

Healthcare acquired infections: malpractice and litigation issues

M. Siracusa¹, S. Scuri¹, I. Grappasonni¹, F. Petrelli¹

Key words: Cross infection, malpractice, litigation

Parole chiave: Infezioni correlate all'assistenza, medicina legale, contenzioso

Abstract

Background. Healthcare acquired infections (HAIs) represent a significant burden for hospitalized patients in terms of mortality, morbidity, length of stay and costs. Also cause medical liability and medical malpractice litigation.

Methods. Specific keywords combinations were analytically searched in PubMed and Scopus databases. Publications concerning medical liability, medical malpractice and litigation issues were reviewed.

Results. The authors outlined the healthcare workers and healthcare settings mandatory duties in consideration of the Italian law. In case of infections occurred in hospital environment the patients must demonstrate the guilty nature of the physicians and healthcare settings, the existence of a harm and causal connection. Physicians and healthcare facilities defence is mainly based on demonstration that protocols and aseptic measures were adopted scrupulously applying the up to date scientific knowledge.

Conclusions. HAI are a complex issue which need a multitask strategy and a surveillance system to control the phenomenon and help physicians and healthcare facilities to reduce malpractice litigation.

Introduction

Healthcare acquired infections (HAIs) represent a significant burden for hospitalized patients in terms of mortality, morbidity, length of stay and costs (1-5). Furthermore, healthcare workers may be affected and this infection category is defined as occupational infections (6).

The World Health Organization (WHO) estimates that millions world wide develop HAIs with a major impact on public health (7). Overall, the European Union estimates an impact of 501 disability-adjusted life years (DALYS) per 100,000 abitanti (8).

According to the European Centre for Disease Prevention and Control which analyzed a total of 310,755 patients in 1,209 hospitals from 28 european countries, 6.5% patients were affected by an HAI and Episodes per year were estimated at 8.9 million (4).

The most frequently isolated microorganisms are Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* among Gram-negatives, and *Staphylococcus aureus*, *Clostridium difficile* and enterococci among Gram-positives (4).

¹ School of Medicinal and Health Products Sciences, University of Camerino, Camerino, Italy

Major risk factors are represented by patients susceptibility, comorbidities and invasive procedures which need to be carried out with scrupulous application of contact precautions (9-12). Healthcare workers non compliance to standards may be influenced by working stress (13, 14) or not appropriate training and personal knowledge (15-20).

Additionally, HAI risk is increased due to the incorrect habit of over-prescription and misuse of antibiotics with the drug-resistance increasing of various pathogens have also associated (21, 22).

The WHO registered an increasing antimicrobial resistance which raises concerns regarding the impact on patients with multidrug resistant organisms (23-27).

As found in the WHO definition about health literacy as “the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health” (28-30).

In Italy already in the 1980s the Ministry of Health issued two Ministerial Circulars (n° 52/1985 “Fight against hospital infections” and n° 8/1988 “Fight against hospital infections: surveillance”) in which basic requirements of control programmes were defined. Every hospital was obliged to establish a committee to control the spread of infections, involving various experts in the field. Later, in order to achieve this task, both the Italian Ministry of Health and the Regional governments encouraged and recommended numerous actions and initiatives to control the phenomenon. National surveillance networks have been implemented (31).

Italian legal system

The historical interpretation of medical negligence, in Italy, was founded in

establishing gross negligence on the part of the treating doctor; this philosophy limited the number and scope of malpractice cases filed against physicians (32). More recently, the professional liability has changed, with increased numbers of claims against doctors, size of payments to injured patients, moving from mere token amounts paid to victims of medical malpractice to the increasingly greater sums of money paid since the late 1980s. In part, this trend may reflect technological advances in healthcare and how judges view these advances.

In the past, physician had an obligation to use all available means to achieve the result without being legally obliged to actually achieve the result, now the physician is more frequently called to answer for any result falling short of patient expectations (32).

