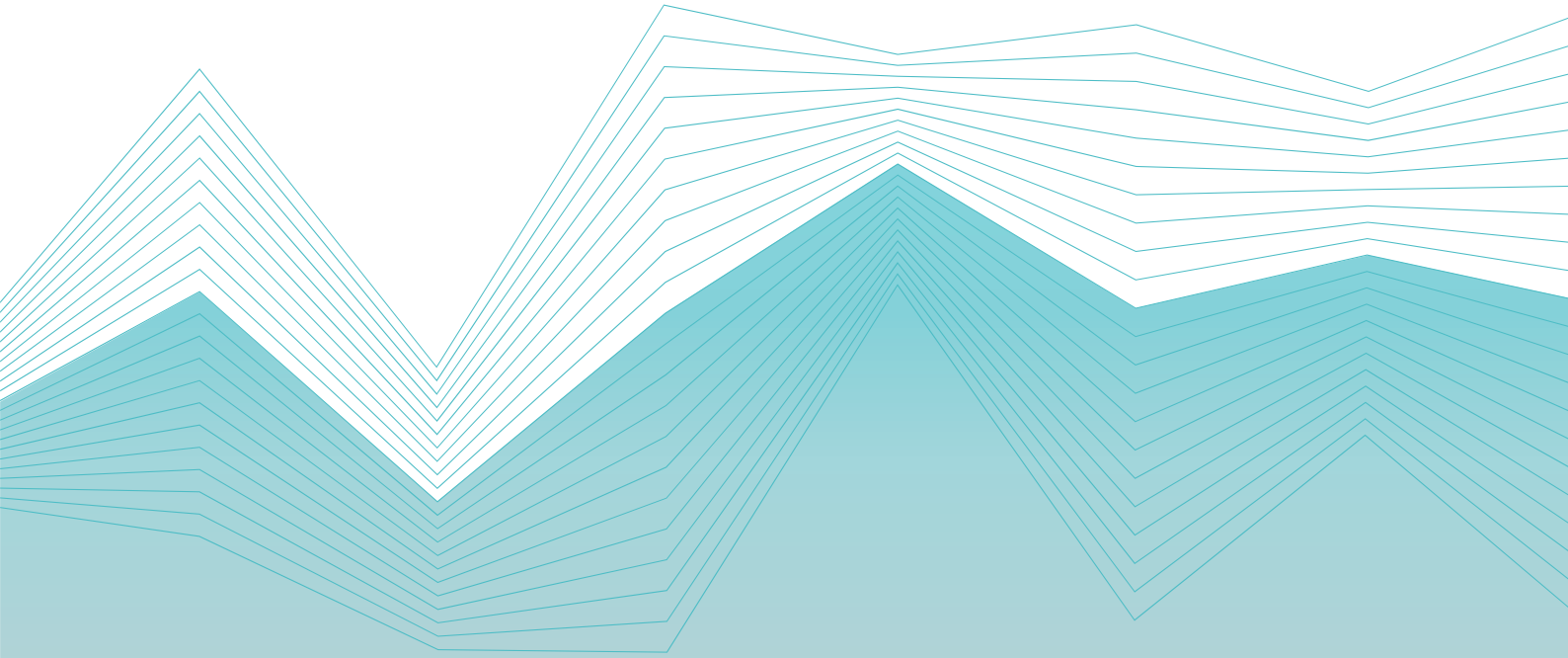
Inducement in the medical device industry

An exploratory literature study



Mees Baartmans, MSc
Prof. dr. Roland Friele

NIVEL
Research for better care

Nivel, Netherlands Institute for Health Services Research, is the national institute for health services research in the Netherlands. It is an independent organization which provides knowledge to improve healthcare in the Netherlands. We do this in conducting high-quality, reliable and independent scientific research on themes of major public interest. ‘Research for better care' is our mission. With our research, we contribute to the continuous improvement and renewal of healthcare. We believe it is important that people are able to participate in society. Ultimately, our research revolves around the question of how we can improve patient care. Nivel publishes all its research publicly, as stipulated in the articles of association. Nivel has been certified ISO 9001 international quality standards.

October 2023

ISBN 978-94-6122-814-7

+31 30 272 97 00
nivel@nivel.nl
www.nivel.nl

Preface

The Dutch Health and Youth Care Inspectorate is responsible for supervising the compliance of the prohibition of inducement in the medical device sector. To enhance their knowledge and understanding of this phenomenon, they asked Nivel to explore the current state of (scientific) literature. In this report we present the findings of our explorative literature study.

As medical device manufacturers operate worldwide to promote the sales of their products, the findings may be relevant to institutions from other countries as well. We therefore wrote this report in English. The initial focus of the study was set on literature from Europe, Asia, and the United States.

We would like to thank Linda Schoonmade, information specialist, for her assistance in setting up and performing the literature search.

The authors,
October 2023

Table of contents

Summary

This report discusses the findings of an exploratory literature study on inducement in the medical device sector. Inducement (or 'gunstbetoon' in Dutch) refers to posing money, services or goods for the apparent objective of promoting the sales of a product. This is prohibited by the Dutch Act on medical devices, with some specific exemptions. While inducement has been extensively studied in the pharmaceutical industry, there exists a knowledge gap when it comes to the medical device sector. This complicates supervision on this phenomenon by the Dutch Health and Youth Care Inspectorate. In this study we explore the state of scientific knowledge on inducement in the medical device sector and specifically focus on the scale, nature, consequences, and policy in Europe, Asia, and the United States.

Our search of scientific databases provided 2756 unique studies. After carefully screening titles and abstracts, 189 publications remained. Full text screening, with a further narrowed scope and additional inclusion criteria, resulted in inclusion of 25 articles. An additional search for specific topics yielded four more publications, leading to a total of 29 included publications.

The output of our search showed inducement in the medical device sector is only minimally studied, in particular for Europe and Asia no scientific literature was identified. For the U.S. we did find some studies that examined payments from device manufacturers to physicians (n=18), as well as studies on the association between industry-physician interactions and device selection and utilization, and quality of care (n=3). Other included publications related to normative articles and codes of conducts on industry-physician interactions (n=8).

From the U.S. literature mapping device industry payments to physicians, we concluded that substantial amounts of money are paid to individual physicians by device manufacturers, which in total even exceed payments made by the pharmaceutical industry. Payments from device industry are not evenly distributed among medical specialties, with some specialties receiving more payments than other – often non-surgical – specialties. Moreover, within specialties, there is great inequality in payment distribution. A small number of physicians receive the majority of value in payments. The highest value payments to individual physicians in the device sector typically relates to the categories of 'royalties, licensing, and investment', and 'consulting and speaker fees'. How research related payments may flow to individual physicians remains unclear from published literature.

The few publications that studied the associations between medical device industry-physician interactions and care practices, show these interactions are associated with device selection and utilization. However, the conclusions drawn from these studies should be interpreted with caution due to their cross-sectional design, which does not allow for establishing causality. Nevertheless from these findings we derive that interactions between device industry and physicians may create mutual dependencies, which may pose risks to patients and society. Providers for example may be incentivized to use more devices of specific manufacturers and could be more reluctant to switch. Yet, the assessed literature does not provide direct and definitive conclusions regarding the consequences for patients and society, and the studied impact on quality of care remains inconsistent.

Furthermore, we discuss some codes of conduct written by the medical device industry and physician associations regarding industry-physician interactions. Both industry and physician associations

recognize the importance of the mutual relationships, but at the same time acknowledge that these relationships can clash with a physician's responsibilities and associated independence in the field of patient care, education, and research. They both emphasize the need for guidance to effectively handle and regulate these relationships. While the studied codes of conduct are based on similar values and cover the same generic topics, they differ in their specifics. For example, some codes do not explicitly address income related to royalties, licensing and investment, while others do. Adoption of the codes is typically voluntary, and compliance is only minimally covered in the publications, raising questions about how this form of regulation works in practice.

The study has some limitations. One important limitation is that the topic is subject to publication bias. Also generalizing the findings to other countries than the U.S., should be done cautiously due to differences in healthcare systems, market scales, physician salaries, and legislation. Since the study had an explorative approach, it does not intend to be exhaustive in all respects, nor does it comply to all methodological requirements of e.g. a systematic literature review.

Some key points of interest from the study include: I) the lack of literature on this topic (in particular for Europe and Asia), II) the insight that substantial payments are made by the device industry to individual physicians that even exceed payments from the pharmaceutical sector, III) the observation that a substantial part of payments relate to royalties, licensing, and investment which are not always explicitly covered in regulations and codes of conduct, and IV) the need for more transparency in financial relationships between the industry and physicians.

From the findings of the study we propose directions for future research to gain further insights, particularly regarding industry payments in Europe and Asia, the association between industry-physician interactions with patient and societal outcomes, the functioning of the codes of conduct in practice, and how research funding is spent. Availability of reliable data is of upmost importance to conduct such research, and so it may be wise to expand payment reporting obligations and improve reporting systems and the associated data output, possibly in an European context.

1 Introduction

In the Netherlands financial relationships between the medical device industry and physicians have been topic of debate. In 2011 serious concerns were raised about inducement[1] (or "gunstbetoon" in Dutch) by medical device companies, and its influence on physician behaviour and patient outcomes. In response, two scans were conducted for the Dutch situation, concluding that inducement was not widespread for medical devices and there were no pressing signs of inducement that could be harmful to patients.(1-3) Recent events have renewed concerns about inducement in the medical device industry.

The Dutch Health and Youth Care Inspectorate (Inspectie Gezondheidszorg en Jeugd) monitors inducement in the medical device sector, and investigates industry-physician relationships.(4, 5) Events covered by media show financial relationships between physicians and device industry remained out of sight of public, employers, and regulators. Industry-physician relationships can thus be untransparent and complex, which can complicate supervision. Also a lack of understanding of industry-physician relationships makes supervision difficult. While for the pharmaceutical sector such relationships have been thoroughly investigated(6, 7), the device industry has not been extensively studied. This, while the medical device sector is a large and growing market, and close collaboration between manufacturers and physicians is common.

Medical devices comprise all products or equipment that are intended by the manufacturer to be used for human beings for one or more specific medical purposes (e.g. diagnosis, prevention, monitoring, treatment, etc.)[2]. Devices comprise relatively simple instruments such as an elastic bandage and a rollator, as well as more complex technologies such as cardiac stents, magnetic resonance imaging systems, and joint or hearing implants. Substantial amounts of money are involved; the world market was valued at $471 billion in 2023 and expected to reach around $850 billion by 2030.(8, 9) The Dutch medical device market was estimated on €4.7 billion in 2023.(10) In a market of such scale and nature, it is plausible that a multitude of vested interests exists.

Collaboration between physicians and the medical device industry has made possible many of the advanced treatments used on a daily basis in clinical settings. Contrarily, these essential relationships create multiple and potentially conflicting roles for physicians.(11) The roles following from physician involvement in product development, testing, clinical trials, education, and product support, may not always align with their interests in their role as independent care giver, entrusted to provide safe and effective care and serve the best interests of patients. It is important to avoid or manage these conflicting interests, while preserving the independency of physicians and at the same time maintaining the important ongoing and close collaboration between physicians and device industry. Therefore this collaboration is explicitly adopted in Dutch legislation.(12)

[1] In this report we focus on inducement defined as 'gunstbetoon' in the Dutch Act on medical devices (Wet medische hulpmiddelen): the prospecting, offering or granting of money or monetizable services or goods by a supplier to an individual involved in the use of a medical device or in vitro diagnostic medical device, or to an institution or health insurer for the apparent purpose of promoting the sale of a medical device or in vitro diagnostic medical device.

[2] Definition derived from the Medical Device Regulation

To avoid conflicts of interests in the medical device sector in the Netherlands, the Act on medical devices (Wet medische hulpmiddelen) prohibits inducement, with some specific exemptions; e.g. small value gifts useful in professional practice are allowed –max €50 per gift and €150 per year.(13) Furthermore, in 2012 field parties established a Code of Conduct for medical devices (Gedragscode Medische Hulpmiddelen)(11) and a voluntary registry for industry payments to physicians was setup (Transparantieregister zorg).(14) The Dutch Health and Youth Care Inspectorate has the legal right to act against inducement. The inspectorate investigates complaints of general public and businesses related to violation of inducement regulations, and carries out (unannounced) inspections where risks exist of improper influencing.(15) For continuing and improving supervision on inducement in the complex sector of medical devices, the Inspectorate has a demand for more knowledge.

