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Conflict of interest among Italian medical oncologists. A national survey

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Original Article: **Conflict of interest among Italian medical oncologists. A national survey.**

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ARTICLE SUMMARY

ABSTRACT 300

Objective

To assess the Italian medical oncologist's opinion regarding the implications of conflict of interest (COI) on medical education, care and research and to evaluate their direct financial relationships.

Design

National survey conducted between March and April 2017 among Italian oncologists.

Setting

Online survey sponsored by the Italian College of Medical Oncology Chiefs through its web site.

Participants:

Italian oncologists who filled out an anonymous questionnaire including 19 items and individual and working characteristics.

Main outcome measures

The proportion of medical oncologists perceiving COI as an outstanding issue and those receiving direct payments from industry.

Results

The number of responders were 321, representing 13% of Italian tenured medical oncologists. Overall, 62% declared direct payments from pharmaceutical industry in the last 3 years. Sixty-eight percent felt the majority of Italian oncologists have a COI with industry but 59% suppose this is not greater than that of other specialties. Eighty-two percent consider that most oncology education is supported by industry. More than 75% believe that current allocation of industry budget on marketing and promotion rather than research and development is unfair but 75% consider appropriate to receive travel and lodging hospitality from industry. A median net profit margin of 5.000€ per patient enrolled in an industry trial was considered appropriate for the employee institution. Sixty percent agree to receive a personal fee for patients enrolled in industry trials but 79% state this should be reported in the informed consent. Over 90% believe that scientific societies should publish a financial report of industry support. Finally, 79% disagree to be co-author of an article written by a medical writer when no substantial scientific contribution is made.

Conclusions

Among Italian oncologists COI is perceived as an important issue influencing costs, education, quality of care and science. A more careful policy on COI should be discussed.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first national survey ever performed by Italian oncologists and one of the few prompted by medical stakeholders on their conflict of interest and physician-industry relationships in Europe.
- The sample size of 321 is quite large, as it represents 13% of 2,260 tenured Italian certified medical oncologists from the 319 Units of the country, making the results of the survey generalizable.
- Another strength of the questionnaire is its anonymous form which favored the disclosure of financial relationships with industry and an open attitude by respondents, an unprecedented opportunity for transparency.
- The study has limitations, including the non-random selection of the respondents and the greater representation of chiefs of staff compared with the overall population of medical oncologists.

INTRODUCTION

A conflict of interest (COI) exists when professional judgment concerning a primary interest such as patients' welfare or the validity of research may be influenced by a secondary interest such as financial gain or career advancement. Financial relationships between industry and physicians and/or researchers are common and may be direct, consisting of stock options, advisory fees, honoraria, speaking fees, travel and lodging expenses, or indirect, such as research support to researchers institutions. COI increasingly affects every aspect of medicine, including care, education, research integrity, patient trust, guideline formulation, regulatory approval and scientific prominence.[1-7]

Collaboration between industry and clinicians and/or researchers creates challenges and opportunities. While these relationships are essential to advancement to the field, there is a need to better understand the positive and negative consequences of COI and how best to report and manage it. Systematic reviews have found that pharmaceutical industry- sponsored studies are more often favorable to the sponsor's product compared with studies having other sources of sponsorship.[4,5] Public opinion on physician–pharmaceutical industry interactions differs depending on context and specific country health care models[8,9], but some studies suggest a significant level of concern regarding interaction involving direct financial benefit to physicians.[9,10]

In medical oncology, financial relationships have increased through the years and have influenced clinical research, scientific prominence and visibility.[11,12] The issue is particularly important given the increasing volume of investments made by the pharmaceutical industry in cancer treatment.[13] In this escalating prize system[14], pharmaceutical companies tend to spend much more for marketing and promotional activities than for research and development.[15,16] Evaluation of the clinical benefits that oncology drugs offer as a function of their cost has become complex and for some clinical

indications, health benefits are diminishing over time[17], do not follow criteria of innovation[18], and provide increasing financial toxicity to patients.[19] There is concern that the substantial increase in drug prices may hamper both the universal and private health care system sustainability in many countries[14, 20-22] and is also of concern to top managers of pharmaceutical industries.[23]

The debate on COI has received attention in the US since the introduction of the Physician Payments Sunshine Act (PPSA), which requires health care product manufacturers to report to the federal government payments of more than $10 to physicians. Bringing transparency, PPSA may provide trustful patient physician relationships and medical professionalism, but has received mixed opinions among physicians and experts in the field.[24,25] Conversely, little is known about the opinion of medical stakeholders from universal health systems such as those in Europe. A recent survey conducted in Italy showed that industry sponsorship of medical conferences is common, while the presence of a structured regulatory system is not. Disclosure of industry funding to medical societies was very limited.[26]

To ascertain the Italian situation, we assessed the opinion of Italian medical oncologists on different aspects and implications of COI in a national survey.

METHODS

The Italian College of Medical Oncology Chiefs (CIPOMO) set up an online national survey of its members. CIPOMO accounts for 184 chiefs of hospital oncology divisions/departments. Medical oncologists working in research institutions and university hospitals do not belong to CIPOMO but were not excluded from the survey. Members of CIPOMO were invited to complete the online survey and spread the survey among their collaborators with the intent to also involve young collaborators.

The questionnaire was authored by three members of CIPOMO and reviewed by eight members of the CIPOMO board of directors. After approval, the questionnaire was written using the "Surveymonkey" platform (www.surveymonkey.com) and presented on line from March 1 to April 15, 2017. CIPOMO members were reminded to complete the survey through three repeated email messages. Completion of the survey was anonymous although baseline information (country area, age, sex, duration of oncology experience, type of institution and position) was requested before proceeding.

The survey was composed of 19 questions investigating feelings, opinions and experience of the respondents on different aspects of COI (Figure 1, table 4 and text). These include the following areas: the influence of COI in medical oncology and drug pricing; influence of the drug industry on continuous medical education; the percentage of direct payments from industry; the acceptability of travel and lodging coverage by the industry and per patient fee for clinical trials and its disclosure in the informed consent; the payment amount of per patient fee to the institution for a trial; the role of disclosure as a deterrent of COI; the influence of COI on scientific societies; the influence of COI on drug prescription; the opinion on ghost writing in scientific articles.

Respondents were requested to quantify in a 4-point Likert scale the extent to which they agreed with the proposed questions or statements. In the analysis, 17 answers were grouped to facilitate understanding of results (i.e., "strongly agree" plus "agree" *versus* "strongly disagree" plus "disagree"). One item on net profit margin led to an answer as a continuous variable, whereas another item on direct payment was dichotomized (Yes, No).

Statistical analysis

Answers were collected by the online platform and transformed in a data sheet for analysis. Usual descriptive statistics were used to show both the respondent characteristics and the general results. Moreover, an exploratory analysis for subgroups was performed considering the following

explicative variables: geographic area (north, center, south), sex (male, female), age (< 45, 45-59, ≥ 60 years), place of work (hospital, university, research institute, other), nature of institution (public, private), job position (assistant chief, chief, other), years of oncology experience (< 15, ≥ 15), direct payment from industry in the last 3 years (No, Yes). All answers to the questionnaire items were in turn used as dependent variables. Due the explorative purpose of analysis, no adjustment for the Bonferroni's inequality was made. Given the cross-sectional study nature where the responders were not randomly chosen, bidirectional chi-square tests assuming alpha=0.05 as significance level were calculated to provide a measure of the strength of association and not with inferential purposes.

RESULTS

The responders were 321, from all 20 Italian regions, representing 13% of 2,260 tenured Italian certified medical oncologists from the 319 Units of the country, according to the White Book of the Italian Association of Medical Oncology.[27] The respondent characteristics are summarized in Table 1. They reflect the main characteristics of the Italian population of oncologists, with the majority of them employed in northern Italy, having equal sex distribution, a third being aged 45 years or younger and working predominantly in public hospitals. However, there was a greater proportion of chiefs of staff because of the nature of the study sponsor.

The questionnaire and answers concerning the COI are described in Figure1. Over two- thirds (68%) believe the majority of Italian oncologists have a COI with industry. A subgroup analysis indicates a greater proportion of believers among females, younger physicians, assistant chiefs and those who did not receive payments from industry in the last 3 years ($p<0.05$, table 2). However, 59% assume the COI in oncology is not greater than in other medical specialties.

Overall, 62% declared general payments from the pharmaceutical industry in the last 3 years, with a significantly greater proportion among those living in southern Italy, males, oncologists working in research institutes and chiefs of staff ($p<0.05$, table 3).

Eighty-one percent believe that most oncology education is supported by industry, with a greater proportion among older physicians and chiefs of staff ($p<0.05$), but over 70% think their continuous medical education (CME) should be supported by their institution or public sources and only less than 10% and 20% think it should be paid for by themselves or the industry, respectively (Table 4). The vast majority stated their first CME tool is scientific journals (89%), but 14% use pharmeceutical representatives as the main CME method.

Furthermore, 54% of the medical oncologists consider inappropriate to organize a scientific meeting within his/her facility with an opinion leader chosen by a pharmaceutical company, especially in the north and among the chiefs of staff ($p<0.05$).

About 77% believe that the greater allocation of budget put by industry on marketing and promotion relative to research and development is inappropriate, with a greater proportion of supporters among younger physicians and non-chiefs of staff ($p<0.05$), but 75% of all respondents consider it appropriate to receive travel and lodging hospitality from industry to attend international meetings, with a significantly greater proportion of supporters among those receiving direct industry payments ($p<0.05$).

A median net profit margin of 5,000€ (mean±SD=9,888±10,414€) per patient enrolled in a trial was considered an appropriate amount for the investigator's institution, although the distribution had a long tail towards higher values.

Sixty percent would agree to receive a personal fee for each patient enrolled in an industry sponsored trial, with a greater proportion among those who received payments from industry ($p<0.05$), but 79% state this should be reported in the patient's informed consent.

Nearly 60% think that disclosing a COI with different companies who are competitors is not a guarantee of impartiality and 71% believe that COI disclosure does not attenuate the risk of scientific bias. However, 48% of those working in private institutions *versus* 27% of those working in public institutions believe that COI disclosure attenuates the problem ($p<0.05$).