Overall, Italian medical litigation is rarely reported in international medical journals. Probably as a consequence of the Italian legal system complexity, which is completely different from the Anglo-Saxon legal derivation. Consequently thus the Italian medical litigation literature is mainly published in nonmedical journals, spread in unpublished theses, legal monographs, or chapters of textbooks for students in law universities. In Italy the legal system is Civil law based on Roman law, whereas Common law legal systems are in use in those nations that trace their legal heritage to Britain. The two legal systems differences also influence the medical liability laws, for example in the Italian civil law system the breach of duty of care does not exist, while negligent personal injuries (*lesioni personali colpose*) that are not included in common law systems are prosecuted. On the contrary in the United States, a successful tort claim requires four legal elements: (1) duty of care; (2) breach of duty; (3) injury; (4) proximate cause (33).

In Italy physicians are both liable to prosecution in a criminal court and in a civil court, and their conduct is evaluated on the basis of negligence, imprudence and

unskillfulness. Negligence (*negligenza*) consists of lack of care, and implies passive behavior that is reflected in the omission of necessary precautions; imprudence (*imprudenza*) consists of a given medical action without taking all the precautions that common experience suggests is necessary, and implies active behavior that translates into a reckless behavior; that is behavior unconscious of the possible dangers verifiable with a reasonable probability; unskillfulness (*imperizia*) consists of a poor attitude in those activities which require special technical knowledge and implies a deficiency of culture, practice, intuition and capacity of observation (33).

We define “healthcare acquired infections” those acquired during hospitalization, and not clinically manifest or incubating at the time of admission. By convention, infections that make themselves evident within forty-eight hours of hospital admission are considered to have been contracted in the community (Community Acquired Infection), while those that occur later are considered to have been contracted in a hospital (Hospital Acquired Infection), unless there is clear information on the incubation in place at the time of admission.

Healthcare workers and healthcare settings

When a patient enters the hospital, stipulates a healthcare contract with the facility. The facility is obliged to ensure the adequate presence of qualified healthcare workers and the proper functioning of the equipment. Therefore, the structure is responsible for both inadequate equipment, and for medical or nursing mistakes, such as forgetting a gauze in the abdomen.

In case of litigation, the injured patient must prove that: 1) he had a contract with the hospital structure; 2) he suffered damage; 3) his health deteriorated because the facility

did not properly perform the healthcare benefits it was contractually obligated.

The hospital must document that: 1) it has carefully observed all the technical requirements, e.g. correct sterilization of the operating rooms; 2) it has predisposed all the measures to ensure the patient’s stay in a healthy environment; 3) the infection derives from a cause not attributable to the structure (art. 1218 cc).

In Italy, first the burden of proof is on the defendant (physician or hospital), second, all laws applicable to professional diligence are pertinent, and third, the statute of limitations (the statute that sets forth the maximum period of time, after certain events, that legal proceedings based on those events may be initiated) is that peculiar to contracts and set at 10 years rather than the 5 for compensation claims not originating from a contract (from tort). This is five times more than the 2 years established by U.S. legislation (33). In other words, in Italy a physician could be called to answer for malpractice 10 years after a medical procedure, and would have to prove his innocence.

The physicians figure in Italy has been related by the Court of Cassation as a “good father of a family” holding that in addition to intentional or grossly negligent conduct, a physician can also be liable for violating the ordinary standard of care relating to professional preparation, scrupulous attention, and adequate training.

The burden of proof in medical negligence cases depends on the nature of the medical procedure. If the medical procedure (nonoperative or operative treatment) is routine, commonly performed, and straightforward, then the physician faced with an adverse outcome is burdened with showing that such an outcome was not the result of negligence, imprudence, or lack of skill. Conversely, if the medical procedure is complex or unusual, the patient is burdened with showing that the procedure was unnecessary, or that physician malice

or serious negligence contributed to a poor outcome.

Preliminary remarks on legal matters

The extent of HAIs (34) brings a multitude of scientific and legal issues to light.

From a subjective viewpoint, the figure of the healthcare worker is central in a legal sense. The term “healthcare worker” may refer to the physician (operating individually or in a medical team) or other personnel such as nurses, postgraduate students, volunteers etc. These figures operate within a healthcare facility, be it publicly or privately owned, under extremely different contractual conditions. Relations between healthcare workers and employers are mediated by insurance companies, which are more often than not given the task of managing the risks associated with medical practice instead of the healthcare facility, which is more likely to deal exclusively with risks related to catastrophic events and pursuant claims. This situation creates a complex tangle of liabilities: strict liability for the healthcare worker; liability of an objective nature relating to organisational/procedural practices in the healthcare institution; and indirect liability for the insurance company in those instances in which/when proceedings are not brought against the party insured.

