Pediatric Surgery International (2019) 35:999–1004
https://doi.org/10.1007/s00383-019-04516-y

ORIGINAL ARTICLE

Non-financial conflicts of interest: contribution to a surgical dilemma by the European Reference Networks for Rare Diseases

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Accepted: 20 June 2019 / Published online: 5 July 2019

Abstract

Purpose Conflicts of interest can impede both research and medical treatment. The European Reference Networks require their members to deal with financial and non-financial conflicts according to an explicit protocol. In a literature review, we identified relevant interests in paediatric surgery, and drafted such a policy.

Methods We conducted a Pubmed query and identified additional publications based on the content of the papers.

Results 58 titles were identified. According to their abstracts, 10 publications were studied in full text. A scientific taxonomy does not yet exist, but a variety of factors are mentioned. Non-financial conflicts of interest are addressed less accurately and less frequently than financial ones, especially regarding surgical treatment. Since the clinical effect of surgical volume was identified as being relevant, additional 29 respective publications were analysed. This volume-quality relationship causes conflicts of interest for the many surgeons treating a broad spectrum of rare conditions. We present a recommendation that may guide referral of patients requiring complex surgery to centres with a higher volume.

Conclusions Non-financial conflicts of interest need to be dealt with more accuracy, especially with regard to surgery in rare, complex congenital conditions. The European Reference Networks offer a framework to mitigate these conflicts.

Keywords Non-financial conflict of interest · Congenital malformation · Volume-outcome relationship · Patient organisation · European Reference Networks · Anorectal malformation

Background

Patients and medical professionals agree in their interest to realise optimal treatment resulting in the best possible outcome. Conflicting interests of members of the medical staff can interfere. Financial and non-financial conflicts of interest in research and guideline making receive growing attention, while those in treatment are less frequently addressed.

The European Reference Networks for patients with rare diseases (ERN), built upon initiative of patient organisations

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This article is based on an oral presentation at The 26th Pediatric Colorectal Club Belgrade 9–11 June 2019.

The patient organisations *SoMA* and *AIMAR* and the *Pediatric Surgical Clinic of Bremen*, Germany, are members of *eUROGEN-ERN*, the European Reference Network for rare uro- recto-genital diseases, the latter being certified therein for the treatment of patients with anorectal malformations. *SoMA* is also member of *ERNICA-ERN*, the European Reference Network for rare inherited and congenital digestive disorders.

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and the EU commission, require from their members to identify and mitigate such conflicts of interest (COI) according to an explicit protocol [1]. In a poll among the ERN-applicants and an Internet research, we were not able to identify such a template. Therefore, we reviewed the relevant literature and drafted the requested policy in a dialogue between clinicians, patient representatives, and the specialist for medical ethics of our clinic.

Methods

In a Pubmed query with the term "(non-financial) AND (conflict OR conflicts)", 58 publications in English language were detected, none of them edited before 1999. According to their titles, 19 relevant publications dealing with COI were identified. In 4 cases, an abstract was missing, the remaining 15 abstracts were studied, and according to their content, 10 papers analysed in full text.

An important non-financial COI was only marginally approached in the identified papers: in surgery, there is a well-described volume–quality relationship, which sheds light on a contrasting surgeon's interest, namely to perform complex types of operations even if they occur infrequently. This is discussed in detail in a recent issue of the European Journal of Pediatric Surgery [2] containing nine articles about the ERNs. We, therefore, identified these and 24 additional specific papers among the respective references.

Results

There is growing awareness and an increasing number of publications dealing with COI in medicine—mostly financial ones [3]. In 2017, a complete issue of the Journal of the American Medical Association (JAMA) was dedicated to the subject, but "out of over 24 articles only two addressed non-financial interests in depth" [4].

A scientific taxonomy of the different interests does not yet exist [5]. They can be differentiated roughly into:

- financial and
- non-financial ones, the latter being
    - systemic (business, cut of costs),
    - individual (personal gain, intellectual passion, religious, political views), and
    - relational (peers, friends, family, company representatives) [4].

In the articles identified by our Pubmed query, non-financial COI are addressed mostly in the context of research [6], concerning publications and academic grant evaluation [7].

A COI "occurs when an individual has competing professional or personal interests that may make it difficult for them to fulfil their duties fairly" [1]. The term "duties" point to the interest of the patient in optimal treatment and of society as a whole concerning responsible use of resources, and trustworthy research, providing an optimal basis for making "expert statements on behalf of others" [8].

These interests of patient and society are often classified as "primary", while additional personal interests of medical professionals are labelled "secondary" [9].

Non-financial COI in surgery are addressed clearly in an issue of the European Journal of Pediatric Surgery dealing mainly with the ERNs [2]. The key feature of the ERNs is centralisation of the treatment of rare conditions, as it is necessary to pool knowledge and patient data to achieve better treatment results and more significant research, but it has to deal with a classic COI in surgery: the surgeon wants to train and increase his or her skills by treating complex cases, even if facing them rarely. Especially in paediatric surgery, the treatment of congenital malformations is a core identity of the discipline, so "job satisfaction" is a strong motive [10].

