EDITORIAL



Defensive medicine in Europe: a 'full circle'?

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Introduction

Defensive Medicine (DM) is a concept originating in the USA in the early 1970s and later extended to other continents, Europe included (Fig. 1). The very first mention of DM in a public speech was probably that of the General Counsel of the American Medical Association in 1974, who recommended it after provocatively suggesting that his colleagues should do no medical action at all as the only way to avoid malpractice lawsuits [1].

Basically, DM refers to all medical care by physicians, aimed primarily at preventing the risk of litigation [2–4]. Interest in DM as a strategy for deterring patients' lawsuits for medical negligence and malpractice has increased in recent decades because of the growing number of litigations in many countries [5–7]. DM-redundant practices induced by the threat of medical liability rather than the benefit of patients [8–10] are expected to artificially increase total healthcare expenditures [11–13].

Defining DM and neighbor concepts

Although many authors have indulged in providing definitions of DM, they are all substantially similar and overlap the very first ones [1]. Stemming from the shorter and easier definitions we found [14–16], DM includes all medical actions that physicians do without considering them the standard of care according to their clinical knowledge; these

actions are meant to shield best physicians from negligence or malpractice lawsuits filed by patients or their families.

DM practice is generally divided into two categories [1, 17]: (1) 'positive' DM occurs when physicians prescribe unnecessary or repetitive tests, referrals and/or procedures; (2) 'negative' DM occurs when physicians refuse care to high-risk patients or avoid risky procedures. DM is likely to be more practiced in high-risk specialties (e.g. emergency medicine, obstetrics and gynecology, surgery) [2, 5], intuitively more prone to litigation [18]. Diagnostic tests and cesarean section operations are the most commonly cited examples of unnecessary practices enhanced by DM [19, 20].

Patients are the 'first victims' of medical negligence and, therefore, DM [21], especially the negative type. However, physicians can become 'second victims' because of increasingly stressful working conditions affecting everyday practice [3]. A legal action may even induce a 'clinical judicial syndrome' [12], at first triggered by sudden notification of legal proceedings, and later by lawyers' harsh and aggressive language during court trials. Although it is still debated whether this stress can really become a clinical syndrome [12], DM may offer psychological benefit to all physicians tackling it, no matter whether they have really experienced a litigation or just heard about bad experiences from colleagues.

Since DM debate has spread widely also in countries where medical negligence is seldom subject to tort laws [12, 22], recently, some authors did not relate DM solely to the fear of litigation, but extended it to being perceived as a low-profile physician among colleagues [1]. There are two complementary 'triggers' potentially enhancing DM, more generally related to physicians' loss of reputation in the workplace on account of medical errors [23]. First, a strong emotional response to complaints can lead to 'shame',



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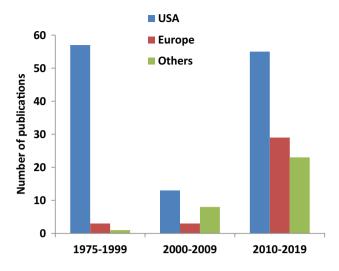


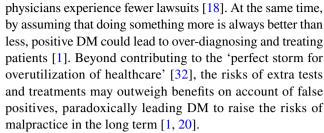
Fig. 1 Trend of articles with 'Defensive medicine' in the title

a desire to withdraw from medical practice and run away due to a feeling of global failure, far beyond guilt about a specific error, eventually undermining the physician's self-esteem [8] and potentially leading to professional 'burnout' [24, 25]. Second, a social culture oriented to individual 'blame' can boost a 'witch-hunt' aimed at identifying physicians who are personally responsible for medical errors as happens with pilots who are held to be the culprits for air crashes and blame them publicly through the mass media to stigmatize their mistakes [12, 26].

DM and the legal framework of nations

Medical malpractice can be legally defined as professional negligence (by an act or omission) generating a treatment which falls below the common standard of medical practice, eventually causing an avoidable injury (or even death) to a patient [27]. DM is inevitably influenced by the domestic legal culture of nations [13], though the relationship is by no means clear [28].

