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1 TITLE

2 Interactions with the pharmaceutical industry and the practice,  
3 knowledge and beliefs of medical oncologists and clinical  
4 haematologists: a systematic review.

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6

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100 ABSTRACT

101 Background: No previous review has assessed the extent and effect of industry interactions on medical  
102 oncologists and haematologists specifically.

103 Methods: A systematic review investigated interactions with the pharmaceutical industry and how  
104 these might affect the clinical practice, knowledge and beliefs of cancer physicians. MEDLINE, Embase,  
105 PsycINFO and Web of Science Core Collection databases were searched from inception to February,  
106 2021.

107 Results: Twenty-nine cross-sectional and two cohort studies met the inclusion criteria. These were  
108 classified into three categories of investigation: 1. Extent of exposure to industry for cancer physicians  
109 as whole (n=11); 2. Financial ties among influential cancer physicians specifically (n=11), and; 3.  
110 Associations between industry exposure and prescribing (n=9).

111 Cancer physicians frequently receive payments from or maintain financial ties with industry, at a  
112 prevalence of up to 63% in the United States (US) and 70.6% in Japan. Among influential clinicians,  
113 86% of US and 78% of Japanese oncology guidelines authors receive payments. Payments were  
114 associated with either a neutral or negative influence on the quality of prescribing practice. Limited  
115 evidence suggests oncologists believe education by industry could lead to unconscious bias.

116 Conclusions: There is substantial evidence of frequent relationships between cancer physicians and  
117 the pharmaceutical industry in a range of high income countries. More research is needed on clinical  
118 implications for patients and better management of these relationships.

119 Registration: PROSPERO identification number CRD42020143353

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129 INTRODUCTION

130 Almost a fifth of the global medication market will be anticancer drugs by 2024, more than four times  
131 the nearest competing therapeutic area.(1) Sales representatives from the pharmaceutical industry  
132 routinely approach medical oncologists and haematologists, the prescribers of these medications,  
133 who are described together here as ‘cancer physicians’. These interactions intend to affect prescribing  
134 practice and to maximize sales, which may have negative consequences for patient care.

135 Previous reviews have investigated the effect of these interactions on physicians in general. In 2000,  
136 Wazana found that physicians’ attitudes towards interactions with industry representatives were  
137 mainly positive and that most studies showed an association between exposure to industry  
138 interactions and behaviours favouring promoted drugs.(2) Lotfi et al showed more variable attitudes  
139 towards these interactions in low-middle income countries, albeit based on a limited available body  
140 of evidence.(3) Regarding prescribing practice per se, Wazana’s review showed consistent evidence  
141 for preferential and more costly prescribing following interaction with the pharmaceutical industry.  
142 Several subsequent systematic reviews supported these findings, demonstrating a general association  
143 between industry-provided information and payments and higher prescribing costs and frequency and  
144 lower prescribing quality.(4-7)

145 To our knowledge, following a literature and systematic review register search, no previous review  
146 has investigated the extent and effect of pharmaceutical industry interactions on the knowledge,  
147 beliefs or clinical practice of cancer physicians specifically. A review by Tibau et al showed in 2015 that  
148 reported rates of financial conflicts of interest for authors of clinical practice guidelines of anticancer  
149 drugs had increased over time, suggesting these interactions among practice-influencing clinicians are  
150 widespread and may lead to potential bias.(8) We performed a systematic review to investigate the  
151 extent of interactions with the pharmaceutical industry their effect on the clinical practice, knowledge  
152 and beliefs of cancer physicians.

153 METHODS

154 Protocol and registration

155 This review was pre-registered on the International Prospective Register of Systematic Reviews  
156 (PROSPERO) with the identification number CRD42020143353, with a limited protocol available  
157 online.(9) The full protocol is available on request to the corresponding author and includes additional  
158 details about pre-specified methods. We followed the Preferred Reporting Items for Systematic  
159 Reviews and Meta-Analyses (PRISMA) criteria in designing and reporting this study (see  
160 Supplementary Appendix [S1]).(10)

161 Eligibility criteria

162 The target population was defined as practising medical oncologists and haematologists globally,  
163 including residents training in these specialties specifically. The investigated intervention was any  
164 interaction with the pharmaceutical industry. We aimed to identify any study that assessed either an  
165 association between interactions and behaviour or a prevalence of these interactions. This was kept  
166 purposefully broad to maximize the number of included studies.