Aim and research question

We aim to increase knowledge on inducement in the medical device sector by exploring the current state of (scientific) literature, and answer the following research question:

"What has been written in the Dutch and international (scientific) literature since 2000 about the scale, nature, consequences and policy regarding inducement in the medical device sector within Europe, Asia and the United States, and what insights does this provide about situations in which risks arise for violating the prohibition on inducement?"

In this report, we describe our exploration of the literature on inducement in the medical device industry. Specifically, we will examine payments made by medical device industry to physicians and potential impact of industry-physician interactions on physician behaviour and decision-making. We will also review normative statements from formal associations on the ties between medical industry and physicians, and a selection of code of conducts. By synthesizing the available literature, we aim to provide a comprehensive understanding of the current state of knowledge on inducement in the medical device sector.

2 Methods

For answering the research question a review of scientific literature published in peer-reviewed journals was conducted. Additionally, for some specific topics non-scientific and Dutch literature was reviewed. During the study period, the Inspectorate was periodically updated about the progress.

Data source and searches

Our search for scientific articles in peer-reviewed journals included three databases: PubMed, Embase and Web of Science. For building a search strategy an expert in literature review studies (LS) was consulted. She build the definite search strategy in Medline, and translated it to the other databases. The final strategy included three main concepts, linked with the AND operator and represented with many keywords and relevant Mesh terms; medical devices (e.g. medical device, implant, consumable, prothesis, apparatus), inducement (e.g. payment, conflict of interest, lobbying, product choice) and industry (e.g. industry, vendor, manufacturer, supplier). We searched these terms in title, abstracts and keywords. Databases were searched on 22th of march 2023, for literature published since 1-1-2000. See Appendix A for the full search strategy.
We supplemented the results of this search with a search of Google Scholar for Dutch literature on the topic, because we expected that not all sources relevant to the Dutch situation would be found with the first search strategy. Those Dutch sources are relevant to the inspectorate, however, because their area of activity concerns the Netherlands. Additionally, for some specific topics we searched Google general search engine using precise search terms. See Appendix A for the search strings.

Screening and study selection

After removal of duplicates, search results were imported in reference management tool Rayyan(16) for title and abstract screening. One reviewer (MB) screened all titles and abstracts, and about 5% were independently double screened by a second reviewer (RF). This 5% included the studies for which the first reviewer doubted about inclusion. Disagreements were resolved in a consensus meeting. Studies were eligible for inclusion if they met the following criteria:

1) Full text in English or Dutch available
2) Literature reviews, empirical studies, or normative publications from formal associations (excluding editorials, commentaries, viewpoints, etc.)
3) Focused on Europe, Asia or the U.S.
4) Studied the relationship between medical device manufacturers and individual care providers

The results from the additional searches were assessed on relevance for a specific topic, and included if the reviewers were convinced of its particular relevance and the reliability of the source.

Data extraction, synthesis and analysis

We extracted basic characteristics from all studies included, i.e. title and author(s), publication year, location, and study type/design. As a variety of study types and topics were included, we extracted different outcomes per topic based on relevance for that specific topic. In the results section, per topic the extracted outcomes are described. Data were extracted by one reviewer (MB) and discussed with a second reviewer (RF) for data synthesis. Due to great diversity in study type, structure, period, and selected outcome measures a narrative approach was used for data analysis.

3 Results

3.1 General findings

The search of scientific literature in peer-reviewed journals resulted in a substantial amount of unique studies (n=2756). After carefully screening titles and abstracts, 189 unique publications were found related to the topic and seemed to meet inclusion criteria. As these 189 studies covered many different topics (e.g. the association between research funding and study outcomes, and physician and public perspectives on industry-physician relationships) we decided to further narrow our scope. Only references that elaborated on one of three of the following topics and met additional requirements were accepted for full-text review:

1) Studies mapping payments from device industry to physicians (only studies that differentiated on payments by medical device industry from total industry payments)
2) Studies on the association between medical device industry-physician interactions and device utilisation and selection, and quality of care
3) (Articles on) Codes of conduct or normative statements that address the relationship between medical device industry and physicians, written or endorsed by formal associations

During full-text screening some references turned out to not meet inclusion criteria and were therefore excluded. For example, studies were eventually found to not differentiate on device industry separately from pharmaceutical industry, or appeared to be the wrong publication type. The screening process eventually resulted in inclusion of 25 unique studies. From the additional search strategies, four additional publications were included. Figure 1 presents details on the study screening process.

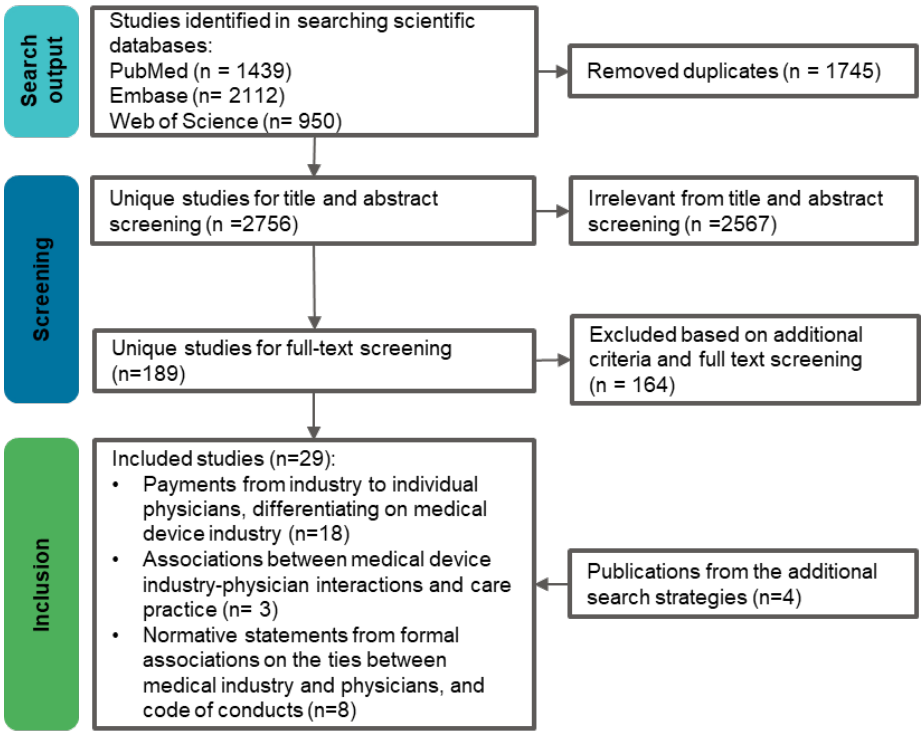


Figure 1. Overview of the study selection process

3.2 Payments from medical device industry to physicians

Based on the articles that analyzed payments from the medical device industry to physicians, we aimed to answer the following question: *"On what scale does medical device industry make payments to physicians, and how does this compare to payments made by the pharmaceutical industry?"*
We first provide some generic information on the included studies and give a generic overview of total registered payments by industry to set the context. Then we present quite a lot of examples and numbers as derived from the individual studies, to illustrate what we found and give an idea of the scale of industry payments. We finish with a reflection paragraph in which the findings are summarized and some concluding remarks are made.

The articles that assessed payments from the device industry to physicians (n=18, Table 1, and Appendix B) all reviewed the U.S. CMS Open Payment Database[3] and were thus focused on the U.S. No studies on payments by industry to healthcare providers were identified for Europe or Asia.

One study(17) provided an overview of medical device industry payments to all types of physicians and differentiated on the top 20 receiving medical specialties. Another study(18) focused on all types of physicians and advanced practice clinicians. The other 16 included studies(19-34) evaluated payments to specific medical professions, e.g. orthopedics, otolaryngology, surgery, urology, and gastroenterology. The selection of medical professions for these studies was made by the authors of the published literature. How this selection took place is not clear from these publications.

The included studies assessed various payment types. Most of the studies reported on general payments only (n=7) or general payments and ownership and investment (n=7). These payment types comprise the bulk of all payments to individual physicians (Figure 2). Four studies included all types of payment, including research funding.
To indicate the distribution between these payments types, the summary data of the CMS Open Payment Database(35) was assessed. From these figures follows that in 2022 in the U.S. of the reported payments by industry (pharmaceutical and device together, $12.59 billion, n=1719 companies) most of the total value paid related to research payments, namely $7.07 billion (Figure 2).(35) Further $3.71 billion related to general payments and $1.29 billion related to ownership and investment. These payments were made to various types of recipients, i.e. physicians, non-physician practitioners, and teaching hospitals. On the individual physician level, reported payments in 2022 related to $2.48 billion in general payments, $1.29 billion in ownership or investment interest, and only $68.84 million in research payments[4].(35) For individual physicians thus the majority of value in payment reported to the database related to general payment and ownership or investment, as also assessed in most included studies.

[3] The CMS Open Payment Database is part of a national transparency program following the U.S. Sunshine Act. The publicly accessible database provides data about financial relationships between drug and medical device industry and health care providers in the U.S.

[4] A substantial amount of total research payments was not related to a specific receiver. The covered recipient research payment total to individual physicians includes: 1) Payments where the company making the payment has named a covered recipient as the primary recipient and 2) Payments to a research institution or entity where a covered recipient is named as a principal investigator on the research project (i.e. associated research funding).

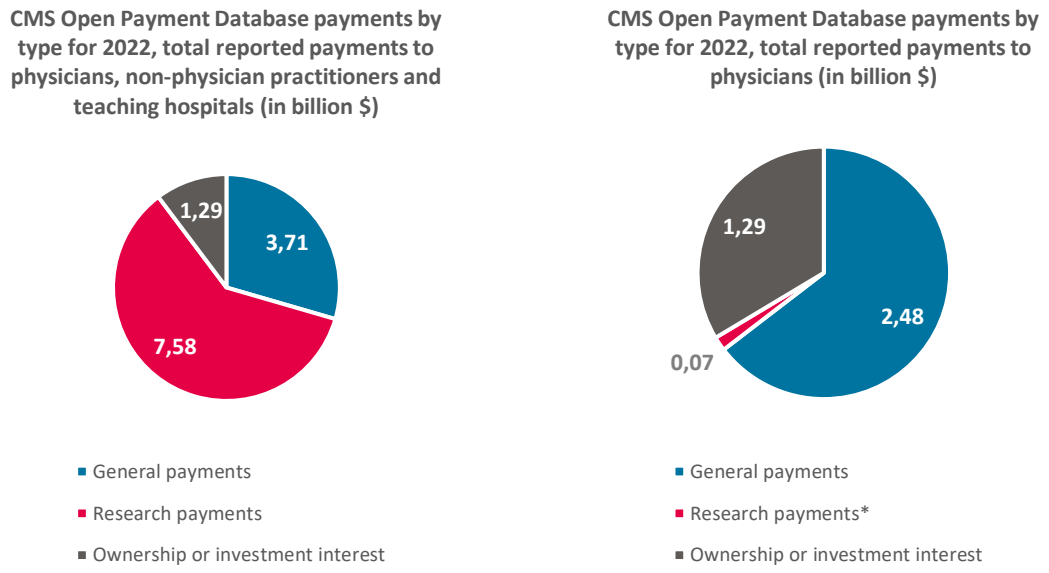


Figure 2. Overview of payments over payment types reported to the U.S. CMS Open Payment Database, figure derived from the database summary data. (34)

*** See [4] for further explanation of the included research payments for individual physicians.**

Publications included differed in study period, included types of payment and reported outcome measures. This made data extraction, synthesis and analysis difficult. We therefore focused in abstracting findings on two 'outcomes' and narratively analyzed these: 1) the scale of payments by medical device industry to care providers, and 2) comparatives between device industry payments and pharmaceutical industry payments.

