P	B → 1P	B → 1P	A → 1P	A → 1P	7
Elliot et al.[39]	A → 1P	A → 1P	A → 1P	A → 1P	A → 2P[k] C → 0P[l]	A → 1P	A → 1P	A → 1P	9[k] 7[l]
Badgwell et al.[40]	A → 1P	A → 1P	A → 1P	A → 1P	C → 0P	A → 1P	A → 1P	A → 1P	7
Kanesvaran et al.[41]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
Hamaker et al.[42]	A → 1P	A → 1P	B → 1P	A → 1P	C → 0P	B → 1P	A → 1P	A → 1P	7
Kristjansson et al.[43]	A → 1P	A → 1P	A → 1P	B → 0P	C → 0P	A → 1P	A → 1P	A → 1P	6

Abbreviations: P, point.

[a] For the association of polypharmacy with hospitalization

[b] For the associations of PIM use with hospitalization and of polypharmacy with overall survival and with treatment-related toxicity

[c] For the outcome overall survival

[d] For the outcome hospitalization

[e] For the outcome overall survival

[f] For the outcome treatment-related toxicity

[g] For the association of PIM use with emergency department visit/hospitalization/overall survival

[h] For the exposure polypharmacy and associations of PIM use with emergency department visit, hospitalization, and overall survival

[i] For the association of polypharmacy with in-patient hospitalization

[j] For the associations of polypharmacy with treatment-related toxicity, of PIM use with hospitalization and with treatment-related toxicity

[k] For the exposure polypharmacy

[l] For the exposure PIM use

(a) Counting of the Study Quality Score

In our modified Newcastle-Ottawa-Scale (NOS), the study quality score ranges from 0 to 9 points, with more points indicating a study has lower risk of bias. Points were allocated to each sub-category as shown below. A modification of the NOS made was that an extra point was given for studies which adjusted for comorbidity because this is an important source for confounding by indication in our research question on polypharmacy and PIM.

Selection:

(1) Representativeness of the exposed cohort: A, truly representative (1 point); B, somewhat representative (1 point); C, selected group of users (0 points); D, no description of the derivation of the cohort (0 points).

(2) Selection of the non-exposed cohort: A, drawn from the same community as the exposed cohort (1 point); B, drawn from a different source (0 points); C, no description of the derivation of the non-exposed cohort (0 points).

(3) Ascertainment of exposure: A, secure record (1 point); B, structured interview (1 point); C, written self-report (0 points); D, no description (0 points).

(4) Demonstration that outcome of interest was not present at start of study: A, yes (1 point); B, no (0 points).

Comparability:

(1) Comparability of cohorts on the basis of the design or analysis: A, study controls for co-morbidities (2P); B, study controls for age and sex (1P) (if studies are conducted in males or females only no control for sex was mandatory); C, no control for age, sex or co-morbidities.

Outcome:

(1) Assessment of outcome: A, independent blind assessment (1 point); B, record linkage (1 point); C, self-report (0 points); D, no description (0 points).

(2) Was follow-up long enough for outcomes to occur: A, yes (1 point); B, no (0 points).

(3) Adequacy of follow up of cohorts: A, complete follow up – all subjects accounted for (1 point); B, subjects lost to follow up were unlikely to introduce bias because a small number (less than 15 %) were lost or description provided of those lost (1 point); C, follow-up rate was lower than 85 % and no description of those lost (0 points); D, no statement (0 points).

Appendix Table A6. Designs of Studies Investigating the Association of Polypharmacy with Adverse Health Outcomes in Older Adults with Cancer