Over 90% believe that scientific societies should have a COI policy and that a detailed report of the financial support by the industry should be published annually. A total of 58% believe that industry support does not influence topic selection in meetings and 61% believe that giving an invited speech by industry does not influence their drug prescription. However, a higher proportion of male and older physicians feel that prescription is influenced by direct industry payments ($p<0.05$).

Finally, 79% see as unfair to being co-author of an article written by a medical writer for an industry-sponsored trial when no substantial scientific contribution is made. However, 25% of those receiving industry payments believe this is appropriate *versus* 15% of those who did not ($p<0.05$).

DISCUSSION

With the introduction of the Open PPSA and the increasing costs of healthcare, the debate on financial COI has received a great deal of attention in the USA.[1,24,25,28] However, a direct perspective by medical stakeholders on this matter is still unclear, particularly in Europe.

The main findings from this anonymous questionnaire indicate that two-thirds of Italian medical oncologists believe that COI is a relevant issue, with a higher perception among females, young physicians, assistant chiefs of staff and those not receiving industry payments in the last 3 years. Although nearly 60% suppose this is not a greater issue in oncology than in other medical specialties, this does not mitigate the potential impact of the problem. Secondly, 62% of the sample declared direct payments from the pharmaceutical industry in the last 3 years, with a greater frequency in southern Italy, research hospitals, chiefs of staff and male physicians.

Over 80% confirm that most oncology education and training is financially supported by industry, with a greater proportion of followers among older physicians and chiefs. Subgroup analyses also show there is a greater awareness of COI as a problem among women and young doctors, who are also among those categories receiving fewer payments from industry. While it is difficult to establish a causal relationship between increased awareness and lower frequency of payments (the younger and female physicians groups might have a more idealistic attitude), the gender disparity in industry relationships is a well-known phenomenon. In recent American analyses, only one-quarter of physicians receiving payments were female, who, on average, also received less money per person than men.[29] In our study, 70% of male *versus* 53% of female physicians received direct payments from industry for speaking fees in the last 3 years. This percentage is in line with that reported by a recent survey through the open payment act in the US, where 63% of oncologists received a general payment in 2014.[30] Oncologists were also more likely to receive a general payment and to hold ownership interest compared with non-oncologists.[30]

Another important source of funding from industry is research. Interestingly, while 60% of physicians agree to receive a percentage fee for every patient enrolled in an industry- sponsored trial, nearly 80% are favorable to disclose it in the patient's informed consent. This is a significant inclination towards transparency among our professional community that has not yet been translated in regulatory acts by the current legislation of clinical trials. This is also important because physician payment for study participation in clinical trials is a potential COI that can adversely affect patient trust.[10,31]

The median net margin for the employee institution that was considered balanced for each patient enrolled in an industry trial was 5,000€, which appears significantly lower than the current level of industry per-patient fee, whose gross fee may now easily exceeds 30,000€. The vast majority of respondents is also contrary to the current escalating trend to spend more for marketing and promotion than for research and development by the industry, a notion which is rarely openly

declared by industry.[15,16] These considerations suggest that the surveyed sample is aware that the current trend to increasing costs has a negative impact also on quality of care once the drug is licensed. In the United States, cancer patients carry rising burdens of healthcare-related out-of-pocket expenses, and a growing number of patients are considered underinsured. To save money, a large proportion of these patients take less or nothing of the prescribed medications, a phenomenon known as financial toxicity which is present also in Italy.[19-32]

Nearly 80% see as unfair being co-author of an article written by a medical writer for an industry-sponsored trial when no substantial scientific contribution has been made. This is in contrast to the present tendency of most industry-sponsored trials to be reported by medical writers, often in concomitance with presentation at premier international meetings.[11] The legal and ethical consequences of ghost writing, including risk of plagiarism and loss of professionalism and genuine intellectual contribution to advancement of science, is a subject of intense debate[33,34]

Over 70% of the oncologists think their CME should be supported by their institution or public sources and less than 10% by personal resources. The vast majority stated their first CME tool is scientific journals but nearly 15% use industry sales representatives as the main CME method. These findings are in line with the public landscape of our national health system stakeholders, where CME is considered a right that should be covered by public resources and not a duty to be at least partially covered with physician resources. Three quarters of Italian oncologists would agree to be financially supported by industry for travel and lodging at international meetings, another important source of industry expenditures. It is possible that this form of financial support is perceived as less conflicting and the only way to attend important meetings given the scarcity of public or private no-profit funding.

Interestingly, over 70% believe that COI disclosure during presentations does not attenuate the risk of scientific bias. However, approximately 60% believe that industry support does not influence

topic selection at meetings and that giving invited speeches does not influence personal drug prescription.

Another important issue raised by our survey is the call for a higher level of transparency by scientific societies, including annual detailed reporting of industry payments. Prior studies have shown that disclosure of COI among Italian scientific societies does not attenuate the problem but actually seems to be a justification to increase financial relationships.[26]

The consequences of financial COI on patient perception has been the subject of recent studies.[8,10,35] In an ASCO survey of COI policies, the majority of non-physician stakeholders and patient advocates felt that full disclosure of COI by physicians was expected and could be a factor in patients' decisions regarding therapy.[36]

Altogether, the answers to the survey clearly show that the economic direct relationship between clinicians and industry is deeply rooted in current practice. Money from industry regularly flows as the result of declared marketing investments in the context of legal pathways. The hidden question is whether a clinician who receives financial support for so many activities in his profession can be impartial and objective in making clinical decisions. This is particularly true in all those clinical settings where uncertainties on the added value of new drugs make treatment choices questionable.[17,18,20-22]. Most recent evidence indicates that the majority of registered cancer drugs in Europe by EMA do not show a benefit in term of survival or quality of life[37], indicating the necessity of raising the evidence bar before market approval[38]. Moreover, in a recent analysis on 10 approved cancer drug in the US, the median cost to develop a drug was $648.0 million, a figure significantly lower than prior estimates, and the revenue since 4 years of approval was substantial (median, $1658.4 million; range, $204.1 million to $22 275.0 million)[39], suggesting the need for a global reconsideration of the pricing system especially in universal health systems.

To our knowledge this is the first national survey ever performed by Italian oncologists and one of the few prompted by medical stakeholders on their COI and physician-industry relationships. The questionnaire in an anonymous form has probably favored the disclosure of financial relationships with industry and an open attitude by respondents, an unprecedented opportunity for transparency. The study has limitations, including the non-random selection of the respondents and the greater representation of chiefs of staff. A strength of our study is the large sample size which reflects the general characteristics of medical oncologists in Italy.[27]

In conclusion, our study indicates that among Italian oncologists COI is perceived as an important issue influencing education, quality of care, science and costs. The overall view on COI calls for a process of rethinking of the relationship between clinicians and industry and, most importantly, a courageous step toward transparency. The surveyed clinicians, particularly younger and female physicians, do not argue against the role of physician- industry relationships but seem to disagree with the tendency toward direct financial relationships and low degree of transparency. Our findings suggest the need for a systematic approach in which all stakeholders in the health professions work together to protect professional judgment and integrity while advancing progress. In the present context of increasing health care costs and financial toxicity, alternative ways to support education and research and strict transparency policies could contribute to increased patient trust and equity in heath care access.

What is already known on this topic?

Several studies have shown that financial conflict of interest increasingly affects every aspect of medicine, including care, education, research integrity, patient trust, guideline formulation, regulatory approval and scientific prominence. This is particularly relevant in medical oncology given the large industry investment and increasing drug costs in the field. However little is known about the medical perception and experience of the problem, particularly in Europe.

What this study adds?

Of a total of 321 Italian oncologists who were surveyed anonymously, 68% felt the majority of them have a conflict of interest and 62% self declared direct payments from the pharmaceutical industry in the last 3 years. However, conflict of interest is perceived as an important issue influencing education, quality of care, research and costs. The majority also disagree with direct payments and call for a higher degree of transparency and a more stringent policy on conflict of interest..

Table 1. Main respondent characteristics

	***No.* (%)**
Geographic Area	
North	161 (50.2%)
Center	108 (33.6%)
South	52 (16.2%)
Age in years	
< 45	103 (32.1%)
45 - 59	133 (41.4%)
≥ 60	85 (26.5%)
Sex*	
Male	170 (53.3%)
Female	149 (46.7%)
Place of Work	
Hospital	283 (88.2%)
University	20 (6.2%)
Research Institute	11 (3.4%)
Other	7 (2.2%)
Nature of Institution	
Public	296 (92.2%)
Private	25 (7.8%)
Job Position	
Assistant Chief	190 (59.2%)
Chief	98 (30.5%)
Other	33 (10.3%)
Years of Experience	
<15	88 (27.4%)
≥15	233 (72.6%)
Direct payment from industries in the last 3 years*	
No	120 (37.6%)
Yes	199 (62.4%)

*Two oncologists did not answer the question

Table 2. Subgroup analysis on question # 1: Do you believe most oncologists have direct conflict of interests with pharmaceutical companies?

	Disagree		**Agree**		***P* < ***
	no.	**%**	**no.**	**%**	
Country area					
North	112	69.6	49	30.4	0.440
Center	68	63.0	40	37.0	
South	37	71.2	15	28.8	
Sex					**0.001**
F	84	56.4	65	43.6	
M	131	77.1	39	22.9	
Age					0.057
< 45	61	59.2	42	40.8	
45 — 59	92	69.2	41	30.8	
≥ 60	64	75.3	21	24.7	
Workplace					
Research Institute	9	81.8	2	18.2	0.583
Hospital	189	66.8	94	33.2	
University	15	75.0	5	25.0	
Other	4	57.1	3	42.9	
Type of structure					0.350
Private	19	76.0	6	24.0	
Public	198	66.9	98	33.1	
Job position					**0.021**
Assistant chief	119	62.6	71	37.4	
Chief	77	78.6	21	21.4	
Other	21	63.6	12	36.4	
Years of experience					**0.023**
< 15	51	58.0	37	42.0	
≥ 15	166	71.2	67	28.8	
Direct payments from industry					**0.029**
No	72	60.0	48	40.0	
Yes	143	71.9	56	28.1	

*Referred to bidirectional chi-square test

Table 3. Subgroup analysis on the question: "Have you received any payment to speak at educational meetings sponsored by a pharmaceutical company in the last 3 years?"