Probably not by chance was DM born in the USA, where negligence lawsuits and tort actions are very frequent [29], although unevenly distributed among the States depending on their different legislations [4]. In general, DM practices are likely to be more common in nations with a higher density of lawyers and recourse to tort lawsuits [2], e.g. Italy has by far the highest proportion of malpractice lawsuits settled in courts among the largest mainland European countries (90% in 2014 compared to 60% in France and 40% in Germany) [15]. This suggests that DM is more affected by environmental than individual factors [28], becoming a sort of 'luxury tax' paid in wealthy countries with tort-based legal systems [29–31], where adopting DM tactics can help



In Northern European countries (such as Denmark, the Netherlands and Sweden), where patients' complaints can be addressed earlier in alternative sites (e.g. medical disciplinary boards) before arriving in the courts [3, 6, 17], physicians are less financially liable for non-gross negligence. In these nations, DM seems to be perceived as a less pressing issue at present, more like a future threat in the case of growing 'Americanization' of European healthcare systems and more frequent recourse to court claims as a consequence [17].

In general, decriminalizing medical mistakes and handling them by medical organizations or in civil courts should help limit DM [15, 33]. Since a fair legal environment is expected to constrain DM, especially the positive type [2], the more recommended legal strategies aim at reducing medical liability for unintentional errors through alternative dispute resolutions [20]. Ideally, patients' damages should be at least co-paid by health employers too [23], although the interests of employers and employees do not always converge [27] and a balanced liability climate should result in [2]: (1) unlikely compensation for patients bringing frivolous lawsuits, (2) appropriate restitution for patients truly wronged because of gross medical negligence.

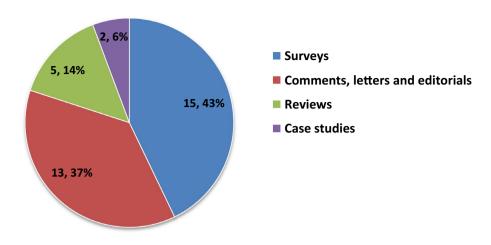
Estimating DM and the economic impact

Estimates of DM activities and the induced costs come from physician surveys worldwide, Europe included (Fig. 2). Various surveys have been run in Europe (mainly in Italy and the UK), on different types of physicians (mainly surgeons and general practitioners). Except in a few studies from northern countries [13, 34] where patients are offered several administrative alternatives to satisfy their complaints before taking legal action (see above), DM appears to be widespread and flourishing in most of Europe [5, 7, 14, 26, 35–37], potentially causing healthcare systems substantial costs [25, 38]. DM was less frequent among senior physicians in the UK [14], while most Italian physicians justified their frequent recourse to DM as a reaction to the weak protection received from their managers against individual lawsuits [25, 26, 38].

However, the standard of care can be legally defined only as what other qualified physicians would have done under similar circumstances [8]. Therefore, lacking an objective reference for standard care, the intrinsic limit of surveys is



Fig. 2 Articles with 'Defensive medicine' in the title published in Europe by type of publication



that answers are necessarily subjective and affected by physicians' beliefs, making it hard to collect reliable information on DM [9]. Regardless of researchers' efforts and beyond physicians' specialties, responses can vary a lot depending on how surveys are framed and questions are set out [39]. Since any medical practice may virtually offer patients some benefit [8, 40, 41], it is hard to draw a line between cautious and defensive practices [19, 21, 30], with participants giving black or white answers to necessarily gray questions [18]. As a consequence, cost estimates of DM sourced from surveys are hardly reliable too [1].

The broad economic impact of DM has also been analyzed using theoretical models. Beyond DM direct expenses, modelers usually consider indirect costs related to physicians' stress, loss of time and reputation. Litigation may damage physicians' reputations and the huge amount of time spent for claims may lower their productivity [42], which is why physicians may find it convenient to practice DM even when they are fully covered by insurance [43]. Paradoxically, increasing safety in clinical practice may raise patients' expectations excessively in the long run, hence litigation rates too when accidents occur, beyond any significant change in the actual level of DM [6]. Consistently, rising malpractice pressure can increase both the quality of care and DM expenses up to a certain threshold, after which they decrease [44]. Although a risky technology (e.g. surgery) might entirely cure patients, negative DM can spur physicians to opt for a safer (even if potentially less effective) strategy in settings with tough malpractice legislation [43].