Scale of payments by medical device industry

The included references that reported on the scale of payments made by medical device industry indicate that the device industry pays substantial amounts to individual care providers. The generic study on all types of physicians by Bergman, Grennan and Swanson(17) found over the period of 2014-2017, medical device vendors paid annually on average $904 million to 196,624 physicians (30 percent of active physicians). Most value of these payments related to the categories 'Royalty, licensing, and investment' ($440 million, 49%), 'Consulting fee' ($145 million, 16%), and 'Speaking fee' ($137 million, 15%).(17) Another study(18) reporting on more recent numbers noted that in 2021 physicians received $740 million in payments that related to medical devices. Several other studies that focused on specific medical specialists or specific manufacturers also reported on the scale of device industry payments(19-24); e.g. one study found urologists in 2014 received $16 million related to medical devices(21) and another study reported one medical device company paid $40 million over five years to colorectal surgeons.(22)

Some medical specialties seem to receive more payments and more total value in payments from device industry than others. For example, the overview study(17) formed a list of the percentages of payment receivers per specialty. Neurosurgeons, orthopedic surgeons, cardiologists, general surgeons, and urologists were in the top 5. Non-surgical specialties such as family medicine, rheumatology, psychiatry, dermatology and internal medicine were among the bottom of this list. Annual value of received payments also differed substantially amongst these specialties. Median annual payments for neuro- and orthopedic surgeons were $454 and $410 respectively for an individual physician, while median payments for non-surgical specialties that were receiving the lowest payments varied between $14 and $44.(17)

Notably, many studies also found substantial inequality between receivers within specialties.(19-21, 24, 26, 29, 30, 32, 33) Some top receivers gain the majority of value in payments, while a substantial group only receives minor or no payments. For example, one study reported the Gini index for measuring income inequality for orthopaedic surgeons. The index was 0.956, where an index of 1 reflects complete inequality among receivers.(24) Another study(30) reported that in otolaryngology the majority of the total reported amount paid to otolaryngologists by industry (about 90%) went to a small number of top earners (10%). For urologists it was found that received annual payments were between $100 and $1000 for most urologists, while some receivers got paid $1 million, and the top receiver got more than $7.5 million over the 5 year study period.(33)

Comparing physician payments from the device and pharmaceutical industry

All included references (17-34) reported -in differing manners- on the proportions of payments made by the device industry as compared to the pharmaceutical industry. Although the studies showed some variety, they indicate that at least for some of the studied professions, medical device industry payments exceed payments from the pharmaceutical industry.

Singh, Hyman and Modi(18) reported that for all types of physicians in 2021, device related payments comprised 56% of the total value of industry payment to physicians, while drug related payments accounted for 28%. For some specialisms medical device industry provides for even higher percentages of total payments. For example, for otolaryngologists more than three quarters (76%) of total payments were made for devices(25) and 80% of total value payments to orthopedic surgeons came from device industry.(24) On the other hand, for several other professional groups (e.g. emergency physicians and pediatricians) most payments were drug-related and thus paid by pharmaceutical companies.(28, 34)

Also over a longer period it was found that total payments from device vendors to individual physicians exceed what pharmaceutical companies pay. For the period of 2014-2017 device vendors paid annually on average about $83 million more than drug manufacturers to individual physicians.(17) Moreover, these payments were made to a smaller proportion of active physicians; 30% of active physicians for devices and 50% of active physicians for drugs. Device manufacturers thus paid larger amounts to fewer physicians. Device industry also paid a larger part of total revenue to physicians than pharmaceutical industry (1.7% and 0.24% respectively).

3.2.1 Reflection

From the analysed studies on payments made by the medical device industry to physicians we made some remarkable observations.

First, we observed that current literature focusses on the U.S., as here the CMS Open Payment Database provided the opportunity to study the payments made by medical device industry. No publications were identified that studied Europe or Asia.

Second, the included studies indicate that the medical device industry pays substantive amounts of money to physicians. Total value of payments made by device industry exceeded total payments by the pharmaceutical industry.

Third, we noticed that payments by the medical device industry were not equally distributed; some specialties received substantially more and higher (median) payments than others. Higher percentages of physicians receiving money and higher median payments were observed for neurosurgery, orthopaedic surgery, cardiology, general surgery, and diagnostic radiology. High total value of payments from device industry was observed for orthopaedics, radiology, urology, colorectal surgery, otolaryngology, neurotology, otology, and oncology. In other, often non-surgical, specialities

payments from device vendors is less common and median payments are substantially lower. Also within specialties great inequality among receivers exists. Often a small proportion of receivers got paid the major share, while others only receive minor or no payments.

Finally, most value of payments to individual physicians from medical device industry related to royalty, licencing and investment, which is not that common in drug industry payments.

Table 1 Overview of studies on payments by medical device industry

Reference	Study period	Profession/specialism	Scale of payment medical device industry	Comparatives medical device and pharmaceutical industry
(17)	2014-2017	All physicians, and differentiation over top 20 medical specialities receiving payments from industry and 'other specialties combined' category	Over the four year study period vendors promoting medical devices paid $904 million to 196 624 physicians (30% of active physicians) each year, on average.	Annual average payments for vendors promoting drugs were $ 821 million to 331 187 physicians (50% of active physicians), which is $ 83 million less annually than device vendors' payments Device-related payments to physicians represented about 1.7 percent of device industry revenue Drug-industry payments to physicians represented about 0.24% of drug industry revenue
(18)	2021	Advanced practice clinicians and physicians	For advanced practice clinicians and physicians payments from medical device industry amounted in one year over $753 million, of which $ 740 million to physicians	For physicians medical device industry was responsible for 56% of total value payment, 28% came from drug manufacturers For nurse practitioners and physician assistants, drug manufacturers were responsible for 68% and 54% of total value payments. While payments from device manufacturers accounted for 10% and 16% of total value payments respectively
(19)	2014-2019	Orthopaedic surgeons	For orthopaedic trauma surgeons, the top five payers were all medical device manufacturers and contributed $33 million in 6 years	For orthopaedic trauma surgeons the top five paying companies were all medical device manufacturers, and contributed for 80% of total payments
(20)	2015	Radiologists (and subspecialties)	For radiologists (and subspecialties) the three companies that made the biggest payments were medical device manufacturers, and together provided payments for the amount of $19 million in one year	Overall in radiology biggest payments were by medical device manufacturers
(21)	2014	Urologists	For urologists payments related to devices totalled $16 million in one year	Although for urologists number of payments that were associated with drugs were higher than those associated with devices, the total payment amount associated with devices (48%) was higher than total payment amount associated with drugs (39%)
(22)	2014-2018	Colorectal surgeons	One medical device company paid $40 million over five years to colorectal surgeons	From all payments made to colorectal surgeons over two third (67%) were associated with devices. The top paying company was a medical device company, accounting for 39% to 59% of total payment amount
(23)	2018	Plastic surgeons	Payments to plastic surgeons from Allergan related to Natrelle breast implants amounted in one year to $6 million	Allergan paid over half (57%) of their payments to plastic surgeons for breast implants, while e.g. botox (drug) only accounted for 2% of total value payments by this company
(24)	2013	Orthopaedic surgeons	For orthopaedic surgeons total payments by the top ten payers, all medical device companies, comprised $87 million in five months	For orthopaedic surgeons, top ten manufacturers or Group Purchasing Organisations were all medical device related. These ten companies accounted for 80% of total payments to orthopaedic surgeons ($87 million)

(25)	2018	Otolaryngologists		For otolaryngologists it was reported that more than three quarters (76%) of total payments were made for devices (e.g. balloon sinus dilatation, sinus implant and cochlear implant). Also the two companies paying the higher amount were medical device industry payers
(26)	2013-2014 (17 months)	Cardiothoracic surgeons and interventional cardiologists		For cardiothoracic surgeons the five biggest companies by total payments were all medical device related. For interventional cardiologists 4 of the top 5 payers were medical device manufacturers
(27)	2015	Neurotology and otology		For neurotology and otology the top 4 paying companies were all primarily focused on medical devices and accounted for almost all (98%) of all general payments. Also the top 3 paying companies accounting for almost all (95%) of all research payments, were all primarily focused on medical devices
(28)	2014	Pediatricians		For orthopaedic surgeons, cardiology, Pediatric surgery, and pediatric radiology Median payments for the majority related to devices For pediatricians most payments are drug related, with some exceptions (i.a. pediatric surgery, pediatric radiology)
(29)	2014	Oncology		For oncologists (radiation, medical and surgical) device manufacturers accounted for 58% of the total payment value
(30)	2013 (5 months)	Otolaryngology		Among the top 20 highest paying sponsors to otolaryngologists, 65% manufactured devices. In the top 5 of highest paying companies, 80% manufactured devices
(31)	2013-2017	Ophthalmology		For ophthalmologists it was reported that 15 companies were responsible for 88% of all payments, these involved predominantly pharmaceutical products manufacturers
(32)	2015	Cardiology		For cardiologists half of the value (52%) of payments came from a pharmaceutical company
(33)	2014-2018	Urology		Largest sums of payments from industry were to those urology subspecialties that most often utilize implantable medical devices
(34)	2014	Emergency physicians		For emergency physicians the top ten payments were related to drugs

3.3 Associations between medical device industry-physician interactions and care practice

The studies on medical device industry payments show substantial amounts of money are paid to physicians by device manufacturers. These studies, however, do not assess the consequences of such payments. This while financial ties between device industry and physicians may influence device selection and usage, and could have consequences for patients and society. The topic is therefore explicitly adopted in the Dutch Act on medical devices.(12) We were curious about the evidence for these hypothesis and analyzed studies that did assess the association between industry-physician interactions and device selection and utilization, and quality of care, to answer the following question: *"What is the evidence for the consequences of medical device industry-physician interactions and product selection and utilization, and quality of care?"*

First the characteristics of the included studies are briefly described. Then the set-up and findings of the studies are elaborated upon more in-depth to explain precisely how the studied industry-physician interactions work. Thereafter some important remarks are summarized in a reflection paragraph.

The search of scientific databases and the subsequent screening process resulted in inclusion of only two studies.(36, 37) During the screening process we identified one other relevant study that took place in Canada.(38) Although this study did not meet our original inclusion criteria due to its location, we decided to include it anyway because of its relevance. The 3 references(36-38) assessed whether device industry-physician interactions were associated with device selection and utilisation, and/or quality of care (Appendix II, Table 2). All three studies had a cross-sectional design. We narratively analyzed these studies and focused on the 1) industry-physician interaction (type and intensity or scale), and 2) association with device selection and utilization, and quality of care.

Industry-physician interactions

Two studies(36, 37) focused on financial interactions. These used data from the CMS Open payment database and were thus focused on the U.S. For data on device selection and use, national registries were consulted (i.e. the National Cardiovascular Data Registry ICD Registry, and Medicare Claims Database). The Canadian study(38) assessed the influence of a non-monetary interaction, i.e. sales representatives' presence when devices were implanted. For data on device selection and use medical records were reviewed.

The studies on associations that assessed payment interactions indicate that specific device manufacturers pay substantial amounts to physicians applying their device(s). For some individual physicians this adds up to serious amounts of money. Annapureddy et al.(36) studied the association between general payments from manufacturers of Implantable Cardioverter Defibrillators (ICD) or Cardiac Resynchronisation Therapy-Defibrillators (CRT-D) and physician device selection and quality of care. They found 94% of the physicians who performed ICD/CRT-D implantations received payments from manufacturers of these devices. Total annual payments equalled $20 million to 4152 physicians, with payments ranging from $2 to $323 559 per physician. Median payment was $1211 (IQR $390-$3702). Many physicians (43%) received in total under a $1000 or between $1000 and $10 000. For a small number of physicians (4%) total payments exceeded $25 000. Payments often came from multiple manufacturers; 92% of physicians received payments from more than one manufacturer.

The other study(37) focused on characterising the association between device industry payments (all types) and utilisation and selection of paranasal balloon catheter dilations (BCDs). Most physicians (83%) who performed BCDs received payments from industry. The physicians using BCDs (n=334), over 17 months received $951 620 in total payments, with payments varying from $43 to $111 685 per physician. Median payment was $301.

Next to financial incentives, there are other ways of how industry may interact with medical device users. The article on a non-monetary interaction(38) studied the presence of sales representatives of stent manufacturers in the catheterisation laboratory during Percutaneous Coronary Intervention(PCI). They found sales representatives of stent manufacturers were present in the catheterization laboratory in 44.2% of days in which PCI was performed, during 47.8% of the treatments, and during deployment of 49.8% of the stents.(38) Thus, during a substantial number of interventions they were present.