167 The interactions could be either financial or non-financial, as long as they involved some form of direct  
168 contact with the pharmaceutical industry or its sales representatives. The relevant comparator was  
169 either a lower level or absence of these interactions. All interventional and observational studies with  
170 quantitative results were included.

171 Where studies investigated effects of interactions, the primary outcomes were any examples of  
172 affected clinical practice (such as prescribing behaviour), knowledge or beliefs following interaction  
173 with the pharmaceutical industry. These could be either objectively assessed or self-reported.

174 Knowledge referred to differences in level of cancer physicians' knowledge about specific aspects of  
175 patient care associated with different levels of exposure to pharmaceutical industry interactions.  
176 Beliefs referred to self-reported attitudes around interactions with the industry, including the  
177 perceived benefits or harms of these interactions.

178 We excluded editorials, perspectives, letters to the editor, case series, case reports and qualitative  
179 studies such as interviews, semi-structured interviews and focus group analyses. We also excluded  
180 both narrative and systematic reviews. Our included studies were limited to those in English, French  
181 or Italian. Studies investigating medical students, interns and pre-vocational resident medical officers  
182 were excluded. We had no geographic or time limit, nor any setting (i.e. clinical versus non-clinical)  
183 restriction.

184 Information sources and search strategy

185 To obtain relevant articles, we performed a systematic search using the MEDLINE, Embase and  
186 PsycINFO databases via the Ovid interface, in addition to the Web of Science Core Collection from  
187 their inception to September 2019, with the initial searches carried out on 9 October 2019. An updated  
188 search of all databases was performed on 19 February 2021. Additional citations were sought through  
189 Google Scholar and via a pre-planned forward citation search of included studies.

190 The search strategies were designed using a combination of keywords and medical subheading (MeSH)  
191 terms, tailored to each database. Each strategy was reviewed by two specialist medical librarians

192 following the Peer Review of Electronic Search Strategies (PRESS) guidelines(11), and are reported in  
193 detail in the Supplementary Appendix (S2).

194 The criteria used in the search were purposefully broad, so as to minimize the risk of omitting any  
195 relevant articles. For example, the initial searches included all articles with physicians as participants,  
196 rather than limiting these to cancer physicians specifically. When studies were identified that were  
197 not found in the initial search, we performed an additional search using an initially omitted MeSH term  
198 and keyword combination ('exp "Conflict of Interest"/ and (conflict of interest or conflicts of  
199 interest).tw and exp Oncologists/') in the Ovid-based databases to ensure no further citations were  
200 missed. These terms were additionally included in the updated search.

#### 201 Study selection

202 A single reviewer (AP) screened all citations during the initial title and abstract screen to identify  
203 articles considered potentially suitable for inclusion. For the full-text screen of these, all papers were  
204 independently screened by five reviewers, working in pairs.

205 Prior to the full-text screen, we performed a pilot screen of five articles by all reviewers for calibration.  
206 When disagreement between two reviewers occurred during the formal full-text screen, a third  
207 reviewer independently adjudicated the final decision. We calculated Cohen's Kappa statistic to  
208 estimate inter-reviewer reliability for the decision to include a paper.

#### 209 Data collection process and extracted items

210 We extracted data from the included studies using the standardized data extraction headings for  
211 systematic reviews of aetiology and risk provided by the Joanna Briggs Institute (JBI) Reviewer's  
212 Manual.(12) Data were initially extracted by a single reviewer (AP) and confirmed by a second (BM).

213 In line with the JBI recommendations, relevant data from each study included baseline details about  
214 the study, its methodology and characteristics, dependent variable (outcomes), the data analysis  
215 methods used and the study results.

#### 216 Quality assessment

217 To assess the quality of individual studies, we used the critical appraisal tools provided by the JBI  
218 Reviewer's Manual. These assessments were performed independently by two reviewers (AP and BM)  
219 and investigated the studies as a whole rather than focusing on specific outcomes. Disagreements in  
220 the quality assessment were resolved by discussion, with no studies requiring third-reviewer  
221 adjudication, although this had been planned if necessary. Authors of any included studies were not  
222 involved in the selection, data extraction and quality assessment of these studies.(13-16) An external

223 reviewer (PD – see acknowledgements) was engaged for three studies to minimize bias in the  
224 assessments, as all other potential reviewer pairings involved either authors of or close professional  
225 relationships with the authors of these studies.(14-16)

#### 226 Summary measures and synthesis

227 We undertook a descriptive analysis of the included studies, presenting their characteristics, settings  
228 and populations. Given the heterogeneous and observational nature of all the identified studies, we  
229 were unable to produce any summary statistics of effect. Instead, we categorized the studies by their  
230 focus of investigation and discussed the results using a qualitative synthesis approach.