Last but not least, the patient who has contracted an infection (cause of disability and in some cases even death) will have to face lengthy, expensive court procedures in an attempt to prove the right to compensation for physical and moral damages is founded (35).

Indeed, speaking objectively, the fact that the micro-organism responsible for the infection is unknown to science in 21% of cases is profoundly disheartening, as this complicates the assessment of legal liability (the etiological link between the event and actual damages).

Hospital and health authority: the holders of a plot of responsibility

In consideration of the relationship between healthcare facility, healthcare staff and patients (art. 7 of L.n. 24/2017; I and III c), in presence of negligent or malicious behavior, the responsibility of both healthcare providers is contractual, with explicit reference to the art. 1218 and 1228 c.c. The patient who relies on healthcare facility or doctor care, creates a real contractual relationship. Also the article n° 7 of the Law n. 24/2017 specifies that, apart from the hypothesis of a contractual obligation between doctor and patient (article n° 7 of the Law n. 24/2017), the doctor’s responsibility is linked also by the art. 2043.

Although healthcare facility and healthcare provider responsibilities are based on the same assumptions, they remain autonomous and independent, as they are valid even in the absence of each other.

Therefore, healthcare facility responsibility is widely objective on organizational basis, not having guaranteed a minimum risk condition. The structure may was “faulty” not having adopted the protocols in order to guarantee environments sanification, equipments, staff. Also, may having adopted them without their compliance supervision (36).

Since 1988, all healthcare facilities are obliged by italian law (D.M. 13/09/1988) to set up infection control committees to ensure infections prevention through surveillance programs, training and of proper antimicrobial stewardship (whose abuse is closely related to the spread of HAIs).

Also, national level guidelines and quality standards are promoted by Regions coordination, and implemented in every healthcare facility. An example is the INF-OSS project (37), promoted by the Ministry of Health, which aims to create a national infections monitoring network to exchange experiences, and improve prevention.

The national and international guidelines are also the basis for healthcare facility responsibility discipline (criminal and civil law) according to the *ex* Law 8 June 2001, n.231. The responsibility is related to programs compliance, whose failure or erroneous adoption causes a risk of crime, whereby the body must respond proving they adopted programs adequately and effectively.

Indeed, there are many criticalities that hinder the application of this legislation, which are currently difficult to overcome (38). First of all, the data for which constitutional bodies, in which health facilities can be traced, are excluded from its application.

However, recent jurisprudence (39) has imposed the necessary differences, recognizing that many healthcare facilities have a private (or mixed public-private) nature and are comparable to corporate bodies aimed at profit production. Secondly: the Law n. 231/2001 establishes that the crime must be actually committed by a physical person, in the entity's interest or benefit.

The culpable event, like injuries or death, in intentional crimes is not wanted and therefore it is not possible that it was produced in the interest or for the benefit of the entity. So the jurisprudence has accomplished an interpretation: what is not wanted is not the final event, but the initial one, for example, the failed or incorrect adoption of compliance programs in order to get the institution to save costs (40). Actually, in the field of HAIs, health management could omit the adoption of some sanitation protocols to achieve cost savings. A non-deceptive obstacle remains: the Law n. 231, 8 June 2001 reports a list of crimes for which only, this type of responsibility can exist and in that list crimes against public or individual health are not included. However, it is possible to speculate a future inclusion based on the recent adoption of the art. 590 *sexies* penal law, which regulates the "culpable

liability for death or personal injury in the health sector".

According to the Court of Cassation (41) to support the doctor's lack of criminal liability, he must have correctly identified the guidelines, recommendations for good practices applicable to the specific case, then erring, for unskillfulness, in their execution.

Therefore, in case of HAIs, this can rarely occur: failure to comply with guidelines, recommendations and good practices regarding the sanitation of people, environments, procedures, etc., is due not so much to the notion of incompetence (understood as a violation of the *leges artis*) as to that of negligence (carelessness, lack of attention) or imprudence (cases of recklessness or insufficient weighting), for which articles 589 and 590 penal law are applicable.