	No		Yes		*P* < *
	no.	**%**	**no.**	**%**	
Country area					**0.002**
North	57	35.4	104	64.6	
Center	52	49.1	54	50.9	
South	11	21.1	41	78.9	
Sex					
F	69	46.6	79	53.4	**0.002**
M	51	30.0	119	70.0	
Age					0.715
< 45	41	39.8	62	60.2	
45 — 59	50	38.2	81	61.8	
≥ 60	29	34.1	56	65.8	
Workplace					**0.003**
Research Institute	0	0.0	11	100.0	
Hospital	106	37.6	176	62.4	
University	8	42.1	11	57.9	
Other	6	85.7	1	14.3	
Type of structure					0.493
Private	11	44.0	14	56.0	
Public	109	37.1	185	62.9	
Job position					**0.016**
Assistant chief	72	38.3	116	61.7	
Chief	29	29.6	69	70.4	
Other	19	57.6	14	42.4	
Years of experience					0.314
< 15	37	42.0	51	58.0	
≥ 15	83	35.9	148	64.1	

*Referred to bidirectional chi-square test

Table 4. Role of public entities and private industry on continuous medical education (CME) support.

	***No.* of important or very important score 4+5 (%)**
Questions	
1. Which method do you primarily use for your CME? You can select multiple choices and attribute different scores from "not at all important" (1) to "very important" (5).	
Medical websites	185 (60.8)
Scientific journals	278 (89.1)
CME courses	181 (59.5)
Conferences	211 (67.4)
Pharmaceutical representatives	42 (13.7)
Books	62 (20.9)
2. Who should pay for your CME? You can select multiple choices and attribute different scores from "not at all important" (1) to "very important" (5).	
- Myself	27 (9.3)
- Hospital	256 (83.1)
- Public Institutions	211 (70.3)
- Pharmaceutical companies	51 (17.3)
- Research Foundations	140 (48.1)

Figure Legend. Figure 1: Questions and answers evaluated with a 4-point Likert scale on CoI (%)

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Contributors

ADC, GN, FR: idea, planning data set, data analysis, wrote the manuscript.

EB, BR, VL: planning data set, statistical analysis, wrote the manuscript.

FA, LF, CV: discussion of results.

MT, MC: discussion of results, standing funding.

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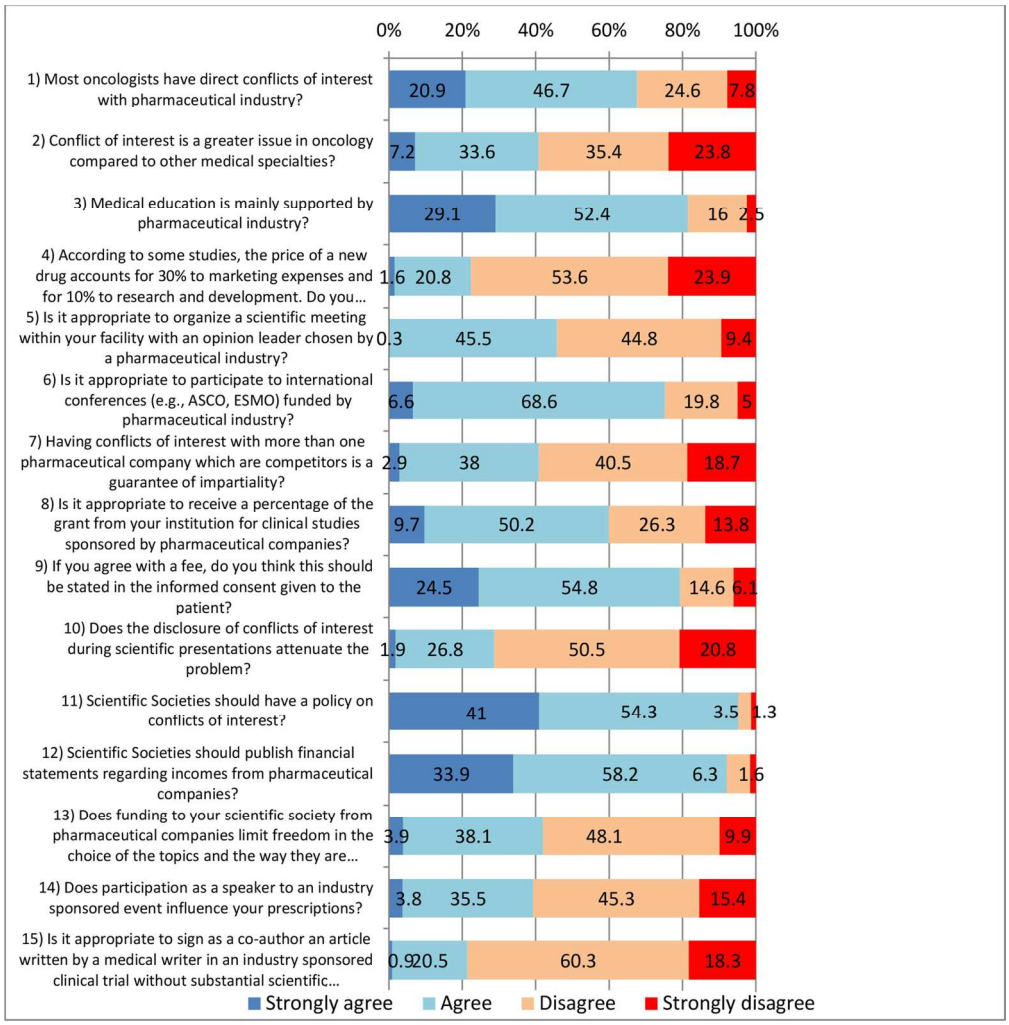

Figure 1: Questions and answers evaluated with a 4-point Likert scale on CoI (%)

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Conflict of interest among Italian medical oncologists. A national survey

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Original Article: **Conflict of interest among Italian medical oncologists. A national survey.**

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ARTICLE SUMMARY

ABSTRACT 300 words

Objective

To assess the Italian medical oncologist's opinion regarding the implications of conflict of interest (COI) on medical education, care and research and to evaluate their direct financial relationships.

Design

National cross-sectional survey conducted between March and April 2017 among Italian oncologists.

Setting

Online survey sponsored by the Italian College of Medical Oncology Chiefs through its web site.

Participants:

Italian oncologists who filled out an anonymous questionnaire including 19 items and individual and working characteristics.

Main outcome measures

The proportion of medical oncologists perceiving COI as an outstanding issue and those receiving direct payments from industry.

Results

The number of responders were 321, representing 13% of Italian tenured medical oncologists. Overall, 62% declared direct payments from pharmaceutical industry in the last 3 years. Sixty-eight percent felt the majority of Italian oncologists have a COI with industry but 59% suppose this is not greater than that of other specialties. Eighty-two percent consider that most oncology education is supported by industry. More than 75% believe that current allocation of industry budget on marketing and promotion rather than research and development is unfair but 75% consider it appropriate to receive travel and lodging hospitality from industry. A median net profit margin of 5.000€ per patient enrolled in an industry trial was considered appropriate for the employee institution. Sixty percent agree to receive a personal fee for patients enrolled in industry trials but 79% state this should be reported in the informed consent. Over 90% believe that scientific societies

should publish a financial report of industry support. Finally, 79% disagree to being co-author of an article written by a medical writer when no substantial scientific contribution is made.

Conclusions

Among Italian oncologists COI is perceived as an important issue influencing costs, education, care and science. A more rigorous policy on COI should be implemented.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first national survey performed by Italian oncologists and one of the few prompted by medical oncologists regarding their conflict of interest and physician-industry relationships in Europe.
- The sample size of 321 is quite large, as it represents 13% of the 2,260 tenured Italian certified medical oncologists from the 319 Units of the country, making the results of the survey well founded.
- Another strength of the questionnaire is its anonymous form which favored the disclosure of financial relationships with industry and an open attitude by respondents.
- The study has limitations, including the non-random selection of the respondents and the greater representation of chiefs of staff compared with the overall population of medical oncologists.

INTRODUCTION

A conflict of interest (COI) exists when professional judgment concerning a primary interest such as patient welfare or the validity of research may be influenced by a secondary interest such as financial gain or career advancement. Financial relationships between industry and physicians and/or researchers are common and may be direct, consisting of stock options, advisory fees, honoraria, speaking fees, travel and lodging expenses, or indirect, such as research support to researcher's institutions. COI increasingly affects every aspect of medicine, including care, education, research integrity, patient trust, guideline formulation, regulatory approval and scientific prominence.[1-7]

Collaboration between industry and clinicians and/or researchers creates challenges and opportunities. While these relationships may contribute to advancement in the field, there is a need to better understand the negative consequences of COI and how best to report and manage it. Systematic reviews have found that pharmaceutical industry- sponsored studies are more often favorable to the sponsor's product compared with studies having other sources of sponsorship.[4,5] Public opinion on physician–pharmaceutical industry interactions differs depending on context and specific country health care models[8,9], but some studies suggest a significant level of concern regarding interaction involving direct financial benefit to physicians.[9,10]

In medical oncology, financial relationships have increased through the years and have influenced clinical research, scientific prominence and visibility.[11,12] The issue is particularly important given the increasing volume of investments made by the pharmaceutical industry in cancer treatment.[13] In this price increase strategy[14], pharmaceutical companies tend to spend much more for marketing and promotional activities than for research and development.[15,16] Evaluation of the clinical benefits that oncology drugs offer as a function of their cost has become complex and for some clinical

indications, health benefits are diminishing over time[17]. Moreover, these benefits do not always follow criteria of innovation[18] and provide increasing financial toxicity to patients.[19] There is concern that the substantial increase in drug prices may hamper both universal and private health care systems sustainability in many countries[14, 20-22] , while this is also of concern to top managers of pharmaceutical industries.[23]

The debate on COI has received attention in the United States since the introduction of the Physician Payments Sunshine Act (PPSA), which requires health care product manufacturers to report payments of more than $10 to physicians to the federal government. Together with transparency, PPSA may increase medical professionalism, but it has received mixed opinions among physicians and experts in the field.[24,25] Conversely, little is known about the opinion of medical doctors in universal health systems such as those in Europe. A recent survey conducted in Italy showed that industry sponsorship of medical conferences is common, while the presence of a structured regulatory system is not. Disclosure of industry funding to medical societies was very limited.[26]

To ascertain the Italian situation, we assessed the opinion of Italian medical oncologists on different aspects and implications of COI in a national survey.