First Author, Year	Polypharmacy Definition	Study Design	Country	Claims Data	Data Collection	Study Population				
						Cancer Type	Population	Total (N)	Female (%)	Age (Years)
Dhakal et al, 2020[2]	≥ 5 drugs	RCS, PU	U.S.	No	2000-2016	AML	Inpatients	235	N.R.	≥ 60[a]
Hong et al, 2020[3]	≥ 5 drugs[b]	PCS, PU	South Korea	No	2014-2015	Solid cancer	Inpatients	301	30.9	70 - 93
Klepin et al, 2020[4]	≥ 5 drugs	RCT, PU	U.S.	No	2011-2014	AML	In- and outpatients	40	40	61-83
Lu-Yao et al, 2020_BC[5]	≥ 5 drugs[c]	PCS, PU	U.S.	Yes	1991-2014	BC	Inpatients	5,490	100	≥ 65
Lu-Yao et al, 2020_LC[5]	≥ 5 drugs[c]	PCS, PU	U.S.	Yes	1991-2014	LC	Inpatients	7,309	N.R.	≥ 65
Lu-Yao et al, 2020_PC[5]	≥ 5 drugs[c]	PCS, PU	U.S.	Yes	1991-2014	PC	Inpatients	1,430	0	≥ 65
Hakozaki et al, 2019[6]	≥ 5 drugs	RCS, PU	Japan	No	2016-2019	NSCLC	In- and outpatients	157	36.3	≥ 65
Karuturi et al, 2019_BC[20]	≥ 5 drugs	RCS, PU	U.S.	Yes	2007-2009	BC	Outpatients	1,595	100	≥ 66
Karuturi et al, 2019_CRC[20]	≥ 5 drugs	RCS, PU	U.S.	Yes	2007-2009	CRC	Outpatients	1,528	50.4	≥ 66
Ku et al, 2019[7]	≥ 3 drugs	PCS, PU	South Korea	No	2010-2014	HNSCC	Outpatients	233	15.5	65-84
Reed et al, 2019[8]	≥ 6 drugs	RCS, PU	Canada	No	N.R.	Any	Inpatients	275	57.5	≥ 70
Sales et al, 2019[9]	N.R.	PCS, PU	Brazil	No	2015-2017	Gynecologic cancer	Outpatients	84	100	60-96
Samuelsson et al, 2019[10]	≥ 5 drugs	PCS, PU	Sweden	No	2010-2016	CRC	Inpatients	49	53.1	≥ 75
Williams et al, 2019[11]	≥ 10 drugs	RCS, PU	U.S.	Yes	2009-2013	Any	In- and outpatients	125	80	65-93
Nishijima et al, 2018[12]	≥ 5 drugs	PCS, PU	U.S.	No	2009-2014	Any	Inpatients	546	72	65-100
Ommundsen et al, 2018[13]	≥ 6 drugs	PCS, PU	Norway	No	2011-2014	CRC	Inpatients	114	49	65-95
Westley et al, 2018[16]	≥ 6 drugs[d]	RCS, PU	Canada	Yes	1998-2012	BC	Inpatients	24,463	100	≥ 65
Kenis et al, 2018_1[18]	≥ 5 drugs	PCS, PU	Belgium	No	2009-2011	BC, CRC, LC, PC, OC	Inpatients	763	67.8	70 - 95
Kenis et al, 2018_2[18]	≥ 5 drugs	PCS, PU	Belgium	No	2011-2012	BC, CRC, LC, PC, OC	Inpatients	402	66.7	70 - 95
Choi et al, 2018[22]	≥ 5 drugs	RCS, PU	South Korea	No	2014-2015	All surgical	Inpatients	475	54.7	65 - 96
Antonio et al, 2018[23]	≥ 6 drugs	PCS, PU	Spain	No	2008-2016	CRC (stage II and III)	Inpatients	193	37.3	75 - 89
Fagard et al, 2017[24]	≥ 5 drugs	PCS, PU	Belgium	No	2009-2015	CRC	Inpatients	190	44.7	70 - 97
Woopen et al, 2016[25]	≥ 5 drugs	RCT, PU	Germany	No	2000-2009	OC	Inpatients	134	100	≥ 70[e]
Park et al, 2016[27]	≥ 5 drugs	RCS, PU	South Korea	No	2008-2013	HNC	Inpatients	229	16.2	65 - 87
Lee et al, 2016[28]	≥ 8 drugs	RCS, PU	South Korea	No	2009-2014	CRC	Inpatients	240	42.5	70 - 96
Jonna et al, 2016[29]	≥ 7 drugs	RCS, PU	U.S.	No	2000-2008	Any	Inpatients	803	48.2	≥ 65
Bourdel-Marchasson et al, 2016[30]	≥ 4 drugs	RCT, PU	France	No	2007-2012	Any except lymphoma	Inpatients	606	47.4	≥ 70
Sud et al, 2015[31]	≥ 6 drugs	RCS, PU	Canada	No	2005-2010	Solid cancer	In- and outpatients	318	44	80 - 92
Kenig et al, 2015[32]	≥ 5 drugs	PCS, PU	Poland	No	2013-2014	Solid abdominal tumors	Inpatients	75	44.0	65 - 93
Ommundsen et al, 2014[34]	≥ 8 drugs	PCS, PU	Norway	No	2006-2008	CRC	Inpatients	178	57.3	70 - 94
Maggiore et al, 2014[35]	≥ 4 drugs[f]	PCS, PU	U.S.	No	2006-2009	Solid tumor	Outpatients	500	56.2	≥ 65
Hamaker et al, 2014[36]	≥ 5 drugs	RCT, PU	Netherlands	No	2007-2011	BC	Inpatients	73	100	66 - 87
Hamaker et al, 2014[37]	≥ 5 drugs	PCS, PU	Austria	No	2009-2013	Hematologic malignancy	Inpatients	108	47	67.1 - 98.9
Elliot et al, 2014[39]	≥ 4 drugs[g]	RCS, PU	U.S.	No	2004-2009	AML	Inpatients	150	39	61 - 87
de Glas et al, 2013[38]	≥ 5 drugs	RCS, PU	Netherlands	No	1997-2011	BC	Outpatients	3,179	100	65 - 98

First Author, Year	Polypharmacy Definition	Study Design	Country	Claims Data	Data Collection	Study Population				
						Cancer Type	Population	Total (N)	Female (%)	Age (Years)
Badgwell et al, 2013[40]	≥ 6 drugs	PCS, PU	U.S.	No	2010-2012	Abdominal cancer	Inpatients	111	45.0	65 - 89
Kanesvaran et al, 2011[41]	≥ 5 drugs	RCS, PU	Singapore	No	2007-2010	Any	Outpatients	249	38.6	70 - 94
Hamaker et al, 2011[42]	≥ 5 drugs	PCS, PU	Netherlands	No	2002-2008	Any	Inpatients	292	48.8	65 - 96
Kristjansson et al, 2010[43]	≥ 5 drugs	PCS, PU	Norway	No	2006-2008	CRC	Inpatients	182	57.1	70 - 94