Healthcare professional criminal liability will be excluded in case of healthcare facility organization deficiencies (42), although doctor's civil responsibility could remain.

Doctors are responsible for organizational deficits communication, since they could be accused of "negligent fulfillment ineptitude" towards the patient (43), having omitted the vigilance on the hospital environment hygienic conditions (44).

Choosing to resort to criminal proceedings must however be *extrema ratio*: the patient or their kin should be able to aim for the best possible compensation for damages instead of taking punitive action against healthcare workers, whose activities when it comes to HAI are inevitably subject to limitation.

Criminal liability could concern the entire medical team, whenever several healthcare professionals carry out a negligent crime together. Specifically, the art. 113 penal law (in conjunction with a specific culpable crime, for example *ex* artt. 589-590 *c.p.*) establishes that all responsibilities for offense are subject to the same penalty. Objectively, each participant must produce an effective

contribution to the causal realization of the offense. Subjectively, each co-participant must be aware of all elements in which it takes place, otherwise, there would be a competition of independent causes ex art. 41, paragraph III, penal law (for which everyone is responsible for the crime committed).

Art. 113 of the Italian penal code describes the dangerous possibility of a conscious meeting of negligent conduct (stemming from more than one person) which reinforces itself, rather than an accidental (and far more unlikely) convergence of negligent conduct. Medical practice and any examples of malpractice which can easily be identified by an average professional must be adequately checked (45). Though the medical establishment has been completely reformed, responsibilities are still divided, and healthcare managers have to make management and organisational decisions as well as allocate resources.

With regard to HAI it's up to the health manager to supervise the prevention and management of the risk (with other healthcare professionals), being able to configure a fault for organizational deficit, for example, in case of a deficient assignment of tasks and jobs to the personnel or of a lacking branch of the instructions to follow and of the tasks to be performed (46).

Moreover, ex art. 9 Law 24/2017 the healthcare facility that has paid compensation for damages (or the insurance company through subrogation) can act in revenge against the doctor, but only in cases where the same has acted with "intent or gross negligence" (as in the absence of a minimum standard of diligence or contemptuous neglect of one's duties), such as having forgotten a gauze in the abdominal cavity or not having applied post-operative antibiotic therapy (47).

If the health facility also happens to be public, corporate liability must also be considered, the jurisdiction of which is entrusted to the Court of Auditors.

Finally, it should be remembered that for healthcare professionals there may also be a disciplinary responsibility, since the code of medical ethics of 2014 establishes, *ex art.14*, that the doctor must guarantee the safety of the patient, preventing and managing, also and in particular by an inter-specialistic cooperation (art. 62 deont. code), any type of adverse event, including HAIs.

The probatory obstacles in litigation: the proof of causation and guilt

Whatever is the responsibility (individual, group of people, healthcare facility), regardless the nature of responsibility (civil, criminal, administrative, etc.), a problem arises on proof, guilty and causation. In case of civil liability (art. 1218 c.c.), it is up to the injured patient to prove the existence of the contractual relationship (even *de facto*), but not also the fault of the structure or the doctor (as the damage coincides with the non-performance) (48).

Instead, the fraud must be proven by the injured part for non-contractual liability (art. 2043 c.c.), together with proof of having suffered unfair damage that is derived from doctor's behaviour. In any case, probative shortcuts are not allowed: the proof of causality must not be confused with guilt. Both are based on the judgments of events probability / predictability / avoidability, but only the first moves on an exquisitely objective level, while the second presents mostly a subjective connotation. For example: a bacterium spreads in a healthcare facility, infecting and causing multiple patients to die. If heirs want compensation they will have to prove: a) existence of the contractual relationship against the healthcare facility and the doctor; b) causal link between the conduct of the facility and / or the doctor and the event of death (i.e. proving that the bacterium was transmitted through unhygienized tubes or cannulae, in

the absence of specific sanitation protocols). If all this is shown, the healthcare facility and / or doctor will not be considered liable only if they prove that all necessary sanitation protocols were adopted or otherwise if, they show that bacterium type, place and time of its diffusion can not be proved. Conversely, outside a contractual relationship, heirs will have to prove that they have suffered unfair damage from the death of the relative and the precise causal link between the damage resulting from the death and the conduct of the individual doctor.