METHODS

The Italian College of Medical Oncology Chiefs (CIPOMO) set up an online national cross-sectional survey of its members. CIPOMO accounts for 184 chiefs of hospital oncology divisions/departments. Questionnaires were not sent directly to CIPOMO members. We used a passive approach to avoid intrusive claims, given the sensitivity of the topic, so the denominators are unknown. The survey was posted on the CIPOMO website for 6 weeks and three reminder emails were sent to the regional delegates of CIPOMO to advertise the survey and to involve

collaborators. Medical oncologists working in research institutions and university hospitals do not belong to CIPOMO but those willing to participate who were informed by word of mouth were not excluded from the survey.

The questionnaire was authored by three members of CIPOMO and was based on outstanding issues in the oncology community and reviewed by eight members of the CIPOMO board of directors. After approval, the questionnaire was written using the "Surveymonkey" platform (www.surveymonkey.com) and presented on line from March 1 to April 15, 2017. CIPOMO members were reminded to complete the survey through three repeated email messages. Completion of the survey was anonymous although baseline information (country area, age, sex, duration of oncology experience, type of institution and position) was requested before proceeding. Ethics approval was not required because the research survey was considered morally acceptable and could not risk harming the study participants. Moreover, Italian legislation does not require ethics approval for research not involving patients.

The survey was composed of 19 questions investigating feelings, opinions and experience of the respondents on different aspects of COI (Figure 1 and text). These include the following areas: the influence of COI in medical oncology and drug pricing; influence of the drug industry on continuous medical education; the percentage of direct payments from industry; the acceptability of travel and lodging coverage by industry and per-patient fee for clinical trials and its disclosure in the informed consent; the payment amount of per-patient fee to the institution for a trial; the role of disclosure as a deterrent of COI; the influence of COI on scientific societies; the influence of COI on drug prescriptions; the opinion on ghost writing in scientific articles. Main outcome measures were the proportion of medical oncologists perceiving COI as an outstanding issue and those receiving direct payments from industry.

Respondents were requested to quantify in a 4-point Likert scale the extent to which they agreed with the proposed questions or statements. In the analysis, 17 answers were grouped to facilitate

understanding of results (i.e., "strongly agree" plus "agree" *versus* "strongly disagree" plus "disagree"). One item on net profit margin led to an answer as a continuous variable, whereas another item on direct payment was dichotomized (Yes, No).

Statistical analysis

Answers were collected by the online platform and transformed in a data sheet for analysis. Usual descriptive statistics were used to show both the respondent characteristics and the general results. Moreover, an exploratory analysis for subgroups was performed considering the following explicative variables: geographic area (north, center, south), sex (male, female), age (< 45, 45-59, ≥ 60 years), place of work (hospital, university, research institute, other), nature of institution (public, private), job position (assistant chief, chief, other), years of oncology experience (< 15, ≥ 15), direct payment from industry in the last three years (No, Yes). All answers to the questionnaire items were in turn used as dependent variables. Due the explorative purpose of the analysis, no adjustment for Bonferroni's inequality was made. Given the cross-sectional nature of the study, where the responders were not randomly chosen, bidirectional chi-square tests assuming alpha=0.05 as significance level were calculated to provide a measure of the strength of association and not with inferential purposes. A sample size of at least 220 respondents was considered adequate as it represents 10% of the total medical oncologist population in Italy.

Patient and public involvement

The issues of increasing health care costs and of a trustful relationship between patients and physicians were the main reasons of the survey and were highlighted in the introduction section. Neither patients nor public were involved in this study. The findings of the survey will be disseminated through a press release and media coverage. A position paper on COI by CIPOMO is under preparation.

RESULTS

The responders were 321, from all 20 Italian regions, representing 13% of the 2,260 tenured Italian certified medical oncologists from the 319 Units of the country, according to the White Book of the Italian Association of Medical Oncology.[27] The respondent characteristics are summarized in Table 1. They reflect the main characteristics of the Italian population of oncologists, with the majority of them employed in northern Italy, having equal sex distribution, a third being aged 45 years or younger and working predominantly in public hospitals. However, there was a greater proportion of chiefs of staff because of the nature of the study sponsor.

The questionnaire and answers concerning the COI are described in Figure 1. Over two- thirds (68%) believe the majority of Italian oncologists have a COI with industry. A subgroup analysis indicates a greater proportion of them among females, younger physicians, assistant chiefs and those who did not receive payments from industry in the last 3 years ($p<0.05$, table 2). However, 59% assume the COI in oncology is no greater than in other medical specialties.

Overall, 62% declared general payments from the pharmaceutical industry in the last 3 years, with a significantly greater proportion among those living in southern Italy, males, oncologists working in research institutes and chiefs of staff ($p<0.05$, Table 3).

Eighty-one percent believe that most oncology education is supported by industry, with a greater proportion among older physicians and chiefs of staff ($p<0.05$), while over 70% think their continuous medical education (CME) should be supported by their institution or public sources and only less than 10% and 20% think it should be paid for by themselves or the industry, respectively (Table 4). The vast majority stated their first CME tool is scientific journals (89%), but 14% use pharmaceutical representatives as their main CME source.

However, 54% of the medical oncologists consider it inappropriate to organize a scientific meeting within his/her facility with an opinion leader chosen by a pharmaceutical company, especially in the north and among the chiefs of staff ($p<0.05$).

About 77% believe that the greater allocation of budget placed by industry on marketing and promotion relative to research and development is inappropriate, with a greater proportion of supporters among younger physicians and non-chiefs of staff ($p<0.05$), but 75% of all respondents consider it appropriate to receive travel and lodging hospitality from industry to attend international meetings, with a significantly greater proportion of supporters among those receiving direct industry payments ($p<0.05$).

A median net profit margin of €5,000 (mean±SD=€9,888±10,414) per patient enrolled in a trial was considered an appropriate amount for the investigator's institution, although the distribution had a long tail towards higher values.

Sixty percent would agree to receive a personal fee for each patient enrolled in an industry sponsored trial, with a greater proportion among those who received payments from industry ($p<0.05$), but 79% state this should be reported in the patient's informed consent.

Nearly 60% think that disclosing a COI with different companies who are competitors is not a guarantee of impartiality and 71% believe that COI disclosure does not attenuate the risk of scientific bias. However, 48% of those working in private institutions *versus* 27% of those working in public institutions believe that COI disclosure attenuates the problem ($p<0.05$).

Over 90% believe that scientific societies should have a COI policy and that a detailed report of the financial support by the industry should be published annually. A total of 58% believe that industry support does not influence topic selection in meetings and 61% believe that giving an invited speech by industry does not influence their drug prescription. However, a higher proportion of male and older physicians feel that prescription is influenced by direct industry payments ($p<0.05$).

Finally, 79% consider it unfair to be co-author of an article written by a medical writer for an industry-sponsored trial when no substantial scientific contribution is made. However, 25% of those receiving industry payments believe this is appropriate *versus* 15% of those who did not ($p<0.05$).

DISCUSSION

With the introduction of the open Physician Payments Sunshine Act and the increasing costs of healthcare, the debate on financial COI has received a great deal of attention in the USA.[1,24,25,28] Particularly in Europe, however, a direct perspective by the medical community on this matter is still unclear.

The main findings from this anonymous questionnaire indicate that two-thirds of Italian medical oncologists believe that COI is a relevant issue, with a higher perception among females, young physicians, assistant chiefs of staff and those not receiving industry payments in the last three years. Although nearly 60% suppose this is not a greater issue in oncology than in other medical specialties, this does not mitigate the potential impact of the problem. Secondly, 62% of the sample declared direct payments from the pharmaceutical industry in the last three years, with a greater frequency in southern Italy, research hospitals, chiefs of staff and male physicians.

Over 80% confirm that most oncology education and training is financially supported by industry, with a greater proportion of followers among older physicians and chiefs. Subgroup analyses also show there is a greater awareness of COI as a problem among women and young doctors, who are also among those categories receiving fewer payments from industry. While it is difficult to establish a causal relationship between increased awareness and lower frequency of payments (the younger and female physicians groups might have a more idealistic attitude), the gender disparity in industry relationships is a well-known phenomenon. In recent American analyses, only one-quarter of physicians receiving payments were female, who, on average, also received less money per

person than men.[29] In our study, 70% of male *versus* 53% of female physicians received direct payments from industry for speaking fees in the last 3 years. This percentage is in line with that reported by a recent survey through the open payment act in the United States, where 63% of oncologists received a general payment in 2014.[30] Oncologists were also more likely to receive a general payment and to hold ownership interest compared with non-oncologists.[30]

Another important source of funding from industry is research. Interestingly, while 60% of physicians would agree to receive a percentage fee for every patient enrolled in an industry-sponsored trial, nearly 80% are favorable to disclose it in the patient's informed consent. This is a significant inclination towards transparency among our professional community that has not yet been translated in regulatory acts by the current legislation regulating clinical trials. This is also important because physician payment for study participation in clinical trials is a potential COI that can adversely affect patient trust.[10,31]

The median net margin for the employee institution that was considered balanced for each patient enrolled in an industry trial was €5,000, which appears significantly lower than the current level of industry per-patient fee, where the gross fee may now easily exceed €30,000. The vast majority of respondents is also contrary to the current escalating trend to spend more for marketing and promotion than for research and development by industry, a notion which is rarely openly declared by industry.[15,16] These considerations suggest that the surveyed sample is aware that the current trend to increasing costs also has a negative impact on quality of care once the drug is licensed. In the United States, cancer patients carry rising burdens of healthcare-related out-of-pocket expenses, and a growing number of patients are considered underinsured. To save money, a large proportion of these patients take less or nothing of the prescribed medications, a phenomenon known as financial toxicity, which has also been described in the context of the Italian healthcare system.[19,32]

Nearly 80% consider it unfair be co-author of an article written by a medical writer for an industry-sponsored trial when no substantial scientific contribution has been made. This is in contrast to the

present trend of most industry-sponsored trials to be reported by medical writers, often in concomitance with presentation at premier international meetings.[11] The legal and ethical consequences of ghost writing, including risk of plagiarism and loss of professionalism and genuine intellectual contribution to the advancement of science, is a subject of intense debate[33,34]

Over 70% of the oncologists think their CME should be supported by their institution or public sources and less than 10% by personal resources. The vast majority stated their first CME tool is scientific journals but nearly 15% use industry sales representatives as the main CME method. These findings are in line with the public landscape of our national health system medical doctors, where CME is considered a right that should be covered by public resources and not a duty to be at least partially covered by physician resources. Three quarters of Italian oncologists would agree to be financially supported by industry for travel and lodging at international meetings, another important source of industry expenditures. It is possible that this form of financial support is perceived as less conflicting and as the only way to attend important meetings given the scarcity of public or private no-profit funding.