DM in the science of medicine debate

The discussion on DM is actually part of a more general debate in the medical literature on the role of modern medicine Europe included (Fig. 3) whether to be considered an already perfect science of certainty or a still imperfect art of probability [33]. The 'body-as-machine' metaphor is very

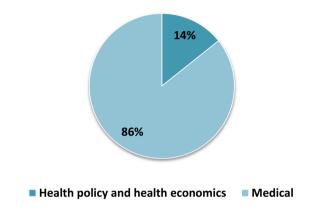


Fig. 3 Articles with 'Defensive medicine' in the title published in Europe by type of journal

useful to describe the biomedical approach [24], the patient's body being the machine and the doctor its 'mechanic' in case of failure. Thanks to scientific progress, physicians can make the right diagnosis and provide the right therapy so any illness seems potentially curable, and behind a complication inevitably a suspicion of clinical error arises [10]. This approach supports a 'zero-mistake' culture of omnipotent medicine [15].

Differently, the multidimensional (bio-psycho-social) approach by far preferred by DM experts reminds us that medicine is still an art of probability rather than a perfect science [1]. Starting from diagnosis, only uncertainty is sure and certainty an illusion, even in the most advanced settings [33]. Therefore, clinical experience and intuition should still drive the art of medicine, with patients' responses often unpredictable and adverse events unavoidable [12, 33]. According to this patient-centered approach, disease varies a lot depending on the individual [24], so the personal physician–patient relationship is still crucial [22]. Clinical protocols and guidelines often mainly based on opinions and observational studies [45] are means for improving population rather than individual health [3]. Therefore, just as a



recipe book cannot guarantee successful cooking, physicians should not follow only clinical guidelines to make their decisions, regardless of their personal experience, and always analyze their patients case by case [33].

By immediately ordering tests and prescribing therapies, DM seems to be a logical reaction to the overwhelming biomedical approach [33], which promises to treat any disease in the overstocked 'factories' of modern medicine. According to some authors, DM is as reasonable as it is necessary to reduce physicians' legal liability [18, 19, 30, 31], a sort of unavoidable fact of modern life whose unnecessary risks are often overestimated and potential benefits for patients overlooked. However, many authors consider DM unethical and at odds with medical deontology [2, 14, 15, 23, 33, 38, 40], adding avoidable risks to individual patients and costs to societies as a whole—especially positive DM [13].

DM, physician-patient trust and attitude toward clinical errors

DM seems to be closely related to the creeping crisis of trust in the modern physician–patient relationship [33, 46]. The former are not yet used to accepting challenges to their professional judgment rarely questioned historically thanks to a rife paternalistic attitude [14], while the latter have dramatically increased their expectations from innovative treatments, fostered by regular searches on modern media such as internet [15], so they fear having received substandard care instead of best care available if the outcome is adverse [47].

In the last few decades, patients' trust in physicians has been undermined mainly because doctors have drastically cut the time spent to discuss with each patient [10], so as to diagnose and treat more and more patients in less and less time, eventually leading to low job satisfaction and DM as a logical consequence. The most effective reaction to DM, therefore, should be to restore trust with patients, the main source of professional satisfaction for physicians [33]. Since patients who do not trust their physician are reluctant to provide important information [12], communication and respect on both sides needs to be strongly encouraged [42], and physicians should listen to their patients before trying to persuade them [15].

A societal strategy struggling against DM should be able to manage medical errors positively [33]. Since medical quality and safety are hardly ever achieved through threat and penalty [15, 29], a cultural revolution supported by all health 'players' health authorities included [26] would be desirable to transform any unwilling error into a learning opportunity [12, 47]. Ideally, all physicians should collaborate with their colleagues too, to discuss and share best patient care [19] for instance, radiologists could help educate referring colleagues about the benefits and risks of tests

prescribed [47]. A climate of clinical collaboration would be conducive to the best use of staff in healthcare services [26], eventually cutting DM costs [30]. At the same time, since cooperation between patients and physicians is the social optimum [6, 42], continuing efforts are needed to educate patients and their relatives that the most reliable information comes from clinical sources rather than social media [33].

DM, everything and its opposite

A recent literature review concluded that the debate on DM is really confusing from any point of view, giving no guidance in practice to policy makers for potential action based on robust evidence and rational logic [11]. Having found everything and its opposite in our analysis on DM, we just share this tough conclusion. However, we can draw at least one sound lesson from the DM debate: an organizational culture aimed at limiting both extreme severity in punishing clinical errors and full discretion in medical practice should be highly recommended in health care systems [26]. While the former fosters DM, the latter has nowadays been overwhelmed by the 'patient empowerment' tendency [48], thanks to which redistribution of power from physicians toward patients has enhanced openness in the relationship. This implies that the legal framework of Northern European countries with their different solutions before legal action should be the best to deter DM. Finally, beyond questionable debates, clearly any physician can ensure good clinical practice on a daily basis, wherever s/he works and regardless of the healthcare organization, just like any health professional who does her/his job in the interest of patients.