In many cases the lethal event might be caused not only by the infection but also by previous pathological situations that lead the patient in a state of considerable physical degradation, debilitation and immunodeficiency.

To prosecute doctors for culpable homicide offenses ex art. 590 penal law will have to be evaluated, first of all, the typicality (concrete conduct must be provided by a rule, such as in culpable homicide) then causation and, finally, guilt.

It must be shown that, on the basis of universal scientific and statistical laws (logical probability), applied to the concrete case (rational credibility) (49), the omitted conduct, if implemented, would have prevented the specific death event (and not another one). Added to this is the assessment of the pre-existing and supervening causes, to understand if they were appropriate to cause the death event, exonerating the doctor from any responsibility.

Pursuant to Art.40 of the Italian penal code, this type of cause must be clearly linked to the event. Furthermore, it must also be shown that the event was exceptional and therefore unable to be controlled by the healthcare facility, which might, for example, not have suspected that there was any likelihood of an outbreak occurring. Obviously, this line of defence does not stand when protocol has not been correctly followed: in fundamental wards like intensive

care, a doctor should not carry on admitting patients in the event of an outbreak, but instead should choose to direct them to another facility (50). Vice versa, third-party liability would stand if the doctor's actions had in any way contributed to death; for example, if the doctor's intervention can be shown to have increased the patient's chances of survival, compensation would be correspondingly reduced.

Then there is the plan of guilt. It will be necessary to demonstrate (art. 590 sexies c.p.) that the doctor is in fault, in light of both the precautionary rule represented by the guidelines / good practices, and the injury / death event produced (not only predictable by the doctor but also avoidable if he had been careful). Furthermore, it's established that the criminal liability of the healthcare professional could be excluded in the hypothesis of undue conduct, when in any case he has respected the guidelines and the good practices accredited.

And if demonstrating this in the case of HAIs is not as easy, it is not impossible to achieve.

An example could be the sterilization of instruments: there are various types of sterilization and one issue is to choose a type of sterilization that is not adequate for specific surgical practice, because it isn't known or because one is not qualified; differently if the doctor knew the sterilization practices appropriate to the specific case, but due to negligence or carelessness, he opted for the one that at the time of the action appears to be faster and easier to implement.

A further obstacle arises: when is it possible to bring the notion of guidelines / good practices back to the notion of expertise?

It is still early to express an opinion, in the absence of practical applications, or sentences. Presumably, the legislator aims at the configuration of the particular type of fault c.d. procedural (51). What is feared, of course, is the suppression of the freedom of

the medical ars, with the sole aim of avoiding accusations of liability or compensation.

While protecting healthcare facilities and their workers, the patient should not be forgotten: compensation for damages

Compensation for damages as understood by art. 7 of Law. no. 24/2017 raises some concerns. The judge decides on a settlement for impairment on the basis of the insurance companies' rating system, (under Legislative Decree no. 209/2005) but has the power, "where necessary", to change the way in which damage is evaluated by examining ways in which the healthcare worker followed, or deviated from, guidelines/recommendations. This carries the risk of distorting the notion of compensation (which should not be seen as a punishment for the healthcare worker, but as a way to recompense the injured patient) (52).

And it does not end here, as this increases the elements which can be taken into consideration when trying to quantify compensation, meaning that the same injury can be evaluated under different conditions (53). The Joint Session of the Court of Cassation tried hard to avoid this in 2008 (54), when it ruled that only one award should be made for damages, and any further information be considered to be purely descriptive.

Conclusions

In conclusion, though attempts are being made to lighten the burden of liability both for the healthcare worker (to avoid defensive medicine) and the healthcare facility (to lessen public spending and the cost of insurance policies), the Gelli-Bianco Law has actually contributed to complicating

procedures. Issues concerning the liability of health workers are unclear, as this can be considered non-contractual in those cases which are not covered by contractual obligation (in a de facto capacity, too?) or when dealing with the criminal liability of the health worker which is regulated by the new provision, art. 590 sexies of the penal code, which allows for exemptions in specific cases.

To the healthcare worker this is a double-edged sword, as it is difficult to enforce and at worst could lead to an extremely rigid application of medical standards; on the other hand, if it were easier to enforce, it might undermine the patient's rights.