Association with device selection, utilisation, and quality of care

Selection and utilisation

Industry-physician interactions were found to be associated with device selection; products of manufacturers with more intense interactions with physicians were chosen more often than products of competitors. Two of the studies(36, 38) assessed whether interactions between specific device manufacturers and physicians resulted in an advantageous position compared to other (competing) manufacturers. One study found that patients were substantially more likely to receive ICD/CRT-D devices made by the manufacturer that provided the largest payment to the physician who performed the implantation than they were from each other individual manufacturer. Absolute differences ranged from 14.5% to 30.6%.(36) The study reports that even stronger associations were found than in previous work on pharmaceutical industry payments and physician medication prescription behaviour.

Also the study on sales representatives presence found an advantageous position in device selection for some manufacturers. The study noted that for all companies marketing drug-eluting stents there was an increase in the sales representative company's drug eluting stents and less use of the competitors product when the representative was present.(38)

With regard to the number of devices used, two studies(37, 38) found that industry-physician interactions were associated with increased device usage. For example, Fujiwara, Shih and Mehra (37) conclude that industry payments were associated with BCD device use for chronic rhinosinusitis treatment. Overall, one payment was associated with an additional 3.05 BCD use. Separate analysis for specific payment types showed one payment for food and beverages and education was associated with 3.81 additional BCDs and one payment for travel and lodging, consulting fees, speaker fees, and honoraria was associated with 5.49 additional BCDs. Also, in the study on stent use in PCIs, Surdarsky et al.(38) found that when a representative was present more drug-eluting stents per case were implanted (1.71 SD 0.9 vs 1.60 SD 0.93). No difference in use was found for other types of stents. The study also noted higher cost per case when a representative was present.

Quality of care

One study assessed the association between industry-physician interactions and outcomes of quality of care. This study(36) did not find an association between payments from ICD/CRT-D manufacturers and the included quality of care measures; for prescription of guideline recommended therapy or in-hospital complications or death there was no consistent relationship observed with physician payments.

3.3.1 Reflection

The associations between medical device industry-physician interactions and care practice was only limitedly studied. Moreover, the three included studies were all very cautious with their conclusions. As these all had a cross-sectional design and thus only studied associations, causality could not be concluded. Nevertheless, for this phenomenon such cross-sectional research may be the best available research method, since an experimental study design is not feasible. The study on the presence of sales representatives comes closest to some sort of quasi experiment, since in some cases the representatives were present and on other moments they were not. Yet, this article also remains very cautious in their conclusions.

The articles do learn us that monetary and non-monetary interactions between device industry and physicians are associated with device selection and utilisation. Manufacturers' efforts were associated with higher usage of the device, and a greater off-take of that specific manufacturers' device. The articles stressed that also other factors may influence device selection and utilisation,

such as patient preferences, clinical scenarios, and hospital contracts. No consistent relation with quality of care was reported. One study did find higher costs per treatment, which may have consequences on a societal level (i.e. higher healthcare expenditure). However, it remains unknown if this extra expenditure was cost-effective.

Direct and hard conclusions on the consequences for patients and society can thus not be derived from existing literature. What the studies do indicate is that the situation in which industry has (financial) ties with (individual) physicians results in mutual dependencies. This may be indicative of a field in which there are risks for patients and/or society, since providers may be incentivized to use more or specific devices and may be reluctant to switch manufacturer.

Table 2 Overview of association studies

Reference	Type of device and treatment	Inducement strategy and characteristics	Consequences for device utilisation, selection and quality of care
(36)	Implantation of Internal Cardioverter-Defibrillators(ICD) and Cardiac Resynchronization Therapy-Defibrillators(CRT-D)	Industry payments, general payments (incl. travel and lodging, food and beverages, and consulting and speaking fees) Most physicians (94%) who perform ICD/CRT-D implantations received payments from manufacturers (range $2 - $323559, median $1211)	Device selection: Patients were more likely to receive ICD/CRT-D devices from the manufacturer that provided the highest total payment to the physician who performed an ICD or CRT-D implantation than each other manufacturer individually. Absolute differences between manufacturers varied between 14.5% and 30.6% Quality of Care: For prescription of guideline-recommended therapy or in hospital complications or death there was no consistent relationship with physicians payments. Use of CRT-D was higher among patients of whom the physician received high value payments, which may help survival of eligible patients.
(37)	Paranasal sinus balloon catheter dilations (BCDs) for chronic rhinosinusitis	Industry payments, all types Most included physicians (83.3%) received payments from BCD manufacturers (range $43 - $111 685, median $301 over 17 months)	Device utilization: BCD use was significantly associated with the number of BCD-related payments. One payment was associated with 3.05 BCDs. One payment for food and beverages 3.81 additional BDCs. One speaker or consulting fee 5.49 additional BCDs
(38)	Bare-metal stents, drug-eluting stents, and balloon catheters for percutaneous coronary interventions (PCIs)	Visits of manufacturers' sales representative's in the catheterization laboratory Industry representatives were present in the catheterization laboratory in 44.2% of the days, and were present during 47.8% of the treatments, and during deployment of 49.8% of the stents	Device utilization: When a representative was present, more drug-eluting stents per case were implanted (1.71 SD 0.9 vs 1.60 SD 0.93). No difference was found for other types of stents. Stent cost per case was higher when a representative was present (CAD $1703 SD 1314 vs CAD $1469 SD 1273). Device selection: For all companies marketing drug eluting stents, there was an increase in the use of the company's drug eluting stent when their representative was present with less use of the competitors' stent

3.4 Normative statements and code of conducts from formal associations on the ties between medical industry and physicians

In this paragraph, we address whether the medical profession and device industry itself have made normative statements on industry-physician interactions. We assessed publications that described or evaluated codes of conduct with regard to industry-physician relationships or managing conflict of

interest in the medical device sector. By assessing these publications we aimed to answer the following question: *"What are the motives to write (about) codes of conduct, what topics are covered, and how do associations regulate themselves?"*
First, we describe the included publications and provide additional information on how these were selected. Subsequently, we focus on the various elements of the question above, and provide detailed examples extracted from the publications. The concluding reflection paragraph brings the findings together.

Our search of scientific databases at first provided a substantial amount of editorials, viewpoints, and commentaries that reflect specific authors' views on managing industry-physician relationships. We narrowed this output to articles written or endorsed by formal associations, to include more widely accepted opinions and codes. Four publications(39-42) were included. All of them were from U.S. associations. None of them were on codes from Europe or Asia. As we suspected also codes from European and Asian parties existed, we widened our search strategy for this specific topic and searched Google and Google Scholar for European and Asian codes (See Appendix A for search strategy). This resulted in inclusion of two publications.(43, 44) We also included the Dutch Code of Conduct for Medical Devices (Gedragscode Medische Hulpmiddelen).(11)

We observed that both medical associations as well as associations of medical device industries published on this topic. From the device industry we assessed the code of conducts of the U.S. Advanced Medical Technology Association(AdvaMed)(39, 45), the MedTech Europe code of the European trade association for the medical technology industry(43), and the APACMed code of ethical conduct of the Asia Pacific medical technology association.(44)
For medical associations, we assessed the Ethics committee statement of The American College for Obstetricians and Gynecologists(40), an elaboration on the code on interactions with companies of the Council of Medical Specialty Societies(41), and recommendations of the Council on ethics of The American Academy of Pain Medicine on this topic.(42) These three publications by medical professions did not specifically focus on the medical device sector but also (partly) comprised the pharmaceutical industry. Other associations have written on this topic as well, but these were not identified in our search or excluded during the screening process (e.g. because they did not match our search strategy, were assessed as wrong publication type, or full text was not available).
The Code of Conduct for Medical Devices in the Netherlands(11) applies to members of umbrella organizations of physicians, hospitals and industry, and is based on reciprocity; what one party may not offer or give, the other party may not ask for or accept. This code therefore relates to industry as well as physician associations.

Data abstraction of the included studies focused on: 1) motives to write the article or code of conduct and underlying values that could be at risk, 2) discussed norms, standards or advices, and 3) the way the code was assured and regulated.

Motives and values

We noticed both industry and physician associations were convinced that relationships between industry and physicians are necessary, but at the same time interests of both parties may not always align, which can lead to conflicting interests. For physicians therefore potential conflicting interests in the field of patient care, education, and research can arise.(39-42) One study(40) for example specifically states that the intentions of industry simply do not always align with those of physicians when it comes to physicians' responsibilities to promote best interests of their patients, provide evidence based instructions, and adhere to scientific integrity. Also, it sees potential risks that (financial) ties between industry and physicians may result in a decrease of public trust in physicians' ethical standards and high quality care.

Codes of device industry acknowledge that compliance with applicable law and adherence to ethical standards is necessary for achieving the associations' missions in creating an environment to promote high quality, safe and effective patient care by innovative technologies, and meet expectations and needs of stakeholders.(43-45) The codes provide guidance in this field, aiming to avoid or manage conflicting interests.

The values that might be at stake and were described in the publications(39-45) generally overlapped and included: (scientific) integrity, altruism (ensuring that the needs of patients come first), openness and transparency (to peers, patients, and the public), and independence.

Norms, standards and advices

Codes of both medical associations and industry covered similar topics. They mainly provide guidance on acceptance of money (in any form), gifts or services, disclosure, research, training and education, and protecting independence.(39-45) Most codes and their eventual explanatory notes get quite specific in their standards and advices. For example, the Dutch code of conduct explicitly states which information must be adopted in a sponsorship agreement, and specifically notes that sponsoring of a dissertation may only be provided to a maximum of €250.(11) Or the APACmed code stating that any given educational item other than medical textbooks or anatomical models may not exceed $100.(44)

We noted that some codes do not explicitly report on investment and ownership, and some also do not write about payments in royalties. For example, the Dutch and Asian Pacific code do not include the term royalties, while the MedTech Europe guideline and U.S. AdvaMed code do explicitly write on this topic. In the Committee statement of the American College for Obstetricians and Gynecologists(40) and the Council of Medical Specialty Societies' statement(41), stock ownership and royalty agreements are described in passing. For example, by stating that when these arise one should withhold from participating in decision-making activities.(40) The American Academy of Pain Medicine does not report on royalties or licensing, but does recommend that physicians generally should not invest privately and directly in a company for which they do research, or in a company that manufacturers products that they will speak or write about.(42)

Assurance and regulation

Overall assurance is only minimally covered in the publications. Adoption of the codes seems to be mainly voluntary and based on self-regulation. Assurance sometimes is stimulated by certification and listing on the code or associations' website.(39, 41) One article also reported on available tools and standard formats to stimulate adherence.(39) The Dutch code and EU code state that compliance will be pursued by including enforcement based on complaints.(11, 43)

3.4.1 Reflection

We did not provide an exhausting overview of all codes of conduct relevant for the medical device sector, but included some relevant publications on this topic. We noted that medical associations as well as industry associations published regarding this matter. Motives and underlying values to write (about) codes of conduct are consistent and include; the avoidance or management of industry-physician relationships which could result in conflicts of interests, and protecting the values integrity, altruism, openness/transparency, and independence. Also the codes of conduct mainly overlap in the topics covered, i.e. acceptance of money, gifts or services, disclosure, and research, training, education and board practices. As the majority of payments from device industry relate to royalties, investment and ownership, we assessed how these topics were covered in the codes. We found that these are not addressed in all codes, for example the Dutch and Asian code do not explicitly cover

royalties. Adoption of the codes is often voluntary and assurance and compliance seems to be based primarily on self-regulation.