Abbreviations: AML, acute myeloid leukemia; BC, breast cancer; CRC, colorectal cancer; HNSCC, head and neck squamous cell carcinoma; HNC, head and neck cancer; LC, lung cancer; N.R., not reported; NSCLC, non-small cell lung cancer; OC, ovarian cancer; PC, prostate cancer; PCS, prospective cohort study; PU, prevalent user design; RCS, retrospective cohort study; RCT, randomized controlled trial

[a] Only patients aged 60 years or above were included in this systematic review and meta-analysis.

[b] Categories "5-9 drugs" and "≥ 10 drugs" have been pooled for the meta-analysis.

[c] Categories "5-9 drugs", "10-14 drugs", and "≥ 15 drugs" have been pooled for the meta-analysis.

[d] Categories "6-10 drugs" and "> 10 drugs" have been pooled for the meta-analysis.

[e] Only patients aged 70 years or above were included in this systematic review and meta-analysis.

[f] Categories "4-9 drugs" and "≥ 10 drugs" have been pooled for the meta-analysis.

[g] Category "2-3 drugs" was not used for the meta-analysis.

Appendix Table A7. Follow-Up and Effect Size Data of Studies Investigating the Impact of Polypharmacy on Health Outcomes in Older Adults with Cancer

First Author, Year	Polypharmacy Definition	Prevalence of Polypharmacy (%)	Outcome	$N_{outcome}$	FUP	HR or OR (95% CI)	Adjusted Covariates		
							Age+ sex[a]	Comor-bidity	Other
Dhakal et al, 2020[2]	≥ 5 drugs	64.3	Overall survival	≈235[b]	12 years	1.12 (0.81-1.57)	-	x	Multiple[c]
Hong et al, 2020[3]	≥ 5 drugs	45.2	Hospitalization	123	30 days	**1.73 (1.18-2.55)**	x	x	ECOG PS
	5-9 drugs	36.5	Grade ≥ 3 CTCAE toxicity	162	28 days	1.13 (0.70-1.83)	-	-	-
	≥ 10 drugs	8.6	Grade ≥ 3 CTCAE toxicity	162	28 days	1.78 (0.75-4.22)	-	-	-
	5-9 drugs	36.5	Overall survival	≈230[b]	2.5 years	**1.51 (1.09-2.08)**	-	-	-
	≥ 10 drugs	8.6	Overall survival	≈230[b]	2.5 years	**2.04 (1.25-3.32)**	-	-	-
Klepin et al, 2020[4]	≥ 5 drugs	30	Overall survival	≈4	14.9 months[d]	1.25 (0.51-3.06)[e]	-	-	-
Lu-Yao et al, 2020_BC[5]	5-9 drugs	39.3	Hospitalization	N.R.	6 months	**1.17 (1.01–1.37)**[f]	-	-	-
	10-14 drugs	28.6	Hospitalization	N.R.	6 months	**1.61 (1.37–1.89)**[f]	-	-	-
	≥ 15 drugs	16.7	Hospitalization	N.R.	6 months	**2.01 (1.68–2.39)**[f]	-	-	-
Lu-Yao et al, 2020_LC[5]	5-9 drugs	31.9	Hospitalization	N.R.	6 months	**1.36 (1.19–1.72)**[f]	-	-	-
	10-14 drugs	33.7	Hospitalization	N.R.	6 months	**1.49 (1.30–1.72)**[f]	-	-	-
	≥ 15 drugs	25.7	Hospitalization	N.R.	6 months	**1.82 (1.57–2.11)**[f]	-	-	-
Lu-Yao et al, 2020_PC[5]	5-9 drugs	37.2	Hospitalization	N.R.	6 months	**1.42 (1.02-1.97)**[f]	-	-	-
	10-14 drugs	30.7	Hospitalization	N.R.	6 months	**1.75 (1.25–2.45)**[f]	-	-	-
	≥ 15 drugs	21.6	Hospitalization	N.R.	6 months	**2.14 (1.49–3.05)**[f]	-	-	-
Hakozaki et al, 2019[6]	≥ 5 drugs	59.9	Overall survival	74	7.1 months[d]	1.97 (1.14-3.42)	-	-	Multiple[g]
			Progression-free survival	111	7.1 months[d]	1.44 (0.95-2.18)	-	-	Multiple[h]
			Grade ≥2 irAE	27	7.1 months[d]	1.74 (0.67-4.93)	-	-	-
			Hospitalization	76	7.1 months[d]	3.14 (1.54-6.58)	-	-	-
Karuturi et al, 2019_BC[20]	≥ 5 drugs	73.7	Emergency room visit	552	9 months	**1.73 (1.31-2.29)**	-	-	-
			Hospitalization	369	9 months	**1.83 (1.29-2.59)**	-	-	-
			Overall survival	34	9 months	N.S.	-	-	-
			Emergency room visit/ Hospitalization/ Overall survival	598	9 months	N.R.	-	-	-
Karuturi et al, 2019_CRC[20]	≥ 5 drugs	71.2	Emergency room visit	552	9 months	**1.23 (1.04-1.47)**	-	-	-
			Hospitalization	369	9 months	N.S.	-	-	-
			Overall survival	34	9 months	N.S.	-	-	-
			Emergency room visit/ Hospitalization/ Overall survival	598	9 months	N.R.	-	-	-
Ku et al, 2019[7]	≥ 3 drugs	N.R.	Overall survival	81	5.83 years	1.13 (0.73–1.74)	-	-	-
			Cancer-specific survival	57		1.26 (0.75–2.12)	-	-	-
			Non-cancer-specific survival	24		1.09 (0.42–2.82)	-	-	-
Reed et al, 2019[8]	≥ 6 drugs	52.7	Grade ≥ 3 CTCAE toxicity	199	1 month	1.16 (0.62–2.18)	-	-	Multiple[i]