This interferes with the well-known volume–outcome relationship in surgery [11–14]. The more complex a procedure, the higher the case number per clinic and year which is necessary to reach the end of the learning curve, where an increase in numbers no longer reduces complications and mortality. In simple, frequently trained procedures (like cholecystectomy without revision of the biliary duct) one case per clinic and year was found to be sufficient, while in more complex ones the necessary numbers ranged between 50 (colectomy) and more than 200 (open-heart surgery). In this study of 840,000 patients, 22–28% of all mortalities could have been prevented by a sufficient caseload per clinic [11].

Subsequent studies determined the described minimal number of cases necessary to reach the plateau of the learning curve: more than 25 cases in thyroidectomy per year [15], 50–55 cases in radical cystectomy [16], 20 cases in laparoscopic fundoplication, 15–25 cases in D2 gastrectomy, 55–80 cases in laparoscopic colorectal surgery; in esophagectomy, there was continuing improvement at 150 cases [17].

The caseload numbers of congenital malformations in the European paediatric surgical centres rarely reach this realm, in a multicenter survey none treats more than 30 ARM-cases per year [18], the numbers for esophageal anastomosis might even be lower [19].

In the field of paediatric surgery, the importance of this COI was shown exemplary by nationwide data on biliary atresia in Great Britain, as recalled in the above mentioned issue of the European Journal of Pediatric Surgery on the ERNs [20]. Results published in 1985 showed a direct relationship between surgical caseload (some centres treating only one case/year, while others were seeing > 20 cases/years), and outcome. "Despite citing reasons for this, including … a learning curve during which outcomes are less optimal, no recommendation was made for centralisation".

Only after the foundation of a patient organisation by a mother whose child had died after operation in a low-volume clinic, and an article in the mass media accusing the surgeons performing the operation rarely, in spite of known inferior results, as "dabblers", centralisation from 15 to 3 centres was imposed by the politicians [20].

Subsequently, surgical treatment of bladder exstrophy in Great Britain was confined from 12 to 2 centres, yielding significantly better results. Nevertheless, the author states that in a nationwide cohort study on patients with esophageal atresia treated in 28 British and Irish paediatric surgical centres, "no volume to outcome analysis was performed, likely because the results would have been too controversial" [20].

According to the requirements of the ERNs, we coined a protocol to deal with these specific COIs (see Table 1).

Discussion

"Like other humans, clinical scientists" (and surgeons, *the authors' addition*) "desire to advance their own career, improve their income, and experience the satisfaction of peer approval and public recognition" [21].

A significant proportion of the legitimate interests of medical professionals (financial and non-financial) coincides with the patient's interest for best treatment, especially the professionals' desire to gain and maintain practical skills. Therefore, elimination of personal interests is neither possible nor desirable [22]. Nevertheless, it is a well-known fact that sometimes the professional's interests may conflict with the patient's wish for optimal treatment. This can, as described in the British example above [20], "result in patient injury, deterioration of the patient-physician relationship, loss of public trust…, as well as pollution/degradation of the medical literature" [23].

The separation into financial and non-financial interests is common, but hardly realistic [5]. To gain reputation in the scientific community, for example, will turn out to be financially rewarding, too, in the long run.

Financial COI, which receive far more interest today [3, 24], may be of even lesser influence than non-financial ones [8].

It is commonly assumed that financial conflicts of interest can be more easily mitigated than non-financial ones [21, 25], while others doubt that public disclosure is a panacea, it might also serve as a moral justification [26].

Both interests and conflict of interests can be conscious or unconscious [26, 27]. Medical professionals sometimes "strongly contest the view that COI have a significant impact in medicine" [9]. Merely mentioning COI might be regarded an "affront to their integrity and an indictment of the ethical conduct of the profession as a whole" [28]. Of course, there is a moral dimension to COI [29].

All these factors make discussing and solving non-financial COIs even more difficult, but must not serve as an excuse "to erode the political will to identify and manage conflicts of interest" [8].

Checklists are published for the professional who doubts whether a certain personal interest causes a conflict with a primary interest of patient or society [8]. In difficult situations, help of the local commissioner for medical ethics should be sought. Yet, most of the described conflicts between the patient's primary and the healthcare official's secondary interest are "strikingly different from situations requiring ethical consideration" [26].

As shown above (in the paper on centralisation of paediatric surgery in Great Britain [20]), an important COI is the tendency of many surgeons to perform complex operations on a rare basis, in spite of the known volume–outcome relationship.

Not only the number of operations per clinic is essential. The surgical experience of the individual surgeon, of course, is even more relevant, but because of the heterogeneous number for various surgeries much more difficult to assess [30]. The experience of the entire team in recognising and managing severe complications can be crucial, too [31]. In entities requiring additional highly specialised non-surgical care, like congenital diaphragmatic hernia (sometimes necessitating ECMO), or in the follow-up of anorectal

Table 1 Our draft of an internal protocol on non-financial conflicts of interest concerning a possible referral for surgical reconstruction

Detailed diagnosis and prognosis
Plan of treatment
Assessment of own experience, results and complication rates
Comparison with other centres (will become easier after the uniform assessment and publication of treatment results in the ERNs)
Recommendation to the patient/parents about treatment in the own or an at an external centre; if necessary discussion of the options under moderation of the committee on clinical ethics
Documentation of the recommendation and patient decision in the patient file

malformations and other complex congenital malformations, sufficient manpower and training of the essential multidisciplinary team gain importance [32–34].