Proposals for deterring DM from health economics and management

Once agreed that DM is a sort of unnecessary and expensive 'side effect' of modern medicine, to be deterred, rather than an objective problem to be tackled, some general recommendations stemming from economics and business administration can be raised to limit the threat.

Healthcare is a classical example of 'market failure' in economic theory, since health is a 'merit good' rather than a common 'consumer good' [49]. Therefore, competition is not the best instrument for addressing equity concerns, and an 'Americanization' of health, with high prevalence of private for-profit 'players' (for both funding and provision), is hardly recommendable: not by chance has the USA skyrocketing healthcare expenditure and spends far more than other wealthy nations for administration [50]. Differently, in the European health systems patients have not been historically considered common consumers, and physicians respond



mainly to 'third-party payers' for healthcare expenditure. The most worrying recent institutional trend in Europe has been the widespread adoption of tariffs instead of global budgets for funding healthcare services. This arguable choice one more 'Americanization' can eventually undermine coordination and synergies among health services [50]. In particular, we share the opinion that fee-for-service systems tending to reward over treatments can eventually induce DM as a further potential distortion [40], so they should be ruled out.

If medicine is firstly a mission aimed at serving patients as often recalled in the medical literature clinical practice should be mainly inspired by collaboration among health professionals, and financial incentives should be considered very arguable means for making them work better for patients [51]. If patients' interests are the cornerstone of physicians' fiduciary relationship with them, success in curing or caring should be the leading motivation for physicians, and business ethics should not be mixed with medical ethics to avoid undermining physician—patient trust [49]. Ideally, there is no doubt that an organizational culture rooted in teamwork and collaboration fits healthcare services much better than a competitive one.

Surprisingly, we found only one reference, in a Chinese article [46], to physicians' dual practice (i.e. the combination of public and private practice) as a potential trigger of DM inside healthcare services. This might be an 'elephant in the room to decloak' for deterring DM in most European countries too [52]. From a management point of view, it is like allowing company employees to deal privately with the same clients in their spare time, a very odd managerial situation, even stranger for a burdensome job prone to burnout such as the physician's. For instance, many Italian gynecologists used to over-recur to cesarean section very often cited in the DM literature as an example of unnecessary practice to exploit their strong relationship with pregnant women and boost private consultations before and after childbirth. Dual practice arouses conflicts of interest in the physician-patient relationship, with self-gain pursued to the detriment of patients and/or colleagues too [52]. When forbidden, the claim to make third payers accountable for legal expenses in case of lawsuits for medical negligence as a DM deterrent [15] would be much more justifiable.

To conclude, we offer a proposal to try to estimate DM and its costs in health systems through a potentially more robust tool than physician surveys. Assuming that physicians are the most informed patients when they (and/or close relatives) fall ill [48], why not set up a permanent European observatory to compare their healthcare patterns of consumption with the general population? To our knowledge, this useful exercise was done only once in the past in Switzerland in the early 1990s [53] and never repeated.

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Compliance with ethical standards

Conflict of interest Anna Padula and Livio Garattini have no conflicts of interest that are directly relevant to this article.