First Author, Year	Polypharmacy Definition	Prevalence of Polypharmacy (%)	Outcome	$N_{outcome}$	FUP	HR or OR (95% CI)	Adjusted Covariates		
							Age+ sex[a]	Comor-bidity	Other
Sales et al, 2019[9]	N.R.	N.R.	Overall survival	9	1 year	2.65 (0.71-9.81)	x	x	Multiple[j]
Samuelsson et al, 2019[10]	≥ 5 drugs	67.3	POCs	16	1 year	2.82 (0.67-11.85)	-	-	-
			Length of stay > 8 days	N.R.	8 days[d]	1.01 (0.29-3.45)	-	-	-
Williams et al, 2019[11]	≥ 10 drugs	41.2	Hospitalization	41	47 months	1.03[f] (0.64-1.65)[k]	x	x	-
			Long-term care stay	20		**0.33**[f] **(0.17-0.64)**[k]	x	x	-
Nishijima et al, 2018[12]	≥ 5 drugs	N.R.	Overall survival	191	5.7 years	**1.46 (1.08–1.98)**	-	-	-
Ommundsen et al, 2018[13]	≥ 6 drugs	51	Overall survival	46	51 months[d]	1.5 (0.8-2.7)	-	-	-
Westley et al, 2018[16]	6-10 drugs	26.2	Emergency department visit	3,129	45 days	**1.23 (1.15-1.31)**	x	-	Multiple[l]
	≥ 11 drugs	5.6	Emergency department visit	3,129	45 days	**1.53 (1.33-1.77)**	x	-	Multiple[l]
Kenis et al, 2018_1[18]	≥ 5 drugs	51.6	Overall survival	471	6.3 years	**1.43 (1.18-1.73)**[e]	-	-	Stage, tumor type
Kenis et al, 2018_2[18]	≥ 5 drugs	54.2	Overall survival	214	4.5 years	1.27 (0.96-1.68)[e]	-	-	Stage, tumor type
Choi et al, 2018[22]	≥ 5 drugs	50.7	Post-discharge institutionalization	14	30 days	**3.96 (1.05-14.86)**[m]	-	-	Transfusion, infection
Antonio et al, 2018[23]	≥ 6 drugs	64.8	Treatment refusal	141	36 weeks[n]	**5.34 (1.55-18.40)**	-	-	Cancer site, VES-13 ≥ 3, oncogeriatric group
			Grade ≥ 3 CTCAE toxicity	105	36 weeks[n]	1.26 (0.43-3.65)	-	-	-
			Completion ≥ 80% of planned dose	105	36 weeks[n]	0.50 (0.20-12.6)	x	-	Social support, toxicity
Fagard et al, 2017[24]	≥ 5 drugs	47.4	CD ≥ 2 30-day POCs	78	30 days	1.11 (0.49-2.54)[o]	x	x	-
Woopen et al, 2016[25]	≥ 5 drugs	N.R.	Grade ≥ 3 CTCAE toxicity	N.R.	19.7 months[d]	1.12 (1.02-1.24)[k]	x	-	Multiple[p]
Park et al, 2016[27]	≥ 5 drugs	29.3	Grade ≥ 3 CTCAE toxicity	21	N.R.	1.55 (0.61-3.94)	-	-	-
			Hospitalization > 1 month	20	1 month[q]	1.70 (0.66-4.36)	-	-	-
			Non-cancer health event[r]	66	2 years	1.81 (0.99-3.31)	-	-	-
Lee et al, 2016[28]	≥ 8 drugs	13.8	Major 30-day POCs[s]	99	30 days	1.02 (0.39-2.67)	-	x	Multiple[t]
Jonna et al, 2016[29]	≥ 7 drugs	N.R.	Overall survival	≈800[b]	6 years	**1.18 (1.02-1.38)**	-	-	-
Bourdel-Marchasson et al, 2016[30]	≥ 4 drugs	62.5	Overall survival	266	1 year	**1.62 (1.07-2.44)**[u]	-	-	Multiple[v]
Sud et al, 2015[31]	≥ 6 drugs	38	Toxicity-related therapy discontinuation	102	30 days	1.31 (0.77-2.22)	-	x	Mulitple[w]
			Hospitalization	102	30 days	**2.28 (1.34-3.88)**	-	x	Mulitple[w]
Kenig et al, 2015[32]	≥ 5 drugs[x]	44.0	All POCs	38	30 days	1.6 (0.7-4.1)	x	-	Type of cancer, severity of surgery
			Major POCs[y]	20	30 days	**4.2 (1.4-12.1)**	x	-	Same as above