231 When articles included cancer physicians as a subgroup, we reported results for these participants  
232 only. If relevant, we additionally reported on comparisons between cancer physicians and other  
233 physician groups.

#### 234 Publication and sponsorship bias

235 We prospectively planned to look for both publication bias and sponsorship bias in the included  
236 studies as a whole. However, publication bias could not be assessed due to the lack of suitable studies  
237 for a meta-analysis required to perform inverted funnel plots of results against sample size. We  
238 collected data on funding sources and author conflicts of interest (if reported) for each included study.

## 239 RESULTS

### 240 Study selection

241 The search flow is displayed in Figure 1, including reasons for exclusion at the full-text review stage.  
242 Of the 5,150 unique articles identified through our searches, 31 reports met our inclusion criteria for  
243 the final qualitative analysis. The kappa statistic for the full-text screening was 0.730, considered  
244 substantial for inter-reviewer reliability.

Figure 1 here

245

### 246 Study characteristics

247 The characteristics of each study are described in Table 1. All identified studies were observational,  
248 with no assessments of planned interventions. All the studies were conducted retrospectively, and a  
249 majority (n=29) were cross-sectional studies with analysis carried out over a single time period. The  
250 remaining two were retrospective cohort studies.



251 Among the 31 study reports, we identified three broad categories of analysis: 1. Exposure  
252 assessments, or investigations of prevalence of exposure to the pharmaceutical industry for cancer  
253 physicians in general, predominantly through receipt of payments or attendance at events, as well as  
254 attitudes and beliefs around such exposure (n=11); 2. Financial ties among influential physicians  
255 specifically (trial and guideline authors), or investigations of potential bias in decision-making,  
256 predominantly through the conduct of clinical trials and clinical guidelines (n=11), and; 3. Prescribing  
257 outcome studies, or investigations of associations between industry exposure and prescribing (n=9).

#### 258 Quality assessment of studies

259 The quality assessments for each study are presented in the Supplementary Appendix (S3 and S4),  
260 showing results across each critical appraisal domain using the JBI Reviewer's Manual using  
261 McGuinness's *robvis* program.(17) The most frequent areas of concern for the quality appraisal were  
262 the non-identification of and control for confounders. The studies that conducted surveys were also  
263 limited by low response rates and use of non-validated survey instruments. Concerns around the  
264 interpretation of specific studies are discussed in detail below.

265

#### 266 Results of individual studies

267 The baseline characteristics of each study is described in Table 1. Summative descriptions of studies  
268 within each identified category are described below. Most studies (21 out of 31 [68%]) were based in  
269 the US, followed by Australia (5), Japan (3), Italy (1) and Canada (1). All studies were published from  
270 2007 onwards, with a majority (n=27) published from 2016 onwards.

Table 1 here
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271

#### 272 Category 1: Investigations of exposure to the industry among cancer physicians in general

Table 2 here
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273

274 As shown in Table 2, 11 studies directly analysed the frequency and types of exposure to the  
275 pharmaceutical industry, five with medical oncologist participants (18-22), one with haematologist  
276 participants (13) and five with both.(14, 15, 23-25) Three studies assessed industry payments made to  
277 all clinicians within the specialist subgroup.(20, 22, 23) These were widespread, with Marshall et al  
278 and Ozaki et al showing that 63% of US and 70.6% of Japanese medical oncologists received general  
279 payments in 2014 and 2016 respectively.(20, 22) In Australia, over a six month period between 2018

280 and 2019, 32% of medical oncologists and 31% of haematologists received non-research  
281 payments.(15) Among US clinicians active on Twitter, 72.4% received general payments in 2014.(24)  
282 Importantly, Inoue et al showed that between 2015 and 2017 80% of all payments made to US  
283 haematologists and oncologists were for non-research purposes.(25)