Interestingly, over 70% believe that COI disclosure during presentations does not attenuate the risk of scientific bias. A recent study[35] also showed that disclosure can be incomplete by using the term of 'unpaid consultant', whereby many doctors fail to identify research funding, conference fees, travel expenses or other benefits. However, approximately 60% believe that industry support does not influence topic selection at meetings and that giving invited speeches does not influence personal drug prescription.

Another important issue raised by our survey is the call for a higher level of transparency by scientific societies, including annual detailed reporting of industry payments. Prior studies have shown that disclosure of COI among Italian scientific societies does not attenuate the problem but in fact seems to be a justification to increase financial relationships.[26]

The consequences of financial COI on patient perception has been the subject of recent studies.[8,10,36] In an ASCO survey of COI policies, the majority of non-physicians and patient advocates felt that full disclosure of COI by physicians was expected and could be a factor in patients' decisions regarding therapy.[37]

Altogether, the answers to the survey clearly show that the direct economic relationship between clinicians and industry is deeply rooted in current practice. Money from industry regularly flows as the result of declared marketing investments in the context of legal pathways. The hidden question is whether a clinician who receives financial support for various activities in his profession can be impartial and objective in making clinical decisions. This is particularly true in all those clinical settings where uncertainties about the added value of new drugs make treatment choices questionable.[17,18,20-22]. Most recent evidence indicates that the majority of cancer drugs registered in Europe by EMA do not show a benefit in term of survival or quality of life[38], indicating the necessity to raise the evidence bar before market approval[39]. Moreover, in a recent analysis of 10 approved cancer drugs in the United States, the median cost of developing a drug was $648,000,000, a figure significantly lower than prior estimates. The revenue after four years of approval was substantial (median, $1658.4 million; range, $204.1 million to $22 275.0 million)[40], suggesting the need for a significant reduction of expenses for marketing and promotional activities, including paying doctors for a variety of activities, to guarantee sustainable health systems. The results of our study are also consistent with the international research context on this topic[2-7], underlying the increasing importance of COI on practice[41] and research[42].

To our knowledge this is the first national survey performed by Italian oncologists and one of the few prompted by medical oncologists regarding their COI and physician-industry relationships. The questionnaire in an anonymous form probably favored the disclosure of financial relationships with industry and an open attitude by respondents. The study has limitations, including the non-random selection of the respondents and the greater representation of chiefs of staff. A strength of our study, however, is the relatively large sample size which may overcome the limitations and possibly reflect the general characteristics of medical oncologists in Italy.[27]

Our study indicates that among Italian oncologists COI is perceived as an important issue influencing education, quality of care, science and costs. The overall view on COI calls for a process of rethinking of the relationship between clinicians and industry and, most importantly, a courageous step toward transparency. The results seem to indicate a need for education about the effect of sponsored education on attitudes and on prescribing behaviour and the extent to which industry sponsorship affects clinical trial results. However, disclosure cannot be the only answer and all components of the healthcare system are called into action. Health institutions should promote and finance professional education and industry should transparently contribute to research and increase quality of care. Most importantly, we suggest that the financial relationships between industry and clinicians should always be indirect and mediated by institutions. In the present context of increasing health care costs and financial toxicity, alternative ways to support education and research and strict transparency policies could contribute to increased patient trust, sustainability and equity in health care access. These principles are being proposed in a forthcoming policy document on COI that will be endorsed by CIPOMO, spread among all Italian oncologists, and proposed to the Italian health authorities.

Table 1. Main respondent characteristics

	***No.* (%)**
Geographic Area	
North	161 (50.2%)
Center	108 (33.6%)
South	52 (16.2%)
Age in years	
< 45	103 (32.1%)
45 - 59	133 (41.4%)
≥ 60	85 (26.5%)
Sex*	
Male	170 (53.3%)
Female	149 (46.7%)
Place of Work	
Hospital	283 (88.2%)
University	20 (6.2%)
Research Institute	11 (3.4%)
Other	7 (2.2%)
Nature of Institution	
Public	296 (92.2%)
Private	25 (7.8%)
Job Position	
Assistant Chief	190 (59.2%)
Chief	98 (30.5%)
Other	33 (10.3%)
Years of Experience	
<15	88 (27.4%)
≥15	233 (72.6%)
Direct payment from industries in the last 3 years*	
No	120 (37.6%)
Yes	199 (62.4%)

*Two oncologists did not answer the question

Table 2. Subgroup analysis on question # 1: Do you believe most oncologists have direct conflict of interests with pharmaceutical companies?

	Disagree		**Agree**		***P* < ***
	no.	**%**	**no.**	**%**	
Country area					
North	112	69.6	49	30.4	0.440
Center	68	63.0	40	37.0	
South	37	71.2	15	28.8	
Sex					**0.001**
F	84	56.4	65	43.6	
M	131	77.1	39	22.9	
Age					0.057
< 45	61	59.2	42	40.8	
45 — 59	92	69.2	41	30.8	
≥ 60	64	75.3	21	24.7	
Workplace					
Research Institute	9	81.8	2	18.2	0.583
Hospital	189	66.8	94	33.2	
University	15	75.0	5	25.0	
Other	4	57.1	3	42.9	
Type of structure					0.350
Private	19	76.0	6	24.0	
Public	198	66.9	98	33.1	
Job position					**0.021**
Assistant chief	119	62.6	71	37.4	
Chief	77	78.6	21	21.4	
Other	21	63.6	12	36.4	
Years of experience					**0.023**
< 15	51	58.0	37	42.0	
≥ 15	166	71.2	67	28.8	
Direct payments from industry					**0.029**
No	72	60.0	48	40.0	
Yes	143	71.9	56	28.1	

*Referred to bidirectional chi-square test

Table 3. Subgroup analysis on the question: "Have you received any payment to speak at educational meetings sponsored by a pharmaceutical company in the last 3 years?"

	No		Yes		*P* < *
	no.	**%**	**no.**	**%**	
Country area					**0.002**
North	57	35.4	104	64.6	
Center	52	49.1	54	50.9	
South	11	21.1	41	78.9	
Sex					
F	69	46.6	79	53.4	**0.002**
M	51	30.0	119	70.0	
Age					0.715
< 45	41	39.8	62	60.2	
45 — 59	50	38.2	81	61.8	
≥ 60	29	34.1	56	65.8	
Workplace					**0.003**
Research Institute	0	0.0	11	100.0	
Hospital	106	37.6	176	62.4	
University	8	42.1	11	57.9	
Other	6	85.7	1	14.3	
Type of structure					0.493
Private	11	44.0	14	56.0	
Public	109	37.1	185	62.9	
Job position					**0.016**
Assistant chief	72	38.3	116	61.7	
Chief	29	29.6	69	70.4	
Other	19	57.6	14	42.4	
Years of experience					0.314
< 15	37	42.0	51	58.0	
≥ 15	83	35.9	148	64.1	

*Referred to bidirectional chi-square test

Table 4. Role of public entities and private industry in continuous medical education (CME) support.

	***No.* of important or very important score 4+5 (%)**
Questions	
1. Which method do you primarily use for your CME? You can select multiple choices and attribute different scores from "not at all important" (1) to "very important" (5).	
Medical websites	185 (60.8)
Scientific journals	278 (89.1)
CME courses	181 (59.5)
Conferences	211 (67.4)
Pharmaceutical representatives	42 (13.7)
Books	62 (20.9)
2. Who should pay for your CME? You can select multiple choices and attribute different scores from "not at all important" (1) to "very important" (5).	
- Myself	27 (9.3)
- Hospital	256 (83.1)
- Public Institutions	211 (70.3)
- Pharmaceutical companies	51 (17.3)
- Research Foundations	140 (48.1)

Figure Legend. Figure 1: Questions and answers evaluated with a 4-point Likert scale on CoI (%)

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Contributors

ADC, GN, FR: idea, planning data set, data analysis, wrote the manuscript.