First Author, Year	Polypharmacy Definition	Prevalence of Polypharmacy (%)	Outcome	$N_{outcome}$	FUP	HR or OR (95% CI)	Adjusted Covariates		
							Age+ sex[a]	Comor-bidity	Other
Ommundsen et al, 2014[34]	≥ 8 drugs	N.R.	Overall survival	93	5 years	**2.2 (1.1-4.3)**	-	-	-
Maggiore et al, 2014[35]	4-9 drugs	50.8	Grade ≥ 3 CTCAE toxicity	257	598 days	1.34 (0.92-1.97)	-	-	-
	≥ 10 drugs	11.5	Grade ≥ 3 CTCAE toxicity	257	598 days	0.82 (0.45-1.49)	-	-	-
	≥ 4 drugs	62.3	Hospitalization	112	598 days	1.34 (0.82-2.18)	-	x	Creatinine clearance
Hamaker et al, 2014[36]	≥ 5 drugs	50.7	Grade ≥ 3 CTCAE toxicity	27	N.R.	**6.38 (1.99-23.47)**	-	-	-
			Overall survival	54	2.67 years[d]	1.41 (0.82-2.44)	-	-	-
Hamaker et al, 2014[37]	≥ 5 drugs	65	Overall survival	≈70[b]	1 year	1.20 (0.64-2.24)	-	-	-
Elliot et al, 2014[39]	≥ 4 drugs	52	Overall survival	29	30 days	**9.98 (1.18-84.13)**	-	x	-
			Complete remission	71	132 days	**0.20 (0.06-0.65)**	-	x	-
			Intensive care unit stay	30	132 days	6.57 (0.80-53.72)	-	x	-
			Length of stay > 35 days	N.R.	132 days	0.94 (0.29-3.08)	-	x	-
de Glas et al, 2013[38]	≥ 5 drugs	13.5	POCs	618	30 days	**1.76 (1.39-2.23)**	x	-	Multiple[z]
Badgwell et al, 2013[40]	≥ 6 drugs	47.7	Length of stay > 7 days	55	35 days	**2.45 (1.09-5.48)**	-	-	Stage, weight loss ≥ 10%
Kanesvaran et al, 2011[41]	≥ 5 drugs	60.5	Overall survival	172	3 years	**1.62 (1.18-2.23)**	-	-	-
Hamaker et al, 2011[42]	≥ 5 drugs	47.8	Overall survival	187	1 year	1.10 (0.81-1.48)	-	-	-
Kristjansson et al, 2010[43]	≥ 5 drugs	25.8	Severe POCs[s]	N.R.	30 days	1.73 (0.87-3.44)	-	-	Tumor location
			All POCs	N.R.	30 days	1.67 (0.82-3.42)	-	-	Tumor location

Values in bold are statistically significant (p<0.05)

Abbreviations: BC, breast cancer; CD, Clavien-Dindo; CI, confidence interval; CTCAE, Common Terminology Criteria for Adverse Effects; ECOG PS, Eastern Cooperative Oncology Group performance status; FUP, follow-up period; HR, hazard ratio; irAE, immune-related adverse events; LC, lung cancer; N.R., not reported; N.S., not significant; OR, odds ratio; PC, prostate cancer; POC, postoperative complication; VES-13, Vulnerable Elders Survey

[a] If the study population consisted only of males or females, no adjustment for sex is necessary and therefore a cross was made even if the study adjusted for age only.

[b] Number of deaths were not reported but estimated from Kaplan-Meier plots.

[c] Karnofsky Performance Status, cytogenetics, intensity of chemotherapy.

[d] Median follow up.

[e] OR was reversed so that no polypharmacy was the reference group.[44]

[f] Incidence rate ratio.

[g] ECOG PS, presence of liver metastasis, presence of bone metastasis, programmed death-ligand 1 (PD-L1) expression, epidermal growth factor receptor (EGFR) mutation, and the Gustave Roussy Immune Score (GRIm-Score).

[h] Smoking status, ECOG PS, presence of liver metastasis, PD-L1 expression, EGFR mutation, initially chosen immune checkpoint inhibitors (ICIs), and GRIm-Score.

[i] Weight loss, ECOG PS, cancer stage, hemoglobin, platelet count, neutrophils, and creatinine clearance.

[j] Site of cancer, cancer stage, malnutrition, and Katz index.