284 Two additional studies reported prevalence findings for payments, though the main findings of these  
285 papers related to associations with prescribing. Nonetheless, these showed that cancer physicians in  
286 the US receive payments at a higher prevalence than any other specialists.(26, 27) Similar findings  
287 were made for payments to Australian cancer physicians.(15) In addition, Behdarvand et al, Fabbri et  
288 al and Robertson et al all found evidence of oncology- and haematology-related industry-sponsored  
289 events in Australia occurring more frequently than or near the highest frequency of any subspecialty  
290 group.(13, 14, 21)

291 Attitudes around and prevalence of continuing medical education provided by the industry were  
292 assessed by DeCensi et al in Italy in 2017 and Lee et al in Australia in 2015.(18, 19) While limited by  
293 low response rates, both these studies showed widespread and poorly managed educational  
294 relationships with the industry. Most participants expressed a belief that they had adequate  
295 separation from industry, while concurrently most believed that unconscious bias in favour of a drug  
296 could arise from education sponsorship.

#### 297 Category 2: Investigations of financial ties among influential cancer physicians

Table 3 here
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298

299 As shown in Table 3, 11 studies analysed financial ties with the pharmaceutical industry among  
300 influential cancer physicians; nine with medical oncologist participants (16, 28-35), and two with  
301 haematologist participants (36, 37).

302 Six studies looked at the authors or editors of oncology or haematology trials or journals, to assess  
303 ties in these groups.(28, 30, 32, 34-36) These demonstrated financial relationships were reported by  
304 between 29 and 80% of clinicians, with one study showing that 79% of haematologists' financial ties  
305 were disclosed incompletely in published literature.(36) Medical oncologist authors were more likely  
306 than any other specialty to have financial ties, and incomplete disclosure of relationships in 32% of  
307 cases.(28, 34)

308 Five studies looked at financial ties among the authors of oncology clinical practice guidelines, leaders  
309 of representative societies and clinicians advocating for cancer drug funding, again consistently noting  
310 that these ties are widespread. (16, 29, 31, 33, 37) In 2014, 84% of National Comprehensive Cancer

311 Network guidelines authors for four common cancers received general payments, while 78.2% and  
312 95% of Japanese oncology and haematology guidelines authors respectively received non-research  
313 payments between January 1 2016 and September 30 2017.(31, 33, 37) Lexchin found that 66.3% of  
314 submissions to the pan-Canadian Oncology Drug Review had some declared conflict, and 44.5% of all  
315 submissions had a financial conflict with the submission's drug manufacturer between 2016 and  
316 2019.(29) Among oncologist leaders of the American Society of Clinical Oncology, approximately 80%  
317 received either general or research payments between 2017 and 2019.(16)

318 Category 3: Investigations of associations between industry exposure and prescribing

Table 4 here
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319

320 As shown in Table 4, nine studies assessed associations between pharmaceutical industry exposure  
321 and prescribing. Four of these had medical oncologist participants (27, 38-40), and five had both  
322 haematologists and oncologists.(26, 41-44) All were based in the US, and eight used the Open  
323 Payments database as an exposure against Medicare prescribing data as a dependent variable.

324 Four studies assessed potential associations between industry payments and prescription rates of  
325 anti-cancer drugs. Two studies showed a small or negligible association between payments and  
326 prescription rates, although quality assessments raised concerns about both of these due to the  
327 identification and control of confounders as well as the validity of the exposure assessment.(27, 38)  
328 Prescribing outcomes were measured one year prior to exposure assessments in both studies, raising  
329 concerns about the validity of the outcome assessment; the results of these studies should therefore  
330 be interpreted with caution.

331 In contrast, Mitchell et al assessed the effect of payments prior to prescriptions in two studies, with  
332 an analytical focus on general payments.(41, 43) In both of these, for almost all cancer subtypes tested  
333 there were higher odds of prescribing specific manufacturers' drugs when oncologists received  
334 general payments by that company, if these were received consistently in the years prior. A single  
335 negative association for imatinib was potentially explained by contemporaneous introduction and  
336 promotion of nilotinib, made by the same manufacturer for the same indication.