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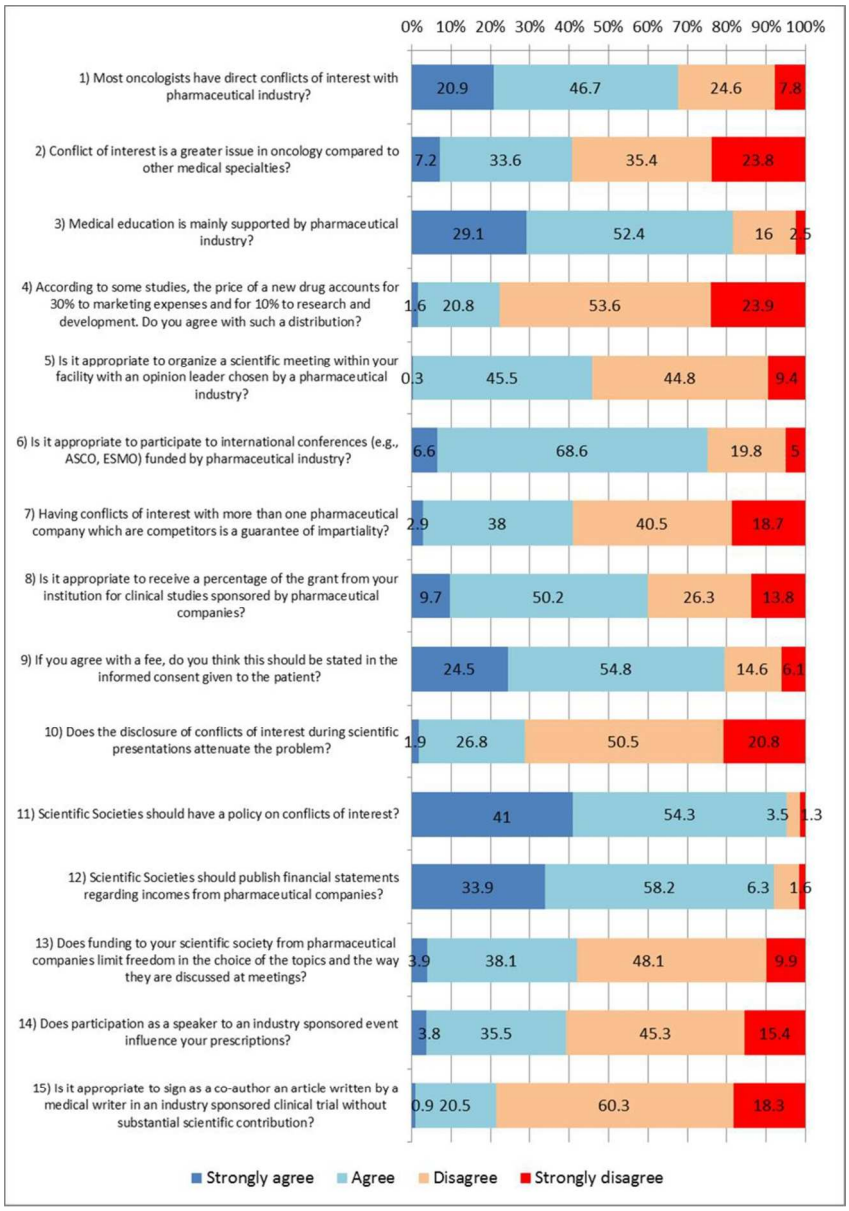

Figure 1: Questions and answers evaluated with a 4-point Likert scale on CoI (%)

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Conflict of interest among Italian medical oncologists. A national survey

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Original Article: **Conflict of interest among Italian medical oncologists. A national survey.**

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ARTICLE SUMMARY

ABSTRACT 300 words

Objective

To assess the Italian medical oncologist's opinion regarding the implications of conflict of interest (COI) on medical education, care and research and to evaluate their direct financial relationships.

Design

National cross-sectional survey conducted between March and April 2017 among Italian oncologists.

Setting

Online survey sponsored by the Italian College of Medical Oncology Chiefs through its web site.

Participants:

Italian oncologists who filled out an anonymous questionnaire including 19 items and individual and working characteristics.

Main outcome measures

The proportion of medical oncologists perceiving COI as an outstanding issue and those receiving direct payments from industry.

Results

The number of responders were 321, representing 13% of Italian tenured medical oncologists. Overall, 62% declared direct payments from pharmaceutical industry in the last 3 years. Sixty-eight percent felt the majority of Italian oncologists have a COI with industry but 59% suppose this is not greater than that of other specialties. Eighty-two percent consider that most oncology education is supported by industry. More than 75% believe that current allocation of industry budget on marketing and promotion rather than research and development is unfair but 75% consider it appropriate to receive travel and lodging hospitality from industry. A median net profit margin of 5.000€ per patient enrolled in an industry trial was considered appropriate for the employee institution. Sixty percent agree to receive a personal fee for patients enrolled in industry trials but 79% state this should be reported in the informed consent. Over 90% believe that scientific societies

should publish a financial report of industry support. Finally, 79% disagree to being co-author of an article written by a medical writer when no substantial scientific contribution is made.

Conclusions

Among Italian oncologists COI is perceived as an important issue influencing costs, education, care and science. A more rigorous policy on COI should be implemented.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first national survey performed by Italian oncologists and one of the few prompted by medical oncologists regarding their conflict of interest and physician-industry relationships in Europe.
- The sample size of 321 is quite large, as it represents 13% of the 2,260 tenured Italian certified medical oncologists from the 319 Units of the country, making the results of the survey well founded.
- Another strength of the questionnaire is its anonymous form which favored the disclosure of financial relationships with industry and an open attitude by respondents.
- The study has limitations, including the non-random selection of the respondents and the greater representation of chiefs of staff compared with the overall population of medical oncologists.

INTRODUCTION

A conflict of interest (COI) exists when professional judgment concerning a primary interest such as patient welfare or the validity of research may be influenced by a secondary interest such as financial gain or career advancement. Financial relationships between industry and physicians and/or researchers are common and may be direct, consisting of stock options, advisory fees, honoraria, speaking fees, travel and lodging expenses, or indirect, such as research support to researcher's institutions. COI increasingly affects every aspect of medicine, including care, education, research integrity, patient trust, guideline formulation, regulatory approval and scientific prominence.[1-7]

Collaboration between industry and clinicians and/or researchers creates challenges and opportunities. While these relationships may contribute to advancement in the field, there is a need to better understand the negative consequences of COI and how best to report and manage it. Systematic reviews have found that pharmaceutical industry- sponsored studies are more often favorable to the sponsor's product compared with studies having other sources of sponsorship.[4,5] Public opinion on physician–pharmaceutical industry interactions differs depending on context and specific country health care models[8,9], but some studies suggest a significant level of concern regarding interaction involving direct financial benefit to physicians.[9,10]

In medical oncology, financial relationships have increased through the years and have influenced clinical research, scientific prominence and visibility.[11,12] The issue is particularly important given the increasing volume of investments made by the pharmaceutical industry in cancer treatment.[13] In this price increase strategy[14], pharmaceutical companies tend to spend much more for marketing and promotional activities than for research and development.[15,16] Evaluation of the clinical benefits that oncology drugs offer as a function of their cost has become complex and for some clinical

indications, health benefits are diminishing over time[17]. Moreover, these benefits do not always follow criteria of innovation[18] and provide increasing financial toxicity to patients.[19] There is concern that the substantial increase in drug prices may hamper both universal and private health care systems sustainability in many countries[14, 20-22] , while this is also of concern to top managers of pharmaceutical industries.[23]

The debate on COI has received attention in the United States since the introduction of the Physician Payments Sunshine Act (PPSA), which requires health care product manufacturers to report payments of more than $10 to physicians to the federal government. Together with transparency, PPSA may increase medical professionalism, but it has received mixed opinions among physicians and experts in the field of COI.[24,25] Conversely, little is known about the opinion of medical doctors in universal health systems such as those in Europe. A recent survey conducted in Italy showed that industry sponsorship of medical conferences is common, while the presence of a structured regulatory system is not. Disclosure of industry funding to medical societies was very limited.[26]

To ascertain the Italian situation, we assessed the opinion of Italian medical oncologists on different aspects and implications of COI in a national survey.

METHODS

The Italian College of Medical Oncology Chiefs (CIPOMO) set up an online national cross-sectional survey of its members. CIPOMO accounts for 184 chiefs of hospital oncology divisions/departments. Questionnaires were not sent directly to CIPOMO members. We used a passive approach to avoid intrusive claims, given the sensitivity of the topic, so the denominators are unknown. The survey was posted on the CIPOMO website for 6 weeks and three reminder emails were sent to the regional delegates of CIPOMO to advertise the survey and to involve

collaborators. Medical oncologists working in research institutions and university hospitals do not belong to CIPOMO but those willing to participate who were informed by word of mouth were not excluded from the survey.

The questionnaire was authored by three members of CIPOMO and was based on outstanding issues in the oncology community and reviewed by eight members of the CIPOMO board of directors. After approval, the questionnaire was written using the "Surveymonkey" platform (www.surveymonkey.com) and presented on line from March 1 to April 15, 2017. CIPOMO members were reminded to complete the survey through three repeated email messages. Completion of the survey was anonymous although baseline information (country area, age, sex, duration of oncology experience, type of institution and position) was requested before proceeding. Ethics approval was not required because the research survey was considered morally acceptable and could not risk harming the study participants. Moreover, Italian legislation does not require ethics approval for research not involving patients.

The survey was composed of 19 questions investigating feelings, opinions and experience of the respondents on different aspects of COI (Figure 1 and text). These include the following areas: the influence of COI in medical oncology and drug pricing; influence of the drug industry on continuing medical education; the percentage of direct payments from industry; the acceptability of travel and lodging coverage by industry and per-patient fee for clinical trials and its disclosure in the informed consent; the payment amount of per-patient fee to the institution for a trial; the role of disclosure as a deterrent of COI; the influence of COI on scientific societies; the influence of COI on drug prescriptions; the opinion on ghost writing in scientific articles. Main outcome measures were the proportion of medical oncologists perceiving COI as an outstanding issue and those receiving direct payments from industry.

Respondents were requested to quantify in a 4-point Likert scale the extent to which they agreed with the proposed questions or statements. In the analysis, 17 answers were grouped to facilitate

understanding of results (i.e., "strongly agree" plus "agree" *versus* "strongly disagree" plus "disagree"). One item on net profit margin led to an answer as a continuous variable, whereas another item on direct payment was dichotomized (Yes, No).

Statistical analysis

Answers were collected by the online platform and transformed in a data sheet for analysis. Descriptive statistics (number, percentage) were used to show both the respondent characteristics and the general results. Moreover, an exploratory analysis for subgroups was performed considering the following explicative variables: geographic area (north, center, south), sex (male, female), age (< 45, 45-59, ≥ 60 years), place of work (hospital, university, research institute, other), nature of institution (public, private), job position (assistant chief, chief, other), years of oncology experience (< 15, ≥ 15), direct payment from industry in the last three years (No, Yes). All answers to the questionnaire items were in turn used as dependent variables. Due the explorative purpose of the analysis, no adjustment for Bonferroni's inequality was made. Given the cross-sectional nature of the study, where the responders were not randomly chosen, bidirectional chi-square tests assuming alpha=0.05 as significance level were calculated to provide a measure of the strength of association and not with inferential purposes. A sample size of at least 220 respondents was considered adequate as it represents 10% of the total medical oncologist population in Italy.