References

- 1. Berlin, L.: Medical errors, malpractice, and defensive medicine: an ill-fated triad. Diagnosis (Berl) 4(3), 133–139 (2017)
- Cote, D.J., Karhade, A.V., Larsen, A.M., Castlen, J.P., Smith, T.R.: neurosurgical defensive medicine in Texas and Illinois: a Tale of 2 States. World Neurosurg. 89, 112–120 (2016)
- Assing Hvidt, E., Lykkegaard, J., Pedersen, L.B., Pedersen, K.M., Munck, A., Andersen, M.K.: How is defensive medicine understood and experienced in a primary care setting? A qualitative focus group study among Danish general practitioners. BMJ Open 7(12), e019851 (2017)
- Agarwal, R., Gupta, A., Gupta, S.: The impact of tort reform on defensive medicine, quality of care, and physician supply: a systematic review. Health Serv. Res. 54(4), 851–859 (2019)
- Ramella, S., Mandoliti, G., Trodella, L., D'Angelillo, R.M.: The first survey on defensive medicine in radiation oncology. Radiol. Med. 120(5), 421–429 (2015)
- Antoci, A., Fiori Maccioni, A., Russu, P.: The ecology of defensive medicine and malpractice litigation. PLoS One 11(3), e0150523 (2016)
- Osti, M., Steyrer, J.: A national survey of defensive medicine among orthopaedic surgeons, trauma surgeons and radiologists in Austria: evaluation of prevalence and context. J. Eval. Clin. Pract. 21(2), 278–284 (2015)
- Anderson, R.E.: Billions for defense: the pervasive nature of defensive medicine. Arch. Intern. Med. 159(20), 2399–2402 (1999)
- 9. Hermer, L.D., Brody, H.: Defensive medicine, cost containment, and reform. J. Gen. Intern. Med. 25(5), 470–473 (2010)
- Lykkegaard, J., Andersen, M.K.K., Nexøe, J., Hvidt, E.A.: Defensive medicine in primary health care. Scand. J. Prim. Health Care 36(3), 225–226 (2018)
- 11. Kapp, M.B.: Defensive medicine: no wonder policymakers are confused. Int. J. Risk Saf. Med. **28**(4), 213–219 (2016)
- Pellino, I.M., Pellino, G.: Consequences of defensive medicine, second victims, and clinical-judicial syndrome on surgeons' medical practice and on health service. Updates Surg. 67(4), 331–337 (2015)
- Yan, S.C., Hulou, M.M., Cote, D.J., Roytowski, D., Rutka, J.T., Gormley, W.B., Smith, T.R.: International defensive medicine in neurosurgery: comparison of Canada, South Africa, and the United States. World Neurosurg. 95, 53–61 (2016)
- Ortashi, O., Virdee, J., Hassan, R., Mutrynowski, T., Abu-Zidan,
 F.: The practice of defensive medicine among hospital doctors in the United Kingdom. BMC Med. Ethics 14, 42 (2013)
- Toraldo, D.M., Vergari, U., Toraldo, M.: Medical malpractice, defensive medicine and role of the "media" in Italy. Multidiscip. Respir. Med. 10(1), 12 (2015)
- Bishop, T.F., Pesko, M.: Does defensive medicine protect doctors against malpractice claims? BMJ 4(351), h5786 (2015)
- Yan, S.C., Hulsbergen, A.F.C., Muskens, I.S., van Dam, M., Gormley, W.B., Broekman, M.L.D., Smith, T.R.: Defensive medicine among neurosurgeons in the Netherlands: a national survey. Acta Neurochir. (Wien) 159(12), 2341–2350 (2017)



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 Bean, J.R.: Defensive medicine: a game in which perception trumps Reality. World Neurosurg. 90, 646–647 (2016)

- Coates, J.: Defensive medicine. N. Z. Med. J. 115(1160), U144 (2002)
- Plebani, M.: Defensive medicine and diagnostic testing. Diagnosis (Berl) 1(2), 151–154 (2014)
- Prabhu, V.C.: Defensive medicine in neurosurgery. World Neurosurg. 95, 587–589 (2016)
- Assing Hvidt, E., Bjørnskov Pedersen, L., Lykkegaard, J., Møller Pedersen, K., Andersen, M.K.: A colonized general practice? A critical habermasian analysis of how general practitioners experience defensive medicine in their everyday working life. Health (London) (2019). https://doi.org/10.1177/1363459319857461
- Keren-Paz, T.: Liability regimes, reputation loss, and defensive medicine. Med. Law Rev. 18(3), 363–388 (2010)
- Cunningham, W., Wilson, H.: Complaints, shame and defensive medicine. BMJ Qual. Saf. 20(5), 449–452 (2011)
- Elli, L., Tenca, A., Soncini, M., Spinzi, G., Buscarini, E., Conte,
 D.: Defensive medicine practices among gastroenterologists in Lombardy: between lawsuits and the economic crisis. Dig. Liver Dis. 45(6), 469–473 (2013)
- Catino, M., Celotti, S.: The problem of defensive medicine: two Italian surveys. Stud. Health Technol. Inform. 148, 206–221 (2009)
- Clark, J.R.: Defensive medicine. Air Med. J. 34(6), 314–316 (2015)
- Prabhu, V.C.: Operant conditioning and the practice of defensive medicine. World Neurosurg. 91, 603–605 (2016)
- 29. Bean, J.R.: Defensive medicine: rational response to irrational risk. World Neurosurg. **94**, 568–569 (2016)
- Fronczak, S.W.: Defensive medicine: a tax/surcharge for the delivery of healthcare. World Neurosurg. 95, 594–596 (2016)
- Bassett, K.L., Iyer, N., Kazanjian, A.: Defensive medicine during hospital obstetrical care: a byproduct of the technological age. Soc. Sci. Med. 51(4), 523–537 (2000)
- Emanuel, E.J., Fuchs, V.R.: The perfect storm of overutilization. JAMA 229, 2789–2791 (2008)
- Vento, S., Cainelli, F., Vallone, A.: Defensive medicine: it is time to finally slow down an epidemic. World J. Clin. Cases 6(11), 406–409 (2018)
- Vandersteegen, T., Marneffe, W., Vandijck, D.: Defensive medicine: implications for clinical practice, patients and healthcare policy. Acta Clin. Belg. 70(6), 396–397 (2015)
- Motta, S., Testa, D., Cesari, U., Quaremba, G., Motta, G.: Medical liability, defensive medicine and professional insurance in otolaryngology. BMC Res. Notes 8, 343 (2015)
- Summerton, N.: Positive and negative factors in defensive medicine: a questionnaire study of general practitioners. BMJ 310(6971), 27–29 (1995)
- 37. Summerton, N.: Trends in negative defensive medicine within general practice. Br. J. Gen. Pract. **50**(456), 565–566 (2000)