[k] 95 % CIs was estimated from reported point estimate and p-value.[45]
[l] Receipt of income supplement, access to primary care, type of surgery, number of surgeries before definitive surgery, benzodiazepine use, anticoagulants use, steroids use, diabetes, active cardiac disease, past hospitalization, institutional volume, postoperative radiotherapy and chemotherapy, clustering by surgical institution.
[m] Model with largest area under the curve (AUC).
[n] Patients were followed at least until 3 months after finishing the chemotherapy, which could last for 24 weeks for fit patients.
[o] Analysis was done in 115 patients with geriatric assessment data available. ORs and 95% CIs were estimated with the original study data, which have been provided by the corresponding author.
[p] International Federation of Gynecology and Obstetrics (FIGO) stage, histology, BMI, number of recurrence, number of administered chemotherapy cycles and study entered.
[q] The follow-up period lasted for at least 1 month.
[r] Defined as readmission to the hospital within 2 years after the initial treatment for any cause that was not directly related to the index cancer or newly developed second primary cancer.
[s] Defined as CD class equal to or greater than II.
[t] Activities of daily living, instrumental activities of daily living, mini mental state examination, Korean Older Depression Scale, delirium, mini nutritional assessment.
[u] The result was obtained from the model with higher AUC done in 565 patients.
[v] Food intake over the last 3 months, protein-rich food intake, calf circumference, cancer origin, metastasis, lymphocytes.
[w] Anemia, leukocytosis, estimated glomerular filtration rate (eGFR) < 60 mL/min, palliative intent, line of therapy ≥ 2, initial dose adjustment.
[x] Only results for ≥ 5 drugs were extracted and no results for ≥ 6 drugs.
[y] Defined as CD class III to V.
[z] Stage, type of surgery, most extensive axillary surgery, neoadjuvant treatment.

Appendix Table A8. Designs of Studies Investigating the Association of Potentially Inappropriate Medication with Adverse Health Outcomes in Older Adults with Cancer

First Author, Year	PIM Criterion Applied	Study Design	Country	Claims Data	Data Collection	Study Population				
						Cancer Type	Population	Total (N)	Female (%)	Age (Years)
Hong et al, 2020[3]	Beers 2015 (avoid)	PCS, PU	South Korea	No	2014-2015	Solid cancer	Inpatients	301	30.9	70-93
Jeon et al, 2019[14]	PDRM[a]	RCS, PU	South Korea	No	2014-2015	All surgical	Inpatients	473	54.8	65-96
Lin et al, 2019[15]	Beers 2015 (all)	RCS, PU	U.S.	No	2001-2016	Hematologic malignancy	Inpatients	527	39	60-78.7
Lin et al, 2018[17]	Beers 2015 (all)	RCS, PU	U.S.	No	2009-2014	Aggressive NHL	Inpatients	171	49	≥ 60
Karuturi et al, 2018 and 2019_BC[b] [19,20]	HEDIS-DAE (avoid); Beers 2012 (all); STOPP criteria	RCS, PU	U.S.	Yes	2007-2009	BC	Outpatients	1,595	100	≥ 66
Karuturi et al, 2018 and 2019_CRC[b] [19,20]	HEDIS-DAE (avoid); Beers 2012 (all); STOPP criteria	RCS, PU	U.S.	Yes	2007-2009	CRC	Outpatients	1,528	50.4	≥ 66
Chun et al, 2018[21]	N.R.	RCS, PU	U.S.	Yes	2007-2011	BC	Outpatients	2,401	100	≥ 66
Choi et al, 2018[22]	Beers 2015 (avoid)	RCS, PU	South Korea	No	2014-2015	All surgical	Inpatients	475	54.7	65 - 96
Samuelsson et al, 2016[26]	Socialstyrelsen criteria (avoid, long-term use)	RCS, PU	Sweden	Yes	2007-2010	CRC	In- and outpatients	7,279	52.4	75 - 98
Park et al, 2016[27]	Beers 2012 (all)	RCS, PU	South Korea	No	2008-2013	HNC	Inpatients	229	16.2	65 - 87
Chiang et al, 2015[33]	Beers 2012 (all)	RCS, NU	U.S.	No	2000-2008	Any	Inpatients	677	47.4	≥ 65
Maggiore et al, 2014[35]	Beers 2012 (avoid[c]) Zhan's classification (all) HEDIS-DAE 2011 (avoid) Combination of all 3 criteria above	PCS, PU	U.S.	No	2006-2009	Solid tumor	Outpatients	500	56.2	≥ 65
Elliot et al, 2014[39]	Beers 2012 (all)	RCS, PU	U.S.	No	2004-2009	AML	Inpatients	150	39	61 - 87

Abbreviations: AML; acute myeloid leukemia; avoid, drugs to avoid; BC, breast cancer; CRC, colorectal cancer; HEDIS-DAE, Healthcare Effectiveness Data and Information Set Drugs to Avoid in the Elderly; HNC, head and neck cancer; long-term use, drugs to avoid long-term use; NHL, non-Hodgkin lymphoma; NU, new user design; PCS, prospective cohort study; PDRM, pre-operative discontinuation requiring medications; PIM, potentially inappropriate medication; PU, prevalent user design; RCS, retrospective cohort study; STOPP, Screening Tool of Older Person's Prescriptions

[a] PDRM were defined as medications that should be discontinued before surgery due to surgical risks.

[b] Studies by Karuturi et al.[19,20] published in 2018 and 2019 were combined because they both used the same study population but different criteria to define PIM use.