337 Three studies assessed the broad cost of prescriptions following industry payments. Perlis et al found  
338 that haematologists and oncologists, combined as one group, had the highest relative non-research  
339 payments received of any specialty, with prescription costs increasing in a statistically significant linear  
340 fashion across all five quintiles of payments.(26) Hadland et al and Zezza et al both investigated the  
341 relationship between payments and the costs of opioid prescriptions, with Hadland specifically looking

342 at non-research payments.(39, 42) Using different methodological approaches, both studies showed  
343 that cancer physicians who received payments related to opioids had higher overall opioid  
344 prescription costs, particularly when payments were consistent over several years. Hollander et al  
345 looked at opioid-related gifts rather than payments per se, and again found higher levels of opioid  
346 prescribing among haematologists and oncologists when a greater value of gifts was received.(44)

347 Eisenberg et al performed the only study assessing the effect of introducing institutional marketing  
348 restriction policies on subsequent opioid prescribing.(40) This showed a small (1%) but significant  
349 difference in the percentage days of opioid prescribing between the period before and after the  
350 introduction of the policies, although it is unclear how these policies were enforced across different  
351 centres, meaning these results should be interpreted with caution.

## 352 Synthesis of results

353 We did not perform any quantitative synthesis (i.e. meta-analysis). This was partly due to the majority  
354 of studies being observational in nature, without measures of effect, and partly due to the  
355 heterogeneous design of the few studies that did measure effect. We were additionally therefore  
356 unable to quantitatively estimate differences in the magnitude or direction of outcomes based on  
357 study quality.

## 358 DISCUSSION

### 359 Key findings

360 This systematic review found strong evidence that cancer physicians frequently receive both general  
361 and research payments from the pharmaceutical industry or maintain financial conflicts of interest.  
362 When compared to other specialties, studies consistently show that cancer physicians receive  
363 payments at the highest or near highest rate of any specialty group. We found further evidence that  
364 'key opinion leader' oncologists and haematologists (i.e. those whose positions within authoritative  
365 bodies are likely to influence broader practice) receive these payments at especially high amounts,  
366 suggesting a risk of bias internationally in the formation of clinical guidelines and high-impact journal  
367 publications.

368 Eight studies assessed prescribing practice of cancer physicians associated with payments from  
369 industry, and one looked at valuable gifts rather than payments. All of these found an association with  
370 prescribing, with either higher prescribing costs or preference for sponsors' drugs over others,  
371 particularly in the context of general payments. These findings are consistent with a recent review  
372 assessing the relationship between payments and physicians across all specialties.(7) All the assessed  
373 studies in this category in our review took place in the United States, which is explained by the greater

374 ease of accessing prescribing data in this study population for these drugs than other jurisdictions. No  
375 studies directly assessed patient outcomes, and only a single trial assessed the effect of limiting  
376 marketing on subsequent prescribing.(40)

377 Notably, all the studies of associations with prescribing practice related to drugs that are either orally  
378 or subcutaneously administered, due to limitations in the prescription data available for analysis. They  
379 did not assess prescription of intravenous anti-cancer medicines, including expensive novel agents  
380 such as immune checkpoint inhibitors.

381 Only two studies asked cancer physicians directly about their knowledge and beliefs around  
382 interactions with the industry, in Italy and Australia.(18, 19) The generalizability of both was limited  
383 by low response rates to the distributed surveys. Both suggested that oncologists believed that  
384 education by industry could lead to an unconscious bias in favour of the companies' products on the  
385 part of prescribers.

#### 386 Strengths and limitations

387 This is the first systematic review directly assessing relationships between the pharmaceutical industry  
388 and cancer physicians specifically. It was strengthened by our clear methodological approach in line  
389 with the Joanna Briggs Institute Reviewer's Manual. Our search strategy underwent review by  
390 academic librarians at two institutions to enhance its validity, following PRESS guidelines, and our  
391 reporting followed PRISMA guidelines.

392 However, the review had two major limitations. First, our initial title and abstract screen was  
393 performed by a single reviewer, which may have led to the inadvertent omission of relevant texts.  
394 Second, the review was limited by its specificity. By focusing directly on cancer physicians, studies  
395 were excluded in which cancer physicians were assessed but not reported as a specified subgroup.  
396 This therefore limited the breadth of results that could be included in the analysis.

397 It is additionally possible that some studies may have been missed due to the specificity of our search  
398 strategy, given that several studies were identified through the in-citation review, though the risk of  
399 this was minimised through our additional post-hoc search described in the Methods. All studies  
400 identified also occurred in high-income countries, limiting the applicability of the results to low and  
401 middle income countries.

#### 402 How results relate to other data

403 The findings of this study are consistent with previous systematic reviews assessing relationships  
404 between the industry and physicians in general.(2-6) However, this review has demonstrated that

405 relationships with the industry are more common and more lucrative for cancer physicians than other  
406 specialty groups. It has additionally identified that 'key opinion leader' cancer physicians are specific  
407 targets of influence for the industry.