The surgeon's interest to operate on as broad a spectrum as possible is not the only factor mentioned which inhibits the necessary centralisation [10]. Politicians want the hospitals they are responsible for to cover as much of the population's health needs as possible. The hospital management or colleagues from neighboured disciplines (paediatrics, neonatology) might resist a referral out of several, also financial reasons [10].

Subspecialisation within a given centre is a often practised model to account for the volume–quality relationship.

Yet it faces the same problems of "concerns about decreased reimbursement, skill levels and/or job satisfaction, … and makes it much more difficult to cover call responsibilities for patients with more complex problems" [35].

Centralisation of surgical care to fewer units cannot be regarded as a remedy for everything.

A smaller unit with not so numerous, but more dedicated staff might yield better results than a huge centre with a big caseload, but a dysfunctional, dispersed team. Uniform, treatment-independent assessment of various outcome indicators is mandatory to guide the process of centralisation, and should include disease-related quality of life and patient-reported outcomes. Nevertheless, current evidence on the volume outcome relationship shows that as long as other relevant quality indicators are not uniformly and comparably assessed and published, the case number remains an important index [36].

Moreover, centralisation makes access to health care more difficult for patients and their relatives, due to greater travelling distances and similar issues. But the patients might be prone to take this burden upon them in return for higher probability of better treatment results and a lower mortality risk. Arora et al. [16] calculate the necessary caseload to reach minimal morbidity after radical cystectomy (50–55 operations per year and clinic) in a scientifically sound way, but then apodictically declare that this would limit access in a non-acceptable way, without even discussing the numbers of centres and their respective distances now and in case of the calculated necessary centralisation. A better way to solve the problem of access would be having a social worker as part of the centre's multidisciplinary team, who helps the patient and family to cover the distances and expenses [37], and a legislation, like in the ERNs, which obliges the health insurances to pay for it [38].

The process of centralisation has to be navigated carefully to avoid deterioration in the following important aspects: who is responsible and qualified for the often lifelong necessary follow-up after the surgical reconstruction: the tertiary centre performing it? The local hospital? Where should the patient go in case of an emergency complication? How to secure sufficient training and experience of the next generation of paediatric surgeons, especially in times of reduced working hours thanks to today's legislation? A well-organised training programme, including the rotation between centres specialised on different entities, might be a solution [39].

Nevertheless, we must not "defend low-volume work when poor outcomes have lifelong functional and quality of life implications for patients" [20]. The resistance of paediatric surgeons against centralisation, as seen in Great Britain in the case of biliary atresia [20], might well be "self-serving bias, leading to self-deception and rationalisation of actions that entrench self-serving behaviour potentially resulting in unethical acts" [40]. The decision, not to report the volume–outcome ratio in a nationwide cohort on esophageal atresia [20] might fall into the category "harm caused by COI restricting information" [9].

In some countries (GB, F, NL) and pathologies (biliary atresia, bladder exstrophy, paediatric oncology), centralisation has already been realised to a higher degree [20, 41]. Obviously, public pressure by patient organisations, paediatricians and politics is helpful in overcoming the surgeons' impeding COIs. The European Reference Networks for Rare Diseases, consisting of 24 thematic networks which strive to offer specialist centres to all EU-patients suffering from the known 6000–8000 rare diseases, have a similar aim.

Their requirement of scientifically based minimal numbers for patients seen and procedures performed [1] cannot yet be fulfilled for many rare diseases, because the necessary data are lacking [42], or because no European clinic yet reaches the necessary case numbers, but it points into the right direction.

Our "consider-referral-policy" (Table 1) is also one of the necessary steps initiated by the ERNs.

Hopefully future generations of paediatric surgeons will be routinely trained [43] in making these decisions in partner-like, fair dialogue with patients and patient representatives.

The closing remarks shall be left to Mark Wijnen, paediatric surgeon from Utrecht and ERN member: "This article does not represent the view of all pediatric surgeons…, but I have tried to describe our struggle to improve the care for a considerably vulnerable group of patients entrusted to us. It has taken several years and we are not yet there, but I believe that we have turned the corner and there is no way back" [10].

Conclusion

Dealing with non-financial conflicts of interest is an important step in developing paediatric surgery and improving patient care.

The increasing interest in the subject has to be welcomed, in spite of many open questions. This holds especially true for the necessary centralisation of surgical care in light of the well-known volume–quality relationship. The European Reference Networks for Rare Diseases address this problem in a new way, mainly because of the driving forces of patient organisations and political will. The broader paediatric surgical community should embark more readily in the process, to co-steer it, to the best of patients and surgeons, instead of denying the necessary changes, which are already underway.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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