Table 3 Overview of code of conduct studies

Reference	Organization/association	Motives & Values	Topics covered	Assurance and regulation
Medical device industry association				
(39, 45)	Advanced Medical Technology Association	Motives: Proactively managing potential conflict of interests in the vital and complex relationships between vascular surgeons and device companies. As competing pressures from the multiple, overlapping roles as clinician/caregiver/investigator/innovator/customer are significant. Code aims to promote the highest ethical standards Values: Openness, altruism (best interest of the patient)	• company conducted training and education • third-party conferences • entertainment and gifts • provision of meals • consulting arrangements and royalties • evaluation and demonstration products • reimbursement information • grants and donations	A compliance section is adopted. A list of the companies that certify for their adoption of the code is publicly available on the AdvaMed's website The website also provided tools that provide information on how a company should approach its interactions with healthcare professionals under the code
(43)	MedTech Europe	Motives: Recognition that compliance with applicable laws and regulations as well as adherence to ethical standards are an obligation and a critical step Values:	• Events (educational, company) • Grants and charitable donations • Consulting • Research • Royalties • Educational, promotional, and demonstrational items • Intermediaries	Complaint handling MedTech Europe Compliance Panel
(44)	Asian Pacific Medical Technology Association	Motives: facilitate independent decision-making, and reinforce public confidence in the integrity of patient care, treatment, and product and service selection Values: integrity	• Consultancy agreements • Training and education • Gifts and entertainment • Evaluation/demonstration products and samples • Research • Charitable donations • Technical support • Sales and marketing intermediaries	Advices on Effective code implementation are adopted
Medical association				
(40)	The American College for Obstetricians and Gynecologists	Motives: Industry priorities not always algin with ethical responsibilities of clinicians to promote best interests of their patients, of educators to provide evidence based instruction, and of researchers to ensure the scientific integrity of their investigations. Secondary financial interests may substantially decrease public trust in physicians' ethical standards and high quality care. Values: (scientific) Integrity, Altruism (patients' best interest), Evidence based Medicine/education	• acceptance of cash donations, vacations, medical or personal services, and gifts • disclosure for institutional decision makers, and in publication and presentation of research findings • providence of medication samples to patients • disclosure of payments of substantial value (royalties, consultation), • participation in speakers' bureaus	-

			• direct involvement of industry in education of trainees • adherence of practice standards that support research • research funding or payments • contribution to manuscript or presentation	
(41)	Council of Medical Specialty Societies	Motives: Helping specialty societies in the profession of medicine to manage their relationships with the pharmaceutical and medical device manufacturers to avoid and manage relationships which result in conflicts of interest to prioritize patient benefits over physician benefits. To protect and promote the independence of specialty societies and their leaders Values: Altruism (ensuring that the needs of patients come first), transparency (to peers, patients, and the public), independence	• definition of conflict of interest • who is addressed in the society's policy • delineation of activities addressed in the policy • disclosures of relationships • consequences for failure to disclose • management and resolution strategies for disclosed conflicts of interest • clarification of circumstances requiring recusal, removal from participation or from the disclosed relationship • adherence to external standards and guidelines • publicly disclosing information on society's websites • management and resolution strategies	Self-regulatory guidance, adoption of the code by specialty societies is voluntary CMSS will not enforce the code Annually societies can certify their continued adherence Adherence to the Code will be identified on the CMSS Web site Standardized model templates for conflict of interest policies, disclosure forms were setup
(42)	The American Academy of Pain Medicine	Motives: Understanding that physicians and industry have fundamentally different goals. In order to ensure that these relationships are principled and ethical, all parties must be aware of the conflicts of interest they present and strive to manage them ethical and with transparency. As a conflict of interest can create bias Values: Transparency	• disclosure • recusal • consultants and advisory boards • continuing medical education • speaker bureaus • meetings with sales and marketing representatives of pharmaceutical companies and device manufacturers • funding for research, • institution review board • physicians investors	-
		Generic		
(11)	Stichting Gedragscode Medische Hulpmiddelen	Motives: prevent improper practice, and provide guidance on legitimate foundations and reasonableness, documentation, and transparency Values: independence, transparency	• Bonusses and discounts • Gifts • Meetings • Remuneration for services • Sponsoring • Involvement in advisory reports and guidelines • Transparency register	Based on self-regulation Rules are enforced based on complaints or signals Monitoring of compliance by an independent Code Commission and Appeals Board

4 Discussion

Recent events in the Netherlands have caused awareness on inducement in the medical device sector. Financial relationships between device manufacturers and physicians may have consequences for patient care. Therefore inducement is explicitly prohibited by the Dutch Act on medical devices.(12) The phenomenon is widely debated and studied for the pharmaceutical industry, but a knowledge gap exists for the medical device sector. This exploratory literature study aimed to provide an overview of the current state of (scientific) insights on this topic, specifically focusing on the scale, nature, consequences and policy regarding inducement in the medical device sector in Europe, Asia and the United States. Therefrom situations may be derived where risks for the violation of the inducement prohibition can emerge.

We found inducement in the medical device sector is only minimally studied. In particular for Europe and Asia no scientific studies were identified. There is some literature from the U.S. covering payments from device industry to physicians(17-34), and a scarce amount of studies was found on industry-physician interactions and its association with device selection and utilization, and quality of care.(36-38)

From the U.S. literature mapping device industry payments(17-34) we conclude that substantial amounts of money are paid to individual physicians. Overall, payments to individual physicians by device manufacturers even exceed payments by the pharmaceutical industry, though this does not hold for all medical specialties independently.
We further found payments are not equally distributed. Some specialties receive more total value payments from device industry than others. Several particular medical specialties receive substantial amounts of money, while some other specialties – often non-surgical – receive only minor or no payments. Also within specialties great inequality exists between receivers. A small number of physicians receives the bulk of value in payments. These payments may collectively add up to a serious source of income for these individual physicians.

Furthermore we observed that highest value payments from device industry to individual physicians often related to royalties, licensing and investment. This seems typical for the device sector. Consulting and speaker fees are also payment types where substantial amounts of money are involved. We noticed that most included studies focused on the categories of general payments and investment and ownership only. Research funding is mainly reported on the organizational level and only a small amount of research payments registered to the CMS database was linked to individual physicians.(35) From the included studies and CMS open payment database overview figures, it remains unclear how these research payments may also flow to individual physicians. Just a few studies comprised all payment types, including research payments.

From the scarce literature on industry-physician interactions and its association with device selection and utilization(36-38), we found that indeed industry-physician interactions are associated with device selection and use. For quality of care no such association was found. Although the study designs do not allow to make any causal claims, they do suggest that mutual dependencies between industry and physicians exist. It remains to be seen to what extent such a system of dependencies leads to undesired influence (or inducement), and what the consequences are for patients and society.

We further observed that device industry(39, 43-45) as well as physician associations(40-42) wrote codes of conducts on industry-physician interactions. Both industry and physician associations

acknowledge the relevance of industry-physician relationships, and agree that such relationships may conflict with a physicians' responsibilities and the associated independence for patient care, education and research. Therefore, both industry and physician associations stress the importance of codes of conduct to manage these relationships. Generally the studied codes of conducts were based on the same values (e.g. integrity, altruism, transparency and independence) and cover similar generic topics (e.g. acceptance of gifts and disclosure principles). Yet, the codes do differ in the specifics. Among other things, the codes vary in the type of financial relations that are addressed; e.g. the Dutch code and the APACmed code do not explicitly cover the payment types of royalties and investment.
Adoption of the codes is typically voluntary based and compliance was only minimally covered in the studied publications. Regulation is often based on self-regulation or depends on complaints. It could be questioned if these code assurance strategies in fact result in adherence in practice.

About the research

This exploratory study has some important limitations that should be addressed. First, the topic is subject to publication bias. Some aspects of inducement are not or only limitedly studied. We were dependent on the conducted studies, the choices of their authors, and the data that were available for these studies. This means that certain elements of the phenomenon may be different in practice than how we could conclude from the published literature. Some elements clearly need further investigation. For example, studies on industry payments in Europe and Asia, association studies on industry-physician interactions and patient and/or societal outcomes, and studies on exactly how research funding is spent.

Almost all included literature was from the U.S., so we have to be cautious with generalizing these findings to other settings, such as the Netherlands. For example, differences may exist across countries in health system, market scale of the healthcare sector, levels of salaries, and legislation. These differences may have consequences for interpretation of the findings. Nonetheless, the medical device market is a global market and thus industry-physician interactions may be similar in other countries.

In addition, we would like to emphasize that this study intended to provide and initial exploration of the literature on this relatively understudied phenomenon. Our explorative approach was structured, but does not adhere to the criteria of e.g. a systematic literature review and meta-analysis. We may therefore not be complete in all aspects and have made choices (e.g. no double screening of all articles but only on a subset, no meta-analysis but narrative analysis of findings etc). Nevertheless, we believe we took adequate measures to present valid and reliable findings for the purpose of this study.

We consider this study a first step in gaining a better understanding of industry-physician relationships. We find that the existing literature is scarce, especially compared to the pharmaceutical domain. Moreover, we note that literature on the Netherlands is virtually non-existent. Nonetheless, this study offers several points of interest that warrant further research and may help in setting a policy agenda to manage potential risks associated with medical device industry-physician relationships.

Points of interest

Some important insights arise from this explorative literature study. From U.S. literature follows that device industry pays substantial amounts of money to individual physicians. These payments go to a small group of high receivers. This could result in situations where inducement prohibition regulations are at risk.

We also found physicians receive high payments from device industry in the form of royalties, licensing and investment, and consulting and speaker fees. While the consulting and speaker fees are often covered in legislation and/or field code of conducts, royalties, licensing and investment are not always explicitly mentioned. For example, it is not explicitly adopted in the Dutch Act on medical devices and Dutch code of conduct. It remains unknown how these payment types are currently addressed. Given the high amounts of money that are apparently involved in this type of payment and the potential for complex and untransparent constructions for these payment types, it would be relevant to see how these are managed in practice.
Also, the category of research funding represents a significant part of total industry payment value. From this study it remains unknown how this money is spent precisely and whether these payments may eventually also flow through to individual healthcare providers, creating potential risks for conflicts of interest.

From this research we further learned that codes of conduct often have a fairly non-committal character and are based on self-regulation. It would be interesting to gain more insights in how the codes work in practice.

Lastly, financial relationships between device industry and physicians can be complex and untransparent. More transparency and insights in these relationships is desirable. This study shows that the U.S. national transparency program following the Sunshine act provided the major and only source of information on these financial relationships. This transparency program led to a publicly accessible database that provides data about financial relationships between drug and medical device industry and health care providers in the U.S. In line with a recent advice from the Dutch Minister of Health Welfare and Sport(46), further expanding the payment reporting system and introducing an obligation to report industry payments could help achieving more transparency. When setting up such a registry system, or expanding the existing system, the need for useful periodic information and suitability of data for specific scientific research should be taken into account. Given the global character of the medical device market, international comparability of payment data may also be important. Using a standardized nomenclature for the various payment types, for example similar to that used in the U.S. registry, could improve international comparison. Setting up an European-wide register could also help to improve transparency and at the same time enable international comparisons.

References

1. Kammeron TMHA, Kuppens IELM, Brackel LGM. Onderzoek naar Marketing, reclame en gunstbetoon omtrent Medische Hulpmiddelen. 2009.
2. Commissie voor Volksgezondheid WeS. Hulpmiddelenbeleid in de gezondheidszorg 2011 [
3. de Bruin M, Schutjens M. Gunstbetoon en medische hulpmiddelen. Tijdschrift voor Gezondheidsrecht. 2012;36(4):280-96.
4. Inspectie Gezondheidszorg en Jeugd. Toezicht op gunstbetoon in de sector van medische hulpmiddelen: Positief dat er dienstverleningsovereenkomsten waren, maar meer transparantie over vergoeding is noodzakelijk. 2019.
5. Inspectie Gezondheidszorg en Jeugd. Toezicht op gunstbetoon in de medische hulpmiddelensector. 2021.
6. Mitchell AP, Trivedi NU, Gennarelli RL, Chimonas S, Tabatabai SM, Goldberg J, et al. Are Financial Payments From the Pharmaceutical Industry Associated With Physician Prescribing? Annals of Internal Medicine. 2021;174(3):353-61.
7. Brax H, Fadlallah R, Al-Khaled L, Kahale LA, Nas H, El-Jardali F, et al. Association between physicians' interaction with pharmaceutical companies and their clinical practices: A systematic review and meta-analysis. PLOS ONE. 2017;12(4):e0175493.
8. Precedence Research. Medical Devices Market (By Type: Cardiovascular Devices, Orthopedic Devices, Diagnostic Imaging, MIS, IVD, Diabetes Care, Wound Management, Dental, Nephrology, Ophthalmic Devices, and Others; By End User: Clinics, Hospitals & Ambulatory Surgical Centers, and Others) - Global Market Size, Trends Analysis, Segment Forecasts, Regional Outlook 2022 - 2030 2023 [Available from: https://www.precedenceresearch.com/medical-devices-market#:~:text=The%20global%20medical%20devices%20market,USD%20198.3%20billion%20in%202022.
9. Statista. Medical Devices - Worldwide: Market insights. health, Medical technology 2023 [Available from: https://www.statista.com/outlook/hmo/medical-technology/medical-devices/worldwide.
10. Statista. Medical Devices - Netherlands: Market insights, Health, Medical Technology 2023 [Available from: https://www.statista.com/outlook/hmo/medical-technology/medical-devices/netherlands.
11. Stichting Gedragscode Medische Hulpmiddelen GMH. Gedragscode Medische hulpmiddelen. 2022.
12. Wet medische hulpmiddelen, (2019).
13. Inspectie Gezondheidszorg en Jeugd. Gunstbetoon: wetten en regels [Available from: https://www.igj.nl/onderwerpen/gunstbetoon/wetten-en-regels.
14. Stichting transparantieregister Zorg. [Available from: https://www.transparantieregister.nl/home.
15. Health and Youth Care Inspectorate. Supervision of inducments [Available from: https://english.igj.nl/medical-technology/supervision-of-inducements.
16. 2022. Available from: https://www.rayyan.ai/.
17. Bergman A, Grennan M, Swanson A. Medical Device Firm Payments To Physicians Exceed What Drug Companies Pay Physicians, Target Surgical Specialists. Health Aff (Millwood). 2021;40(4):603-12.
18. Singh A, Hyman MJ, Modi PK. Evaluation of Industry Payments to US Advanced Practice Clinicians in 2021. JAMA Netw Open. 2022;5(11):e2242869.
19. Frane N, Partan MJ, White PB, Iturriaga C, Tarazi JM, Roy T, et al. Orthopaedic Trauma Surgeons' Financial Relationships With Industry: An Analysis of the Sunshine Act Reporting of