[c] Beers criteria's drugs to avoid except for lorazepam, prochlorperazine, metoclopramide, and atropine–diphenoxylate.

Appendix Table A9. Follow-Up and Effect Size Data of Studies Investigating the Impact of Potentially Inappropriate Medication on Health Outcomes in Older Adults with Cancer

First Author, Year	PIM Criterion	PIM Prevalence (%)	Outcome	$N_{outcome}$	FUP	HR or OR (95% CI)	Adjusted Covariates		
							Age + sex[a]	Comor-bidity	Other
Hong et al, 2020[3]	Beers 2015 (avoid)	45.5	Hospitalization	123	30 days	1.40 (0.98-1.99)	-	-	-
Jeon et al, 2019[14]	PDRM[b]	57.5	Readmission after surgery	37	30 days	**2.18 (1.01-4.70)**	x	x	Multiple[c]
Lin et al, 2019[15]	Beers 2015 (all)	46	Delirium	112	100 days	**1.79 (1.22-2.65)**	-	-	Multiple[d]
			Fall	34	100 days	1.36 (0.69-2.66)	-	-	-
			Non-relapse survival	167	11.9 years	**1.54 (1.14-2.09)**	-	-	-
			Overall survival	298	11.9 years	**1.28 (1.02-1.6)**	-	-	-
Lin et al, 2018[17]	Beers 2015 (all)	47	Treatment delay and/or dose reduction	101	N.R.	1.95 (0.99-3.84)	-	-	Albumin at diagnosis, IPI
			Grade ≥ 3 CTCAE toxicity	112	N.R.	**2.91 (1.42-5.97)**[e]	-	-	Albumin at diagnosis
			Progression-free survival	N.R.	28 months[f]	**2.81 (1.36-5.81)**	-	-	WBC, IPI
			Overall survival	41	28 months[f]	**3.12 (1.49-6.52)**	x	-	WBC, IPI
Karuturi et al, 2018 and 2019_BC[g19,20]	HEDIS-DAE (avoid)	22.2	Emergency department visit	552	9 months	0.96 (0.78-1.18)	x	x	Multiple[i]
			Hospitalization	369	9 months	0.96 (0.75-1.23)	x	x	Multiple[i]
			Overall survival	34	9 months	**2.31 (1.07-4.96)**	x	x	Multiple[i]
			Composite outcome[h]	598	9 months	0.96 (0.79-1.17)	x	x	Multiple[i]
	Beers 2012 (all)	27.6	Emergency department visit	552	9 months	1.02 (0.85-1.24)	x	x	Multiple[i]
			Hospitalization	369	9 months	1.00 (0.79-1.26)	x	x	Multiple[i]
			Overall survival	34	9 months	1.86 (0.88-3.96)	x	x	Multiple[i]
			Composite outcome[h]	598	9 months	0.99 (0.82-1.19)	x	x	Multiple[i]
	STOPP criteria	39	Emergency department visit	552	9 months	N.S.	-	-	-
			Hospitalization	369	9 months	**1.28 (1.02-1.61)**	-	-	-
			Overall survival	34	9 months	N.S.	-	-	-
			Composite outcome[h]	598	9 months	1.07 (0.89-1.29)	-	x	Multiple[j]
Karuturi et al, 2018 and 2019_CRC[g19,20]	HEDIS-DAE (avoid)	15.5	Emergency department visit	621	9 months	0.99 (0.8-1.23)	x	x	Multiple[i]
			Hospitalization	450	9 months	1.02 (0.79-1.32)	x	x	Multiple[i]
			Overall survival	76	9 months	0.80 (0.40-1.59)	x	x	Multiple[i]
			Composite outcome[h]	687	9 months	0.96 (0.78-1.19)	x	x	Multiple[i]
	Beers 2012 (all)	24.8	Emergency department visit	621	9 months	0.96 (0.79-1.16)	x	x	Multiple[i]
			Hospitalization	450	9 months	1.01 (0.81-1.27)	x	x	Multiple[i]
			Overall survival	76	9 months	0.80 (0.40-1.59)	x	x	Multiple[i]
			Composite outcome[h]	687	9 months	0.96 (0.78-1.19)	x	x	Multiple[i]
	STOPP criteria	30.9	Emergency department visit	621	9 months	N.S.	-	-	-
			Hospitalization	450	9 months	N.S.	-	-	-
			Overall survival	76	9 months	N.S.	-	-	-
			Composite outcome[h]	687	9 months	1.11 (0.94-1.33)	x	x	Multiple[k]