#### 408 Meaning of results

409 This review has shown consistent evidence that cancer physicians are targeted by the pharmaceutical  
410 industry, and often more intensively than other specialists, and some evidence that there is a high  
411 likelihood their prescribing is influenced as a result. The results also demonstrate that cancer  
412 physicians frequently either have little awareness of this, or little resolve to alter their behaviour. The  
413 mandatory disclosure of payments from industry in several jurisdictions internationally has exposed  
414 ethically dubious relationships. While there is some evidence to suggest disclosing payments may lead  
415 advisors to avoid these,(45) there are no real world data so far that suggest disclosures have led cancer  
416 physicians to reduce their acceptance of payments from the pharmaceutical industry.

417 There is therefore a need for policy to manage these relationships. At the very least, cancer physicians  
418 in influential positions, such as guideline authors and journal editors, should be discouraged or  
419 prohibited from accepting general payments from industry. At least one previous study suggested that  
420 US Food and Drug Administration Oncology Drug Advisory Committee recommendations are not  
421 associated with financial conflicts of interest, although its interpretation is limited by an unclear  
422 number of clinicians on the Committee.(46)

#### 423 Implications and future research

424 This is an area of ongoing research and investigation. No studies assessed the effect of industry  
425 interactions in a controlled, randomized manner, and only a single study looked at behaviour change  
426 following alteration of institutional policies.(40) While not impossible, performing a randomized trial  
427 would be practically very difficult, as the research question is one of unconscious behaviour in the  
428 standard practice of independent practitioners. Notably, controlled trials have been used in other  
429 specialties to assess the role of educational interventions on subsequent behaviour, for example in  
430 psychiatry residents.(47)

431 A reasonable alternative would be to perform further trials of mandated decreased interaction with  
432 industry, such as the Eisenberg study, with a focus on lucrative anti-cancer drugs rather than opioids.  
433 This review also demonstrated a clear paucity of quantitative research exploring the knowledge and  
434 beliefs of cancer physicians. If issues with recruitment could be overcome, studies could be performed  
435 to understand why cancer physicians as a group interact with the industry to such an extent. This  
436 would be valuable to help formulate management policies globally.

437 Conclusions

438 The power of cancer physicians to prescribe anti-cancer medicines is more lucrative to the  
439 pharmaceutical industry than any other specialty group. It is therefore imperative to understand how  
440 the industry attempts to influence these physicians, so that later research can focus on strategies to  
441 avoid or, at minimum, manage these interactions to the benefit of patient care.

442 In this review, consistent evidence was found internationally that cancer physicians maintain financial  
443 conflicts of interest with the pharmaceutical industry, particularly when in positions that are likely to  
444 influence wider practice. Additional evidence was found that these interactions are likely to affect  
445 prescribing practice in a negative way. There is limited evidence that cancer physicians acknowledge  
446 and understand that interactions with industry may lead to bias, but no studies assessed or discovered  
447 any intent to change the current level of interactions that occur. More studies are needed to  
448 investigate how these interactions affect practice.

449

450 ADDITIONAL INFORMATION

451 ACKNOWLEDGEMENTS

452 Thank you to Dr Patrick Donald, medical oncologist, Darwin, Australia, for his assistance in assessing  
453 the quality appraisal of three included studies.

454 AUTHORS' CONTRIBUTIONS

455 All authors contributed to the protocol development, selection of studies, interpretation of data and  
456 final manuscript. AP undertook the literature searches and extracted data. AP, BM and AF performed  
457 the quality appraisals.

458 ETHICS APPROVAL

459 No ethics approval was necessary as all data analysed exist in the public domain.

460 DATA AVAILABILITY

461 No additional data available.

462 COMPETING INTERESTS

463 In 2020, Barbara Mintzes acted as an expert witness for Health Canada in a legal case related to  
464 marketing of an unregistered product in Canada. There are no other conflicts to declare.

465 FUNDING INFORMATION

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591 FIGURE AND TABLE LEGENDS

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Figure 1: PRISMA flow diagram
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Table 1: Characteristics of included studies
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Table 2: Prevalence of industry exposure among cancer physicians in general: key results.
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Table 3: Financial ties among influential cancer physicians (authors of clinical trials and guidelines): key results.
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Table 4: Associations between industry exposure and prescribing: key results.
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