The patient is actually the main focus of so-called 'anonymous damages'. In order to take the focus away from the facility (since any reduction in spending would damage its activity and have a negative effect on the patient's right to health) and consider the liability of the healthcare worker as exceptional (in order to allow them to adequately perform their duties), the French solution could be taken as an example: a specific fund that guarantees standardised compensation is offered to anyone who has suffered damages. Nationals are free to donate to this fund, which operates on a no-fault basis (36).

The Gelli-Bianco Law also provides for a fund, but it must be financed by insurance companies and contains measures that are similar to those offered by the companies themselves, while payment for damages ultimately falls to the healthcare facility.

This reasoning should not be allowed to stand; rather, the community should be asked to shoulder the cost of compensation resulting from a healthcare associated infection. These cases can not be predicted or prevented by medical science, and it can be said that this is attributable to the increase of bad habits in modern society (the abuse of antibiotics and subsequent increase in antimicrobial resistance comes to mind).

Riassunto

Infezioni correlate all'assistenza: aspetti di negligenza e contenzioso

Introduzione. Le infezioni correlate all'assistenza (ICA) determinano un aumento significativo di morbosità, mortalità dei pazienti ricoverati in ospedale con un aumento dei costi. Inoltre causano un importante contenzioso medico legale.

Metodi. Specifiche combinazioni di parole chiave sono state analiticamente ricercate sui database di PubMed e Scopus. Le pubblicazioni che riguardavano il contenzioso medico legale sono state revisionate.

Risultati. Gli autori hanno sottolineato gli obblighi legali di operatori e strutture sanitarie nel quadro della legislazione italiana. Nel caso si verifichi un'infezione in ambito sanitario il paziente deve dimostrare la natura colposa nell'operato dei medici o delle strutture sanitarie e l'esistenza di un danno ed un legame causale. La difesa di medici ed ospedali è basata principalmente sulla dimostrazione dell'applicazione scrupolosa di protocolli e misure di prevenzione, applicando le conoscenze scientifiche aggiornate.

Conclusioni. Le ICA sono un fenomeno complesso che necessita di una strategia multidisciplinare e di un sistema di sorveglianza per controllarne le dimensioni. In questo modo è possibile aiutare i medici e le strutture sanitarie per ridurre le dimensioni del contenzioso legale.

References

1. Siracusa M, Grappasonni I, Petrelli F. The pharmaceutical care and the rejected constitutional reform: what might have been and what is. *Acta Biomed* 2017; **88**(3): 352-9. doi: 10.23750/abm.v88i3.6376.
2. Petrelli F, Contratti CM, Tanzi E, Grappasonni I. Vaccine hesitancy, a public health problem. *Ann Ig* 2018; **30**(2): 86-103. doi: 10.7416/ai.2018.2200.
3. Signorelli C, Odone A, Gozzini A, et al. The missed Constitutional Reform and its possible impact on the sustainability of the Italian National Health Service. *Acta Biomed* 2017; **88**(1): 91-4. doi: 10.23750/abm.v88i1.6408
4. Suetens C, Latour K, Kärki T, et al. Prevalence of healthcare-associated infections, estimated incidence and composite antimicrobial resistance index in acute care hospitals and long-term care facilities: results from two European point prevalence surveys, 2016 to 2017. *Euro Surveill* 2018; **23**(46): 1800516. doi: 10.2807/1560-7917.ES.2018.23.46.1800516.
5. Marani A, Napoli C, Berdini S, et al. Point prevalence survey on healthcare acquired infections in medical and surgical wards of a teaching hospital in Rome. *Ann Ig* 2016; **28**(4): 274-81. doi: 10.7416/ai.2016.2106.
6. Grappasonni I, Paci P, Mazzucchi F, De Longis S, Amenta F. Awareness of health risks at the workplace and of risks of contracting communicable diseases including those related to food hygiene, among seafarers. *Int Marit Health* 2012; **63**(1): 24-31.
7. World Health Organization (WHO). The burden of health care-associated infection worldwide. 2016. Available on: https://www.who.int/gpsc/country_work/burden_hcai/en/ [Last accessed: 2019, June 25].
8. Cassini A, Plachouras D, Eckmanns T, et al. Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modeling Study. *PLoS Med* 2016; **13**(10): e1002150. doi: 10.1371/journal.pmed.1002150.
9. Siracusa M, Petrelli F. Trade of food supplement: food or drug supplement? *Recenti Prog Med* 2016; **107**(9): 465-71. doi: 10.1701/2354.25224.
10. Grappasonni I, Petrelli F, Scuri S, Mahdi SS, Sibilio F, Amenta F. Knowledge and Attitudes on Food Hygiene among Food Services Staff on Board Ships. *Ann Ig* 2018; **30**(2): 162-72. doi: 10.7416/ai.2018.2207.
11. Grappasonni I, Marconi D, Mazzucchi F, Petrelli F, Scuri S, Amenta F. Survey on food hygiene knowledge on board ships. *Int Marit Health* 2013; **64**(3): 160-7.
12. D'Alessandro D, Fabiani M, Cerquetani F, Orsi GB. Trend of Legionella colonization in hospital water supply. *Ann Ig* 2015; **27**(2): 460-6. doi: 10.7416/ai.2015.2032.
13. Orsi GB, Villari P, Mondillo V et al. A plasma expander related *Pseudomonas aeruginosa* outbreak. *Scand J Infect Dis* 2006; **38**(11-12): 1085-88.
14. Petrelli F, Scuri S, Tanzi E, Nguyen C, Grappasonni I. Public health and burnout: a survey on lifestyle changes among workers in the healthcare sector. *Acta Biomed* 2018; **90**(1): 24-30. doi: 10.23750/abm.v90i1.7626.