Physician Open Payments From 2014 to 2019. J Am Acad Orthop Surg Glob Res Rev. 2021;5(11).
20. Jutras M, Khosa F. The Physician Payment Sunshine Act: Evaluating Industrial Payments in Radiology. Academic Radiology. 2019;26(1):86-92.
21. Maruf M, Sidana A, Fleischman W, Brancato SJ, Purnell S, Agrawal S, et al. Financial Relationships between Urologists and Industry: An Analysis of Open Payments Data. Urology Practice. 2018;5(3):180-6.
22. Kaleem SZ, Parikh S, Yang K, Poggio JL. Industry Payments in Colon and Rectal Surgery: A Cross-Sectional Analysis of Open Payments Data. J Surg Res. 2020;254:369-77.
23. Isbester K, Boas S, Summerville L, Wee C, Kumar A. Industry Payments by Allergan, Inc to Plastic Surgery and Related Specialties in 2018. Annals of Plastic Surgery. 2021;86(1):4-8.
24. Samuel AM, Webb ML, Lukasiewicz AM, Bohl DD, Basques BA, Russo GS, et al. Orthopaedic Surgeons Receive the Most Industry Payments to Physicians but Large Disparities are Seen in Sunshine Act Data. Clin Orthop Relat Res. 2015;473(10):3297-306.
25. Ramsey T, Curran K, Ostrowski T, Ruffner R, Leapman NG. Financial Transactions from Manufacturers to Otolaryngologists in 2018. Laryngoscope. 2021;131(2):E388-e94.
26. Parreco J, Donath E, Kozol R, Faber C. Comparing industry compensation of cardiothoracic surgeons and interventional cardiologists. J Surg Res. 2017;208:51-9.
27. Ziai K, Sahyouni R, Moshtaghi O, Vu K, Goshtasbi K, Ghavami Y, et al. An Analysis of the Open Payment Database in Neurotology. Otolaryngol Head Neck Surg. 2018;158(2):319-22.
28. Parikh K, Fleischman W, Agrawal S. Industry Relationships With Pediatricians: Findings From the Open Payments Sunshine Act. Pediatrics. 2016;137(6).
29. Jairam V, Yu JB. Examination of Industry Payments to Radiation Oncologists in 2014 Using the Centers for Medicare and Medicaid Services Open Payments Database. Int J Radiat Oncol Biol Phys. 2016;94(1):19-26.
30. Rathi VK, Samuel AM, Mehra S. Industry ties in otolaryngology: initial insights from the physician payment sunshine act. Otolaryngol Head Neck Surg. 2015;152(6):993-9.
31. Slentz DH, Nelson CC, Lichter PR. Characteristics of Industry Payments to Ophthalmologists in the Open Payments Database. JAMA Ophthalmol. 2019;137(9):1038-44.
32. Jaiswal D, Checketts JX, Vassar M. Industry Payments in Cardiology: A Cross-sectional Analysis of Open Payments Data. J Am Osteopath Assoc. 2018;118(12):781-7.
33. Clennon EK, Lam M, Manley A, Chakiryan NH, Acevedo M, Duty B, et al. Patterns of Industry Payments to Urologists From 2014-2018. Urology. 2020;140:44-50.
34. Fleischman W, Ross JS, Melnick ER, Newman DH, Venkatesh AK. Financial Ties Between Emergency Physicians and Industry: Insights From Open Payments Data. Ann Emerg Med. 2016;68(2):153-8.e4.
35. CMS Open Payment Database. The facts about Open Payments data, summary 2022 [Available from: https://openpaymentsdata.cms.gov/summary.
36. Annapureddy AR, Henien S, Wang Y, Minges KE, Ross JS, Spatz ES, et al. Association Between Industry Payments to Physicians and Device Selection in ICD Implantation. JAMA. 2020;324(17):1755-64.
37. Fujiwara RJT, Shih AF, Mehra S. Cross-sectional Analysis of the Relationship between Paranasal Sinus Balloon Catheter Dilations and Industry Payments among Otolaryngologists. Otolaryngology–Head and Neck Surgery. 2017;157(5):880-6.
38. Sudarsky D, Charania J, Inman A, D'Alfonso S, Lavi S. The impact of industry representative's visits on utilization of coronary stents. American Heart Journal. 2013;166(2):258-65.
39. Van Haute A. Managing perceived conflicts of interest while ensuring the continued innovation of medical technology. Journal of Vascular Surgery. 2011;54(3, Supplement):31S-3S.
40. Shalowitz DL, Ethics; tACoOaGCo. Professional Relationships With Industry: ACOG Committee Statement No. 2. Obstet Gynecol. 2022;140(5):904-11.

41. Kahn NB, Jr., Lichter AS. The new CMSS code for interactions with companies managing relationships to minimize conflicts. J Vasc Surg. 2011;54(3 Suppl):34s-40s.
42. Dubois MY. American academy of pain medicine ethics council statement on conflicts of interest: interaction between physicians and industry in pain medicine. Pain Med. 2010;11(2):257-62.
43. MedTech Europe. MedTech Europe Code of Ethical Business Practice. MedTech Europe; 2022.
44. Association APMT. Code of ethical conduct for interactions with health care professionals. 2016.
45. AdvaMed. ADVAMED CODE OF ETHICS - On interactions with U.S. Healthcare Professionals. 2023.
46. E.J. Kuipers MvV, Welzijn en Sport. Brief regering: Voorkomen van ongewenste beïnvloeding van medisch professionals door bedrijven. 2023.

Appendix A Search strategy

A.1 Search string scientific databases

Results March 22th 2023

Database	Results	After duplication removal
PubMed	**1439**	**1431**
Embase.com	**2112**	**1077**
Web of Science Core Collection	**950**	**249**
Total	**4501**	
After duplicate removal	**2757**	**2757**

Search history PubMed March 22th 2023

Search	Query	Results
#1	"Equipment and Supplies"[MeSH Terms] OR "medical device*"[tiab] OR "implant*"[tiab] OR "prosthes*"[tiab] OR "prothes*"[tiab] OR "orthopedic device*"[tiab] OR "cardiac device*"[tiab] OR "stent*"[tiab] OR "pacemaker*"[tiab] OR "medical apparatus"[tiab] OR "medical consumable*"[tiab] OR "surgical consumable*"[tiab] OR "medical instrument*"[tiab] OR "surgical instrument*"[tiab] OR "dental device*"[tiab] OR "diagnostic device*"[tiab] OR "in vitro diagnostic device*"[tiab] OR "In-vitro diagnostics"[tiab]	1,964,686
#2	"Fraud"[Mesh] OR "Conflict of Interest"[Mesh] OR "Lobbying"[Mesh] OR "gift*"[tiab] OR "conflict of interest*"[tiab] OR "interest conflict*"[tiab] OR "bribe*"[tiab] OR "lobbying*"[tiab] OR "corrupt*"[tiab] OR "fraud*"[tiab] OR "scams"[tiab] OR "partnership*"[tiab] OR "collaborati*"[tiab] OR "funding*"[tiab] OR "sponsor*"[tiab] OR "fee"[tiab] OR "fees"[tiab] OR "bonus*"[tiab] OR "discount*"[tiab] OR "payment*"[tiab] OR "incentive*"[tiab] OR "financial relationship*"[tiab] OR "buyer-supplier relationship*"[tiab] OR “product choice*”[tiab]	438,091
#3	"vendor*"[tiab] OR "industry"[tiab] OR "industries"[tiab] OR "manufacturer*"[tiab] OR "distributor*"[tiab] OR "producer*"[tiab] OR "supplier*"[tiab]	304,871
#4	#1 AND #2 AND #3	1,500
#5	#1 AND #2 AND #3 Filters: from 2000/1/1 - 3000/12/12	1,439

Search history Embase.com March 22th 2023

Search	Query	Results
#1	'medical device'/exp OR ('medical device*' OR 'implant*' OR 'prosthes*' OR 'prothes*' OR 'orthopedic device*' OR 'cardiac device*' OR 'stent*' OR	4,171,383

Search	Query	Results
	'pacemaker*' OR 'medical apparatus' OR 'medical consumable*' OR 'surgical consumable*' OR 'medical instrument*' OR 'surgical instrument*' OR 'dental device*' OR 'diagnostic device*' OR 'in vitro diagnostic device*' OR 'in-vitro diagnostics'):ti,ab,kw	
#2	'fraud'/exp OR 'conflict of interest'/exp OR 'lobbying'/exp OR ('gift*' OR 'conflict of interest*' OR 'interest conflict*' OR 'bribe*' OR 'lobbying*' OR 'corrupt*' OR 'fraud*' OR 'scams' OR 'partnership*' OR 'collaborati*' OR 'funding*' OR 'sponsor*' OR 'fee' OR 'fees' OR 'bonus*' OR 'discount*' OR 'payment*' OR 'incentive*' OR 'financial relationship*' OR 'buyer-supplier relationship*' OR 'product choice*'):ti,ab,kw	613,205
#3	('vendor*' OR 'industry' OR 'industries' OR 'manufacturer*' OR 'distributor*' OR 'producer*' OR supplier*):ti,ab,kw	394,478
#4	#1 AND #2 AND #3	3,782
#5	#4 NOT ('conference abstract'/it OR 'conference review'/it)	2,307
#6	#12 NOT ('conference abstract'/it OR 'conference review'/it) AND [2000-2023]/py	2,112

Search history Web of Science Core Collection March 22th 2023

Search	Query	Results
#1	TS = ("medical device*" OR "implant*" OR "prosthes*" OR "prothes*" OR "orthopedic device*" OR "cardiac device*" OR "stent*" OR "pacemaker*" OR "medical apparatus" OR "medical consumable*" OR "surgical consumable*" OR "medical instrument*" OR "surgical instrument*" OR "dental device*" OR "diagnostic device*" OR "in vitro diagnostic device*" OR "In-vitro diagnostics")	806,640
#2	TS = ("gift*" OR "conflict of interest*" OR "interest conflict*" OR "bribe*" OR "lobbying*" OR "corrupt*" OR "fraud*" OR "scams" OR "partnership*" OR "collaborati*" OR "funding*" OR "sponsor*" OR "fee" OR "fees" OR "bonus*" OR "discount*" OR "payment*" OR "incentive*" OR "financial relationship*" OR "buyer-supplier relationship*" OR "product choice*")	943,635
#3	TS = ("vendor*" OR "industry" OR "industries" OR "manufacturer*" OR "distributor*" OR "producer*" OR "supplier*")	1,089,113
#4	#1 AND #2 AND #3	983
#5	#4 AND Timespan: 2000-01-01 to 2024-12-31 (Index Date)	950

A.2 Search string Google Scholar

Gunstbetoon|omkoping|lobby|corruptie|fraude|belangenconflict|bonus|sponsor|partner|betalingen+industrie|fabrikant|distributeur|producent|supplier+hulpmiddelen|protheses|implantaten|stents|pacemakers|instrumenten+zorg|medisch
+ filter 2000

Gunstbetoon + Medische hulpmiddelen
+filter 2000

Results march 22th 2023

de Bruin, M. E., & Schutjens, M. D. B. (2012). Gunstbetoon en medische hulpmiddelen. Tijdschrift voor Gezondheidsrecht, 36(4), 280-296.
van den Bos, H., & Franken, R. (2018). The Netherlands Introduces A Statutory Ban On Inducement Related To Medical Devices. EPLR, 2, 37.
Regels Gunstbetoon Redelijk Goed Bekend Bij Artsen, Toepassing Soms Nog Lastig

A.3 Search string Google

European Code of Conduct Medical devices

Results june 8th 2023

The MedTech Europe Code of Ethical Business Practice
Eucomed Code Of Business Practice (no full text)

Asian Code of Conduct Medical Devices

Results june 8th 2023

APACMed Code of Ethical Conduct

Appendix B Payments studies

In the table on the following pages study characteristics are listed for the studies on medical device industry payments to physicians.