Patient and public involvement

The issues of increasing health care costs and of a trustful relationship between patients and physicians were the main reasons of the survey and were highlighted in the introduction section. Neither patients nor public were involved in this study. The findings of the survey will be disseminated through a press release and media coverage. A position paper on COI by CIPOMO is under preparation.

RESULTS

The responders were 321, from all 20 Italian regions, representing 13% of the 2.260 tenured Italian certified medical oncologists from the 319 Oncology Units of the country, according to the White Book of the Italian Association of Medical Oncology.[27] The respondent characteristics are summarized in Table 1. They reflect the main characteristics of the Italian population of oncologists, with the majority of them employed in northern Italy, having equal sex distribution, a third being aged 45 years or younger and working predominantly in public hospitals. However, there was a greater proportion of chiefs of staff because of the nature of the study sponsor.

The questionnaire and answers concerning the COI are described in Figure 1. Over two- thirds (68%) believe the majority of Italian oncologists have a COI with industry. A subgroup analysis indicates a greater proportion of them among females, younger physicians, assistant chiefs and those who did not receive payments from industry in the last 3 years ($p<0.05$, table 2). However, 59% assume the COI in oncology is no greater than in other medical specialties.

Overall, 62% declared general payments from the pharmaceutical industry in the last 3 years, with a significantly greater proportion among those living in southern Italy, males, oncologists working in research institutes and chiefs of staff ($p<0.05$, Table 3).

Eighty-one percent believe that most oncology education is supported by industry, with a greater proportion among older physicians and chiefs of staff ($p<0.05$), while over 70% think their continuing medical education (CME) should be supported by their institution or public sources and only less than 10% and 20% think it should be paid for by themselves or the industry, respectively (Table 4). The vast majority stated their first CME tool is scientific journals (89%), but 14% use pharmaceutical representatives as their main CME source.

However, 54% of the medical oncologists consider it inappropriate to organize a scientific meeting within his/her facility with an opinion leader chosen by a pharmaceutical company, especially in the north and among the chiefs of staff ($p<0.05$).

About 77% believe that the greater allocation of budget placed by industry on marketing and promotion relative to research and development is inappropriate, with a greater proportion of supporters among younger physicians and non-chiefs of staff ($p<0.05$), but 75% of all respondents consider it appropriate to receive travel and lodging hospitality from industry to attend international meetings, with a significantly greater proportion of supporters among those receiving direct industry payments ($p<0.05$).

A median net profit margin of €5,000 (mean±SD=€9,888±10,414) per patient enrolled in a trial was considered an appropriate amount for the investigator's institution, although the distribution had a long tail towards higher values.

Sixty percent would agree to receive a personal fee for each patient enrolled in an industry sponsored trial, with a greater proportion among those who received payments from industry ($p<0.05$), but 79% state this should be reported in the patient's informed consent.

Nearly 60% think that disclosing a COI with different companies who are competitors is not a guarantee of impartiality and 71% believe that COI disclosure does not attenuate the risk of scientific bias. However, 48% of those working in private institutions *versus* 27% of those working in public institutions believe that COI disclosure attenuates the problem ($p<0.05$).

Over 90% believe that scientific societies should have a COI policy and that a detailed report of the financial support by the industry should be published annually. A total of 58% believe that industry support does not influence topic selection in meetings and 61% believe that giving an invited speech by industry does not influence their drug prescription. However, a higher proportion of male and older physicians feel that prescription is influenced by direct industry payments ($p<0.05$).

Finally, 79% consider it unfair to be co-author of an article written by a medical writer for an industry-sponsored trial when no substantial scientific contribution is made. However, 25% of those receiving industry payments believe this is appropriate *versus* 15% of those who did not ($p<0.05$).

DISCUSSION

With the introduction of the open Physician Payments Sunshine Act and the increasing costs of healthcare, the debate on financial COI has received a great deal of attention in the USA.[1,24,25,28] Particularly in Europe, however, a direct perspective by the medical community on this matter is still unclear.

The main findings from this anonymous questionnaire indicate that two-thirds of Italian medical oncologists believe that COI is a relevant issue, with a higher perception among females, young physicians, assistant chiefs of staff and those not receiving industry payments in the last three years. Although nearly 60% suppose this is not a greater issue in oncology than in other medical specialties, this does not mitigate the potential impact of the problem. Secondly, 62% of the sample declared direct payments from the pharmaceutical industry in the last three years, with a greater frequency in southern Italy, research hospitals, chiefs of staff and male physicians.

Over 80% confirm that most oncology education and training is financially supported by industry, with a greater proportion of followers among older physicians and chiefs. Subgroup analyses also show there is a greater awareness of COI as a problem among women and young doctors, who are also among those categories receiving fewer payments from industry. While it is difficult to establish a causal relationship between increased awareness and lower frequency of payments (the younger and female physicians groups might have a more idealistic attitude), the gender disparity in industry relationships is a well-known phenomenon. In recent American analyses, only one-quarter of physicians receiving payments were female, who, on average, also received less money per

person than men.[29] In our study, 70% of male *versus* 53% of female physicians received direct payments from industry for speaking fees in the last 3 years. This percentage is in line with that reported by a recent survey through the open payment act in the United States, where 63% of oncologists received a general payment in 2014.[30] Oncologists were also more likely to receive a general payment and to hold ownership interest compared with non-oncologists.[30]

Another important source of funding from industry is research. Interestingly, while 60% of physicians would agree to receive a percentage fee for every patient enrolled in an industry-sponsored trial, nearly 80% are favorable to disclose it in the patient's informed consent. This is a significant inclination towards transparency among our professional community that has not yet been translated in regulatory acts by the current legislation regulating clinical trials. This is also important because physician payment for study participation in clinical trials is a potential COI that can adversely affect patient trust.[10,31]

The median net margin for the employee institution that was considered balanced for each patient enrolled in an industry trial was €5,000, which appears significantly lower than the current level of industry per-patient fee, where the gross fee may now easily exceed €30,000. The vast majority of respondents is also contrary to the current escalating trend to spend more for marketing and promotion than for research and development by industry, a notion which is rarely openly declared by industry.[15,16] These considerations suggest that the surveyed sample is aware that the current trend to increasing costs also has a negative impact on quality of care once the drug is licensed. In the United States, cancer patients carry rising burdens of healthcare-related out-of-pocket expenses, and a growing number of patients are considered underinsured. To save money, a large proportion of these patients take less or nothing of the prescribed medications, a phenomenon known as financial toxicity, which has also been described in the context of the Italian healthcare system.[19,32]

Nearly 80% consider it unfair be co-author of an article written by a medical writer for an industry-sponsored trial when no substantial scientific contribution has been made. This is in contrast to the

present trend of most industry-sponsored trials to be reported by medical writers, often in concomitance with presentation at premier international meetings.[11] The legal and ethical consequences of ghost writing, including risk of plagiarism and loss of professionalism and genuine intellectual contribution to the advancement of science, is a subject of intense debate[33,34]

Over 70% of the oncologists think their CME should be supported by their institution or public sources and less than 10% by personal resources. The vast majority stated their first CME tool is scientific journals but nearly 15% use industry sales representatives as the main CME method. These findings are in line with the public landscape of our national health system medical doctors, where CME is considered a right that should be covered by public resources and not a duty to be at least partially covered by physician resources. Three quarters of Italian oncologists would agree to be financially supported by industry for travel and lodging at international meetings, another important source of industry expenditures. It is possible that this form of financial support is perceived as less conflicting and as the only way to attend important meetings given the scarcity of public or private no-profit funding.

Interestingly, over 70% believe that COI disclosure during presentations does not attenuate the risk of scientific bias. A recent study[35] also showed that disclosure can be incomplete by using the term of 'unpaid consultant', whereby many doctors fail to identify research funding, conference fees, travel expenses or other benefits. However, approximately 60% believe that industry support does not influence topic selection at meetings and that giving invited speeches does not influence personal drug prescription.

Another important issue raised by our survey is the call for a higher level of transparency by scientific societies, including annual detailed reporting of industry payments. Prior studies have shown that disclosure of COI among Italian scientific societies does not attenuate the problem but in fact seems to be a justification to increase financial relationships.[26]

The consequences of financial COI on patient perception has been the subject of recent studies.[8,10,36] In an ASCO survey of COI policies, the majority of non-physicians and patient advocates felt that full disclosure of COI by physicians was expected and could be a factor in patients' decisions regarding therapy.[37]

Altogether, the answers to the survey clearly show that the direct economic relationship between clinicians and industry is deeply rooted in current practice. Money from industry regularly flows as the result of declared marketing investments in the context of legal pathways. The hidden question is whether a clinician who receives financial support for various activities in his profession can be impartial and objective in making clinical decisions. This is particularly true in all those clinical settings where uncertainties about the added value of new drugs make treatment choices questionable.[17,18,20-22]. Most recent evidence indicates that the majority of cancer drugs registered in Europe by EMA do not show a benefit in term of survival or quality of life[38], indicating the necessity to raise the evidence bar before market approval[39]. Moreover, in a recent analysis of 10 approved cancer drugs in the United States, the median cost of developing a drug was $648,000,000, a figure significantly lower than prior estimates. The revenue after four years of approval was substantial (median, $1658.4 million; range, $204.1 million to $22 275.0 million)[40], suggesting the need for a significant reduction of expenses for marketing and promotional activities, including paying doctors for a variety of activities, to guarantee sustainable health systems. The results of our study are also consistent with the international research context on this topic[2-7], underlying the increasing importance of COI on practice[41] and research[42].