- Panella M, Rinaldi C, Leigheb F, Knesse S, Donnarumma C, Kul S, Vanhaecht K, Di Stanislao F: Prevalence and costs of defensive medicine: a national survey of Italian physicians. J. Health Serv. Res. Policy 22(4), 211–217 (2017)
- Baicker, K., Wright, B.J., Olson, N.A.: Reevaluating reports of defensive medicine. J. Health Polit. Policy Law 40(6), 1157–1177 (2015)
- Kachalia, A., Mello, M.M.: Defensive medicine–legally necessary but ethically wrong?: Inpatient stress testing for chest pain in lowrisk patients. JAMA Intern Med. 173(12), 1056–1057 (2013)
- Sloan, F.A., Shadle, J.H.: Is there empirical evidence for "Defensive Medicine"? A reassessment. J. Health Econ. 28(2), 481–491 (2009)
- Osti, M., Steyrer, J.: A perspective on the health care expenditures for defensive medicine. Eur. J. Health Econ. 18(4), 399–404 (2017)
- Feess, E.: Malpractice liability, technology choice and negative defensive medicine. Eur J Health Econ. 13(2), 157–167 (2012)
- Montanera, D.: The importance of negative defensive medicine in the effects of malpractice reform. Eur. J. Health Econ. 17(3), 355–369 (2016)
- 45. Yeung, E.Y.H.: Evidence based versus defensive medicine. BMJ 363, k4114 (2018). https://doi.org/10.1136/bmj.k4114
- Chen, X.Y.: Defensive medicine or economically motivated corruption? A confucian reflection on physician care in China today.
 J. Med. Philos. 32(6), 635–648 (2007)
- Chawla, A., Gunderman, R.B.: Defensive medicine: prevalence, implications, and recommendations. Acad. Radiol. 15(7), 948– 949 (2008)
- Garattini, L., Padula, A.: Patient empowerment in Europe: is no further research needed? Eur. J. Health Econ. 19(5), 637–640 (2018)
- Garattini, L., Padula, A.: Conflict of interest disclosure: striking a balance? Eur. J. Health Econ. 20(5), 633–636 (2019)
- Garattini, L., Padula, A.: Competition in health markets: is something rotten? J. R. Soc. Med. 112(1), 6–10 (2019)
- Garattini, L., Padula, A.: Clinical governance in Italy: 'Made in England' for import? Appl. Health Econ. Health Policy 15(5), 541–544 (2017)
- Garattini, L., Padula, A.: Dual practice of hospital staff doctors: hippocratic or hypocritic? J. R. Soc. Med. 111(8), 265–269 (2018)
- Domenighetti, G., Casabianca, A., Gutzwiller, F., Martinoli, S.: Revisiting the most informed consumer of surgical services. The physician-patient. Int. J. Technol. Assess. Health Care 9(4), 505– 513 (1993)

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