Title, Authors, year of publication, country	Study design	Study period	Profession/clinical area	Scale and ratio device-pharma	Inequality
(18) Evaluation of Industry Payments to US Advanced Practice Clinicians in 2021 Singh et al. 2022 V.S.	Retrospective review of Open Payment Database	2021	Advanced practice clinicians (nurse practitioners, physician assistants, clinical nurse specialists, certified registered nurse anesthetists, certified nurse midwives, and anesthesiologist assistants) and physicians (doctors of medicine and osteopathy)	Total payments from medical device manufacturers comprised $753 526 283 in 2021. For physicians, medical device industry was responsible for 56% of total value payment, 28% came from drug manufacturers. For nurse practitioners and physician assistants, payments from device manufacturers accounted for 10% and 16% of total value payments respectively. Drug manufacturers were responsible for 68% and 54% of total value payments.	
(19) Orthopaedic Trauma Surgeons' Financial Relationships With Industry: An Analysis of the Sunshine Act Reporting of	Retrospective review of Open Payment Database	2014-2019	Orthopaedic trauma surgeons	Medical device industry provided most of the registered funding. The top five companies (all medical device manufacturers) contributed a total of $32 993271 between 2014 and 2019, which constituted 79.7% of total payments to orthopaedic trauma surgeons.	Between 2014 and 2019, 82.6% (N = 2648) of the orthopaedic trauma surgeons receiving payments acquired a yearly total payment of less than $10 000, which made up 8.2% of the total industry payment. Those receiving a yearly total payment greater than $500 000 accounted for 0.2% of surgeons, these received 14.98% of the sum payments

Physician Open Payments From 2014 to 2019 Frane et al. 2021 V.S.				Stryker had the highest total payments which totaled $9 195 263, 22.2% of total contributions, followed by DePuy Synthes ($8 610 968; 20.8%), Zimmer Biomet Holdings ($7 917 019; 19.1%), Smith and Nephew($4 327 935; 10.5%), and Arthrex ($2 942 085;7.1%).	
(17) Medical Device Firm Payments To Physicians Exceed What Drug Companies Pay Physicians, Target Surgical Specialists Bergman, Grennan and Swanson 2021 V.S.	Retrospective review of Open Payment Database	2014-2017	All types of Physicians, differentiating on the top 20 receiving medical specialities	During 2014–2017 vendors promoting medical devices paid $904 million to 196 624 physicians (30% of active physicians) each year, on average. During the same period, vendors promoting drugs paid $821 million to 331 187 physicians (50 %). This represented about 1.7% of device industry revenue, and 0.24% of drug industry revenue	Between specialties: Median annual payments from device vendors to neurosurgeons and orthopedic surgeons were $454 and $410, respectively. Median annual payment magnitudes ranged from $14 to $44 for some nonsurgical specialties, e.g. medical oncology.
(25) Financial Transactions	Retrospective review of Open	2018	Otolaryngologists	76.4% of the total payments made were for devices, 16.6% were for drugs,	

from Manufacturers to Otolaryngologists in 2018 Ramsey et al. 2021 V.S.	Payment Database			6.7% were for biological products, and 0.14% were for medical supplies. The two companies that contributed the highest amount were Stryker Corporation and Intersect ENT Inc (both medical device manufacturers). Sinus conditions had the most products within the top 25 products associated with payments. The top five products with the highest payments received were for balloon sinus dilation, nasal spray, sinus implant, botox, and cochlear implant. Of which 3 can be categorised as medical device.	
(23) Industry Payments by Allergan, Inc to Plastic Surgery and Related Specialties in 2018 Isbester et al. 2021 V.S.	Retrospective review of Open Payment Database	2018	plastic surgeons and physicians of other related specialties	Payments attributed to Natrelle breast implants totalled $7 641 675, 13.5% of Allergan's total spent on physician or teaching hospital payments in 2018. Payments related to Botox (not a medical device) made up only 6.2%. A total of 2 000 plastic surgeons received payments relating to Natrelle, accounting for $5 685 924 (74.4%). To plastic surgeons, the breast implant line, Natrelle, accounted for 57% ($5 685 924) of Allergan's total payments to plastic surgeons, while e.g. botox only accounted for 2%.	

(22) Industry Payments in Colon and Rectal Surgery: A Cross-Sectional Analysis of Open Payments Data Kaleem et al. 2020 V.S.	Retrospective review of Open Payment Database	2014-2018	Colorectal surgeons	Payments from 2016 to 2018 were associated with a total of 39 649 medical devices, 15 897 pharmaceutical drugs, 2 672 biologicals, and 1 488 medical supplies. Research payments within the study period (2016-2018) were associated with a total of 719 medical devices, 104 pharmaceutical drugs, 10 biologicals, and 114 medical supplies. From 2016 to 2018, there was aa 18.1% decrease in general payments associated with devices. Intuitive Surgical, Inc paid the most in general payments every year, ranging from 39.0% to 58.8% of the total payment amount, totalling $39.8 million. Intuitive Surgical, Inc's product, da Vinci Surgical System, had the greatest number of payments, totalling 21 191 general payments. Da Vinci Surgical System (DVSS) made up 39.0-58.8% of the total amount of money paid to colorectal and rectal surgeons within the study period. It also made up 28.4-38.5% of the total annual number of payments to colorectal and rectal surgeons from 2014 to 2018.	

(33) Patterns of Industry Payments to Urologists From 2014-2018 Clennon et al. 2020 V.S.	Retrospective review of Open Payment Database	2014-2018	Urologists	Only 4 manufacturers—1 pharmaceutical corporation (Astellas) and 3 medical device manufacturers (Boston Scientific, Cook, and Coloplast)—gave more than $10 million to urologists over 5 years, accounting for more than 41% of all value transfer. Subspecialties receiving the largest sums from industry were those that most often utilize implantable medical devices, such as devices for reconstruction, Female Pelvic Medicine and Reconstructive Surgery, and andrology.	The majority of urologists received between $100 and $1 000 annually. About one-fifth of the receivers received under $1 000, and approximately 5% received over $10 000. Maximum individual payments exceeded $1 million 4 out of 5 years, and one urologist received more than $7.5 million over the study period.
(20) The physician payment Sunshine act: Evaluating industrial payments in radiology Jutras and Khosa 2019 V.S.	Retrospective review of Open Payment Database	2015	Radiologists (and subspecialties)	Overall in radiology biggest payments were by Medtronic Neurovascular $ 11 779 770, Medtronic Vascular, Inc. $ 5 130 465, Cook Incorporated $ 1 984 896 (all medical device manufacturers) In the top 3 of payers for all subspecialties only 1 of the 21 companies was a pharmaceutical oriented company Medical device manufacturers primarily focused on minimally invasive procedures	Payments were unequally distributed across the six subspecialties of radiology ($p < 0.01$), with general radiologists receiving the largest number of total payments (44 695), and neuroradiologists receiving significantly higher median payments than any other subspecialty ($80 vs $32 for all radiologists; $p < 0.01$). Our results revealed Gini indices >0.5 for all subspecialties, with the exception of paediatric radiology and nuclear radiology, which had much smaller sample sizes than the other specialties

(31) Characteristics of Industry Payments to Ophthalmologists in the Open Payments Database Slentz, Nelson, and Lichter 2019 V.S.	Retrospective review of Open Payment Database	2013-2017	Opthalmologists	Fifteen companies were responsible for 87.7% of all funds distributed ($476 719 470) and were mostly involved in the production of pharmaceutical agents (anti–vascular endothelial growth factor agents, glaucoma eyedrops, and ocular lubricants) and surgical devices (cataract and glaucoma). 16 of the 20 product with most value in payments in general and research payments were drugs. But the number 1 in value general payments related to a device 'Cypass Microstent'.	
(32) Industry Payments in Cardiology: A Cross-sectional Analysis of Open Payments Data Jaiswal, Checketts, Vassar 2018 V.S.	Retrospective review of Open Payment Database	2015	Cardiologists	The biggest payer responsible for 51.9% of total value of all payments was a pharmaceutical company. The other 4 top 5 companies making payments to cardiologists were primarily focused on medical devices. Combined they were responsible for 42.6% of total value payments.	Payments to cardiologists were highly variable. The minimum payment made to a cardiologist was $1.16 and the maximum, $2 805 825.

(27) An Analysis of the Open Payment Database in Neurotology Ziai et al. 2018 V.S.	Retrospective review of Open Payment Database	2015	Neurotology and otology	Top 4 paying companies accounting for 97.7% of all general payments, were all primarily focused on medical devices. Top 3 paying companies accounting for 95,2% of all research payments, were all primarily focused on medical devices.	
(21) Financial Relationships between Urologists and Industry: An Analysis of Open Payments Data Maruf et al. 2018 V.S.	Retrospective review of Open Payment Database	2014	Urologists	Among 232 207 payments 169 638 (73.1%) were associated with drugs only, 54 878 (23.6%) with devices only and 264 (0.1%) with at least 1 medication and 1 device, while for 7 427 (3.2%) payments, information was missing on the associated device and drug. Payments associated with drugs and devices comprised 38.8% ($12.6 million) and 48.3% ($15.7 million) of total payment amount, respectively. Sacral neuromodulation, a device used in the management of overactive bladder and urinary retention, was the	Payments to the top 10% of the urologists with financial relationships (862) amounted to $26 million, comprising 81% of the total payments. Median payments to these urologists was $13 674 (IQR $8 872 to $29 918).

				most common payment-associated device. American Medical Systems, now Boston Scientific, reported the highest total payment amount of $3.8 million, constituting 11.8% of total amount paid to urologists.	
(26) Comparing industry compensation of cardiothoracic surgeons and interventional cardiologists Parreco et al. 2017 V.S.	Retrospective review of Open Payment Database	2013-2014, August 1, 2013 and December 31, 2014 (17 months)	cardiothoracic surgeons and interventional cardiologists	Top five companies by total payments to cardiothoracic surgeons were all medical device related. 4 of the top 5 payers to interventional cardiologists were medical device manufacturers, but the number one was a pharmaceutical company.	Mean total payments to cardiothoracic surgeons was $7 770 (SD, $52 608) compared with a mean of $15 221 (SD, $98 828) to interventional cardiologists. The median total payments to cardiothoracic surgeons were $1 050 (IQR, $233-$3 612) compared to $1 851 (IQR, $607-$5 462) for interventional cardiologists. Payments made to cardiothoracic surgeons and interventional cardiologists appear to be markedly higher than most other specialties. Among all specialties, the Gini index was 0.932. Gini index was 0.862 for interventional cardiologists and 0.860 for cardiothoracic surgeons.
(28) Industry Relationships With Pediatricians:	Retrospective review of Open Payment Database	2014	Pediatricians	Most payments were drug related. For most physician subspecialites the main share of their median payments came from drug industry. Only for	

Findings From the Open Payments Sunshine Act Parikh, Fleischman and Agrawal 2016 V.S.				orthopaedic surgeons, cardiology, pediatric surgery, and pediatric radiology the median payments for the majority related to devices.	
(34) Financial Ties Between Emergency Physicians and Industry: Insights From Open Payments Data Fleischman et al. 2016 V.S.	Retrospective review of Open Payment Database	2014	Emergency physicians	Top ten most common product associated with payments to emergency physicians were all drugs	The majority of payments (83%) to emergency physicians were less than $100, and the top 5% of payments accounted for 84% of the sum of payments.
(29) Examination of Industry Payments to	Retrospective review of Open	2014	Oncologists (radiation, medical and surgical)	Just over half of the sponsors were medical device companies (52%). 45% of sponsors made pharmaceuticals, 1%	The mean and median payments to individual oncologic physicians were $5 233 and $297, respectively.