To our knowledge this is the first national survey performed by Italian oncologists and one of the few prompted by medical oncologists regarding their COI and physician-industry relationships. The questionnaire in an anonymous form probably favored the disclosure of financial relationships with industry and an open attitude by respondents. The study has limitations, including the non-random selection of the respondents and the greater representation of chiefs of staff. A strength of our study,

however, is the relatively large sample size which may overcome the limitations and possibly reflect the general characteristics of medical oncologists in Italy.[27]

Our study indicates that among Italian oncologists COI is perceived as an important issue influencing education, quality of care, science and costs. The overall view on COI calls for a process of rethinking of the relationship between clinicians and industry and, most importantly, a courageous step toward transparency. The results seem to indicate a need for education about the effect of sponsored education on attitudes and on prescribing behaviour and the extent to which industry sponsorship affects clinical trial results. However, disclosure cannot be the only answer and all components of the healthcare system are called into action. Health institutions should promote and finance professional education and industry should transparently contribute to research and increase quality of care. Most importantly, we suggest that the financial relationships between industry and clinicians should always be mediated by the employee's institution. In the present context of increasing health care costs and financial toxicity, alternative ways to support education and research and strict transparency policies could contribute to increased patient trust, sustainability and equity in health care access. These principles are being proposed in a forthcoming policy document on COI that will be endorsed by CIPOMO, spread among all Italian oncologists, and proposed to the Italian health authorities.

Table 1. Main respondent characteristics

	***No.* (%)**
Geographic Area	
North	161 (50.2%)
Center	108 (33.6%)
South	52 (16.2%)
Age in years	
< 45	103 (32.1%)
45 - 59	133 (41.4%)
≥ 60	85 (26.5%)
Sex*	
Male	170 (53.3%)
Female	149 (46.7%)
Place of Work	
Hospital	283 (88.2%)
University	20 (6.2%)
Research Institute	11 (3.4%)
Other	7 (2.2%)
Nature of Institution	
Public	296 (92.2%)
Private	25 (7.8%)
Job Position	
Assistant Chief	190 (59.2%)
Chief	98 (30.5%)
Other	33 (10.3%)
Years of Experience	
<15	88 (27.4%)
≥15	233 (72.6%)
Direct payment from industries in the last 3 years*	
No	120 (37.6%)
Yes	199 (62.4%)

*Two oncologists did not answer the question

Table 2. Subgroup analysis on question # 1: Do you believe most oncologists have direct conflict of interests with pharmaceutical companies?

	Disagree		**Agree**		***P* < ***
	no.	**%**	**no.**	**%**	
Country area					
North	112	69.6	49	30.4	0.440
Center	68	63.0	40	37.0	
South	37	71.2	15	28.8	
Sex					**0.001**
F	84	56.4	65	43.6	
M	131	77.1	39	22.9	
Age					0.057
< 45	61	59.2	42	40.8	
45 — 59	92	69.2	41	30.8	
≥ 60	64	75.3	21	24.7	
Workplace					
Research Institute	9	81.8	2	18.2	0.583
Hospital	189	66.8	94	33.2	
University	15	75.0	5	25.0	
Other	4	57.1	3	42.9	
Type of structure					0.350
Private	19	76.0	6	24.0	
Public	198	66.9	98	33.1	
Job position					**0.021**
Assistant chief	119	62.6	71	37.4	
Chief	77	78.6	21	21.4	
Other	21	63.6	12	36.4	
Years of experience					**0.023**
< 15	51	58.0	37	42.0	
≥ 15	166	71.2	67	28.8	
Direct payments from industry					**0.029**
No	72	60.0	48	40.0	
Yes	143	71.9	56	28.1	

*Referred to bidirectional chi-square test

Table 3. Subgroup analysis on the question: "Have you received any payment to speak at educational meetings sponsored by a pharmaceutical company in the last 3 years?"

	No		**Yes**		***P* < ***
	no.	**%**	**no.**	**%**	
Country area					**0.002**
North	57	35.4	104	64.6	
Center	52	49.1	54	50.9	
South	11	21.1	41	78.9	
Sex					
F	69	46.6	79	53.4	**0.002**
M	51	30.0	119	70.0	
Age					0.715
< 45	41	39.8	62	60.2	
45 — 59	50	38.2	81	61.8	
≥ 60	29	34.1	56	65.8	
Workplace					**0.003**
Research Institute	0	0.0	11	100.0	
Hospital	106	37.6	176	62.4	
University	8	42.1	11	57.9	
Other	6	85.7	1	14.3	
Type of structure					0.493
Private	11	44.0	14	56.0	
Public	109	37.1	185	62.9	
Job position					**0.016**
Assistant chief	72	38.3	116	61.7	
Chief	29	29.6	69	70.4	
Other	19	57.6	14	42.4	
Years of experience					0.314
< 15	37	42.0	51	58.0	
≥ 15	83	35.9	148	64.1	

*Referred to bidirectional chi-square test

Table 4. Role of public entities and private industry in continuing medical education (CME) support.

	***No.* of important or very important score 4+5 (%)**
Questions	
1. Which method do you primarily use for your CME? You can select multiple choices and attribute different scores from "not at all important" (1) to "very important" (5).	
Medical websites	185 (60.8)
Scientific journals	278 (89.1)
CME courses	181 (59.5)
Conferences	211 (67.4)
Pharmaceutical representatives	42 (13.7)
Books	62 (20.9)
2. Who should pay for your CME? You can select multiple choices and attribute different scores from "not at all important" (1) to "very important" (5).	
- Myself	27 (9.3)
- Hospital	256 (83.1)
- Public Institutions	211 (70.3)
- Pharmaceutical companies	51 (17.3)
- Research Foundations	140 (48.1)

Figure Legend. Figure 1: Questions and answers evaluated with a 4-point Likert scale on CoI (%)

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Contributors

ADC, GN, FR: idea, planning data set, data analysis, wrote the manuscript, final approval of the version to be published.

EB, BR, VL: planning data set, statistical analysis, wrote the manuscript, final approval of the version to be published.

FA, LF, CV: revision of the manuscript for important intellectual content, final approval of the version to be published.

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All authors: Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data sharing statement: All data are stored in the server of CIPOMO and are available on request.

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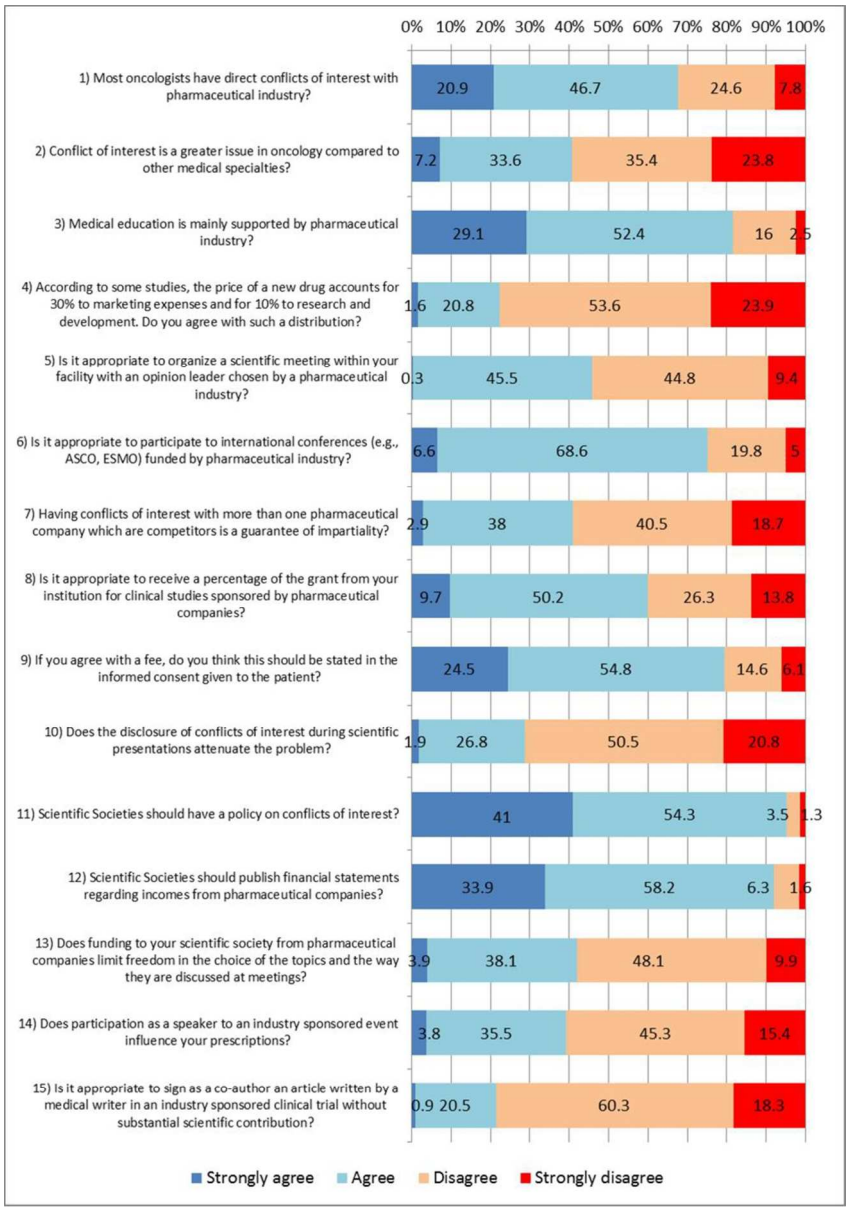

Figure 1: Questions and answers evaluated with a 4-point Likert scale on CoI (%)

106x151mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		AU: Added in the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
		AU: OK
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
		AU: OK, pages 5-6
Objectives	3	State specific objectives, including any prespecified hypotheses
		AU: added in the method section, page 7
Methods		
Study design	4	Present key elements of study design early in the paper
		AU: OK page 6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
		AU: OK page 6-7
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants
		AU: OK page 6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
		AU: OK page 6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
		AU: OK page 6-8
Bias	9	Describe any efforts to address potential sources of bias
		AU: OK page 8
Study size	10	Explain how the study size was arrived at
		AU: added on page 8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
		AU: OK page 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
AU: OK page 8		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
AU: OK page 8-9		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram

Descriptive data **AU: OK page 8-9**	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data **AU: OK page 9-10**	15*	Report numbers of outcome events or summary measures
Main results **AU: OK page 9-10**	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses **AU: OK page 9-10**	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results **AU: OK page 10-11**	18	Summarise key results with reference to study objectives
Limitation **AU: OK page 4 and 14**	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation **AU: OK page 10-14**	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability **AU: OK page 4 and 14**	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding **AU: OK title page**	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.