First Author, Year	PIM Criterion	PIM Prevalence (%)	Outcome	$N_{outcome}$	FUP	HR or OR (95% CI)	Adjusted Covariates		
							Age + sex[a]	Comor-bidity	Other
Chun et al, 2018[21]	N.R.	30.2	Emergency department visit	504	6 months	0.95 (0.76-1.18)[l]	x	x	Multiple[m]
Choi et al, 2018[22]	Beers 2015 (avoid)	26.7	Post-discharge institutionalization	14	30 days	0.76 (0.21–2.78)	-	-	-
Samuelsson et al, 2016[26]	Socialstyrelsen criteria (drugs to avoid as long-term use)	22.5	Length of stay ≥ 10 days	N.R.[n]	30 days	**1.14 (1.00 -1.29)**	x	-	Multiple[o]
			Overall survival	368	30 days	**1.43 (1.11-1.85)**	x	-	Multiple[o]
Park et al, 2016[27]	Beers 2012 (all)	24.0	Grade ≥3 CTCAE toxicity	21	N.R.	1.30 (0.48-3.53)	-	-	-
			Length of stay > 1 month	20	1 month[p]	2.30 (0.89-5.95)	-	-	-
			Non-cancer health event[q]	68	2 years	1.35 (0.71-2.57)	-	-	-
Chiang et al, 2015[33]	Beers 2012 (all)	28.3 (in N=675)	30-day unplanned readmission	238	30 days	1.36 (0.94-1.99)	x	-	Multiple[r]
Maggiore et al, 2014[35]	Beers 2012 (avoid[s])	30.1 (in N=488)	Grade ≥3 CTCAE toxicity	258	598 days	0.97 (0.66-1.43)	-	-	-
			Hospitalization	109	598 days	1.01 (0.64-1.61)	-	-	-
	Zhan's classification (all)	10.8 (in N=498)	Grade ≥3 CTCAE toxicity	264	598 days	1.03 (0.59-1.82)	-	-	-
			Hospitalization	114	598 days	0.64 (0.31-1.37)	-	-	-
	HEDIS-DAE 2011 (avoid)	13.8 (in N=499)	Grade ≥3 CTCAE toxicity	265	598 days	0.90 (0.54-1.49)	-	-	-
			Hospitalization	115	598 days	0.67 (0.35-1.29)	-	-	-
	Combination of all 3 PIM criteria above	29.7 (in N=498)	Grade ≥3 CTCAE toxicity	264	598 days	0.98 (0.67-1.44)	-	-	-
			Hospitalization	114	598 days	1.01 (0.64-1.59)	-	-	-
Elliot et al, 2014[39]	Beers 2012 (all)	19	Overall survival	29	30 days	0.89 (0.31-2.58)	-	-	-
			Complete remission	71	132 days	0.96 (0.42-2.19)	-	-	-
			Intensive care unit stay	30	132 days	0.42 (0.12-1.51)	-	-	-
			Length of stay > 35 days	N.R.	132 days	0.87 (0.32-2.34)	-	-	-

Values in bold are statistically significant (p<0.05)

Abbreviations: avoid, drugs to avoid; BC, breast cancer; CI, confidence interval; CRC, colorectal cancer; CTCAE, Common Terminology Criteria for Adverse Effects; FUP, follow-up period; HEDIS-DAE, Healthcare Effectiveness Data and Information Set Drugs to Avoid in the Elderly; HR, hazard ratio; IPI, international prognostic index; long-term use; N.R., not reported; N.S., not significant; OR, odds ratio; PDRM, pre-operative discontinuation requiring medications; PIM, potentially inappropriate medication; STOPP, Screening Tool of Older Person's Prescriptions; WBC, white blood cell count at diagnosis.

[a] If the study population consisted only of males or females, no adjustment for sex is necessary and therefore a cross was made even if the study adjusted for age only.

[b] PDRM were defined as medications that should be discontinued before surgery due to surgical risks.

[c] Transfusion, gastrointestinal cancer, if the cancer stage is stage 4.

[d] Prior falls, platelet count on admission, creatinine clearance.

[e] OR was obtained from the meeting abstract being published before the main publication.

[f] Median follow up.

[g] Studies by Karuturi et al.[19,20] published in 2018 and 2019 were combined because they both used the same study population but different criteria to define PIM use.

[h] Composite outcome includes emergency department visit, hospitalization, and overall survival.
[i] Year of diagnosis, race, stage, poverty, education, number of baseline care providers, chemotherapy regimen, baseline emergency room visit/hospitalization.
[j] Year of diagnosis, poverty, education, number of care providers, chemotherapy regimen, baseline medications, cancer stage, and baseline emergency room visit/hospitalization.
[k] Year of diagnosis, poverty, education, number of care providers, chemotherapy regimen, race, and baseline emergency room visit/hospitalization.
[l] The original poster abstract reported an adjusted risk difference. The authors provided the OR and 95% CI shown in the table in reply to an inquiry from the review authors.
[m] Race, marital status, stage at diagnosis, claims-data based predicted frailty, medication burden.
[n] The number of cases with LOS ≥ 10 days was not reported but it can be estimated that almost half of the study population, which was n=7,279, had an LOS ≥ 10 days because the median LOS was 9 days in subjects without PIM and 10 days in subjects with PIM.
[o] American Society of Anesthesiologists classification of physical status class, type of surgical procedure, T stage, clinical stage, postoperative surgical complications, urgency of surgery
[p] The follow-up period lasted for at least 1 month.
[q] Defined as readmission to the hospital within 2 years after the initial treatment for any cause that was not directly related to the index cancer or newly developed second primary cancer.
[r] Race, Katz index feeding item, Lawton-housework questionnaire, reason for index admission.
[s] Beers criteria's drugs to avoid except for lorazepam, prochlorperazine, metoclopramide, and atropine–diphenoxylate.

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