Radiation Oncologists in 2014 Using the Centres for Medicare and Medicaid Services Open Payments Database Jairam and James 2016 V.S.	Payment Database			produced both, and 2% produced neither. Seven of the top 10 sponsors were medical device companies. Pharmaceutical companies made more than 3 times (12 675) the number of payments as medical device companies (4 088), whereas device manufacturers accounted for 58% of the total payment value. Mean and median payments per transaction for pharmaceutical companies were $141 and $15, respectively, compared with $619 and $39 for device companies.	
(24) Orthopaedic Surgeons Receive the Most Industry Payments to Physicians but Large Disparities are Seen in Sunshine Act Data	Retrospective review of Open Payment Database	2013 (1 august - 31 december, 5 months)	Orthopaedic surgeons	Top ten manufacturers/GPO's that made payments to orthopaedic surgeons were all (primarily) medical device manufacturers. These ten companies accounted for 80% of total payments to orthopeadic surgeons ($87 million)	The Gini index of disparity for industry payments to orthopaedic surgeons was 0.956

Samuel et al. 2015 V.S.					
(30) Industry Ties in Otolaryngology: Initial Insights from the Physician Payment Sunshine Act Rathi, Samuel, and Mehra 2015 V.S.	Retrospective review of Open Payment Database	2013 (1 august -31 december, 5 months)	Otolaryngologists	Among the top 20 highest paying sponsors, 65.0% (n=13) manufactured devices, 20.0% (n=4) manufactured pharmaceuticals, and 15.0% (n=3) manufactured both. Among the top 5 highest paying sponsors, 80.0% (n=4) manufactured devices, with a single device manufacturer accounting for 15.8% ($405 868) of all nonresearch payment	Within the field of otolaryngology not all surgeons are alike in receiving payments from industry for purposes other than research. Distribution was highly skewed by top earners; about 90% of the total reported amount paid went to the top 10% of earners. This skewed distribution and the high Gini Index indicate that the field is similar to other surgical specialties in that there appears to be a small number of surgeons who maintain significant financial ties with industry.

Appendix C Association studies

In the table on the following pages study characteristics are listed for the studies on the potential association between inducement strategies by medical device industry and device selection/utilisation and quality of care.

Titel, Auteurs, publicatie jaar, land	Design, data used, setting/specialty	Main findings: nature, scale and consequences of inducement	Conclusion
(36) Association Between industry Payments to Physicians and Device Selection in ICD implantation Annapureddy et al., 2020, V.S.	Cross sectional review of patients receiving ICD/CRT-D (n=145 900), physicians (n=4 435), 4 major manufacturers Open Payments Program's payment data & National Cardiovascular Data Registry ICD Registry Physicians who performed implantation	Nature: general payments (incl. travel and lodging, food and beverages, and consulting and speaking fees) Scale: Most physicians (94%) who perform ICD/CRT-D implantations receive payments from manufacturers (range $2 - $323 559, median $1 211 over three years) Consequences: • Device selection/utilization: Patients were more likely to receive ICD/CRT-D devices from the manufacturer that provided the highest total payment to the physician who performed an ICD or CRT-D implantation than each other manufacturer individually. Absolute differences between manufacturers varied between 14.5% and 30.6% • Quality of Care: For prescription of guideline-recommended therapy or in-hospital complications or death there was	Most physicians received industry payments. Patients were more likely to receive ICD/CRT-D devices from the manufacturer that provided the highest total payment to the physician who implanted the device, than each other manufacturer individually. These physicians were also substantially more likely than physicians that did who received no payment.

		no consistent relationship with physicians payments. Use of CRT-D was higher among patients of whom the physician received high value payments, which may help survival of eligible patients.	
(37) Cross-sectional Analysis of the Relationship between Paranasal Sinus Balloon Catheter Dilations and Industry Payments among Otolaryngologists Fujiware, Shih, and Mehra, 2017, V.S.	Cross-sectional analysis, multivariate controlled linear regression Medicare B Public Use Files & Open Payment Data Otolaryngologists, allopathic or osteopathic physicians	Nature: All types of payment Scale: Most physicians (83.3%) received Balloon Catheter Dilations(BCD) manufacturer industry payments (n= 4392 payments, range $43.29 – $111 685.10). Median payment food and beverage $ 19.26, speaker or consulting $409.45. Consequences: • Device selection/utilization: One payment was associated with 3.05 BCDs One payment for food and beverages 3.81 additional BDCs One speaker or consulting fee 5.49 additional BCDs	Payments by manufacturers of BCD devices were associated with increased use of BCD for chronic rhinosinusitis

(38) The impact of industry representative's visits on utilization of coronary stents Sudarsky et al., 2013, Canada	Cross-sectional, retrospective patient record review of patients who underwent percutaneous coronary intervention in an academic center (n= 1 145) Percutaneous coronary interventions, catheterization laboratory	Nature: visits of manufacturers' sales representatives in the catheterization laboratory Scale: Industry representatives were present in the catheterization laboratory in 44.2% of the days. Consequences: • Device selection/utilization: More drug-eluting stents (DES) per case were implanted when a representative was present. For other types of stents there was no difference. Stent cost per case was higher when a presentative was present. For all companies marketing DES, there was increase in the use of the company's DES when their representative was present with less use of the competitors' stent	Sale representative presence was associated with increased use of the representative company's stents. The effect was more pronounced on use of the company's DES and resulted in higher procedural costs.

Appendix D Normative studies/code of conducts

In the table on the following pages study characteristics are listed for the studies evaluating code of conducts by formal associations.

Title, Authors, publicaton year, country	Organisation/association	Motives and concerns	Underlying values	Norms and topics	Assurance
(40) Professional Relationships With Industry: ACOG Committee Statement No. 2 Shalowitz (American College of Obstetricians and Gynecologists' Committee on Ethics) 2022 V.S.	The American College for Obstetricians and Gynecologists	Industry priorities not always algin with ethical responsibilities of clinicians to promote best interests of their patients, of educators to provide evidence based instruction, and of researchers to ensure the scientific integrity of their investigations. Secondary financial interests may substantially decrease public trust in physicians' ethical standards and high quality care.	(scientific) Integrity Altruism (patients' best interest) Evidence based medicine/education	Guidance on: • acceptance of cash donations, vacations, medical or personal services, and gifts, • disclosure for institutional decision makers, and in publication and presentation of research findings • providence of medication samples to patients, • disclosure of payments of substantial value (royalties, consultation), • participation in speakers' bureaus, • direct involvement of industry in	-

				education of trainees • adherence of practice standards that support research • research funding or payments • contribution to manuscript or presentation.	
(39) Managing perceived conflicts of interest while ensuring the continued innovation of medical technology Van Haute (Advanced Medical Technology Association) 2011	Advanced Medical Technology Association	Vital and complex relationships between vascular surgeons and device companies create multiple and potentially conflicting roles for surgeons and must be appropriately managed. Competing pressures from the multiple, overlapping roles as clinician/caregiver/investigator/innovator/customer are significant. Code stimulates proactive management of potential conflict of interests while promoting the highest ethical standards.	Openness high ethical standards Altruism (best interest of the patient)	Code for manufacturers, updates on: • company conducted training and education • third-party conferences • entertainment and gifts • provision of meals • consulting arrangements and royalties • evaluation and demonstration products • reimbursement information	In the code, a compliance section is adopted. This lists the companies that certify for their adoption of the code, and is publicly available on the AdvaMed's website. Also tools are available on this website that provide information on how a company should approach its interactions with healthcare

V.S.				• grants and donations	professionals under discrete sections of the code.
(41) The new CMSS code for interactions with companies managing relationships to minimize conflicts Kahn and Lichter (Council of Medical Specialty Societies) 2011 V.S.	Council of Medical Specialty Societies	helping specialty societies in the profession of medicine to manage their relationships with the pharmaceutical and medical device manufacturers to avoid, and when unavoidable, manage, relationships which result in conflicts of interest to prioritize patient benefits over physician benefits. To protect and promote the independence of specialty societies and their leaders.	Altruism (ensuring that the needs of patients come first), Transparency (to peers, patients, and the public), Independence	Guidance on: • definition of conflict of interest • who is addressed in the society's policy • delineation of activities addressed in the policy • disclosures of relationships • consequences for failure to disclose, • management and resolution strategies for disclosed conflicts of interest, • clarification of circumstances requiring recusal, removal from participation, • or from the disclosed relationship,	Self-regulatory guidance, adoption of the code by specialty societies is voluntary. CMSS will not enforce the code. Annually societies can certify their continued adherence.

				• adherence to external standards and guidelines, • publicly disclosing information on society's websites, • developing standardized model templates for conflict of interest policies, disclosure forms, • management and resolution strategies	
(42) American academy of pain medicine ethics council statement on conflicts of interest: interaction between physicians and industry in pain medicine	The American Academy of Pain Medicine	Physicians and industry have fundamentally different goals. In order to ensure that these relationships are principled and ethical, all parties must be aware of the conflicts of interest they present and strive to manage them ethically and with transparency. As a conflict of interest can create bias.	Ethics Transparancy	Guidance on: • disclosure, • recusal, • consultants and advisory boards, • continuing medical education, • speaker bureaus, • meetings with sales and marketing representatives of pharmaceutical companies and device manufacturers,	-

Dubois (The American Academy of Pain Medicine (AAPM) Council on Ethics) 2010 V.S.				• funding for research, • institution review board, • physicians investors	
(39, 45) ADVAMED CODE OF ETHICS On Interactions with U.S. Health Care Professionals 2023 V.S.	Advanced Medical Technology Association	Proactively managing potential conflict of interests in the vital and complex relationships between vascular surgeons and device companies. As competing pressures from the multiple, overlapping roles as clinician/caregiver/investigator/innovator/customer are significant. Code aims to promote the highest ethical standards	Openness, altruism (best interest of the patient)	• company conducted training and education • third-party conferences • entertainment and gifts • provision of meals • consulting arrangements and royalties • evaluation and demonstration products • reimbursement information • grants and donations	A compliance section is adopted. A list of the companies that certify for their adoption of the code is publicly available on the AdvaMed's website The website also provided tools that provide information on how a company should approach its interactions with healthcare

					professionals under the code
(43) MedTech Europe Code of Ethical Business Practice 2022 EU, Belgium	MedTech Europe, European trade association representing the medical technology industries	Recognition that compliance with applicable laws and regulations as well as adherence to ethical standards are an obligation and a critical step	-	• Events (educational, company) • Grants and charitable donations • Consulting • Research • Royalties • Educational, promotional, and demonstrational items • Intermediaries	Complaint handling MedTech Europe Compliance Panel
(44) APACMed Code of Ethical Conduct 2020 Asia Pacific, Singapore	Asia Pacific Medical Technology Association	To facilitate independent decision-making, and reinforce public confidence in the integrity of patient care, treatment, and product and service selection	Integrity	• Consultancy agreements • Training and education • Gifts and entertainment • Evaluation/demonstration products and samples • Research • Charitable donations • Technical support • Sales and marketing • Intermediaries	Advices on effective code implementation are adopted
(11) Code of Conduct for Medical Devices 2022 2022 Netherlands	Stichting Gedragscode Medische Hulpmiddelen	To prevent improper practice, and provide guidance on legitimate foundations and reasonableness, documentation, and transparency	independence, transparency	• Bonusses and discounts • Gifts • Meetings • Remuneration for services • Sponsoring • Involvement in advisory reports and guidelines • Transparency register	Based on self-regulation Rules are enforced based on complaints or signals Monitoring of compliance by an independent

					Code Commission and Appeals Board