15. Scuri S, Petrelli F, Tesauro M, Carrozzo F, Kracmarova L, Grappasonni I. Energy drink consumption: a survey in high school students and associated psychological effects. *J Prev Med Hyg* 2018; **59**(1): E75-E79. doi: 10.15167/2421-4248/jpmh2018.59.1.898.
16. Kračmarová L, Klusoňová H, Petrelli F, Grappasonni I. Tobacco, alcohol and illegal substances: experiences and attitudes among Italian university students. *Rev Assoc Med Bras* 2011; **57**(5): 523-8.
17. Spacilova L, Klusonova H, Petrelli F, Signorelli C, Visnovsky P, Grappasonni I. Substance use and knowledge among Italian high school students. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2009; **153**(2): 163-8.
18. Petrelli F, Grappasonni I, Peroni A, Kracmarova L, Scuri S. Survey about the potential effects of economic downturn on alcohol consumption, smoking and quality of life in a sample of Central Italy population. *Acta Biomed* 2018; **89**(1): 93-8. doi: 10.23750/abm.v89i1.7059.
19. Petrelli F, Scuri S, Tanzi E, Nguyễn TTC, Grappasonni I. Lifestyles and discomfort in a sample of young Romanian students. *J Prev Med Hyg* 2018; **59**(3): E230-E235. doi: 10.15167/2421-4248/jpmh2018.59.3.985.
20. Grappasonni I, Scuri S, Tanzi E, Kracmarova L, Petrelli F. The economic crisis and lifestyle changes: a survey on frequency of use of medications and of preventive and specialistic medical care, in the Marche Region (Italy). *Acta Biomed* 2018; **89**(1): 87-92. doi: 10.23750/abm.v89i1.7068.
21. Cioffi P, Laudadio L, Nuzzo A, Belfiglio M, Petrelli F, Grappasonni I. Gemcitabine-induced posterior reversible encephalopathy syndrome: a case report. *J Oncol Pharm Pract* 2012; **18**(2): 299-302. doi: 10.1177/1078155211424628.
22. Falcone M, Vena A, Mezzatesta M, et al. Role of empirical and targeted therapy in hospitalized patients with bloodstream infections caused by ESBL-producing *Enterobacteriaceae*. *Ann Ig* 2014; **26**(4): 293-304. doi: 10.7416/ai.2014.1989.
23. Conte MP, Venditti M, Chiarini F, et al. Extended spectrum beta lactamase producing *Klebsiella pneumoniae* outbreaks during a 3rd generation cephalosporin restriction policy. *J Chemother* 2005; **17**(1): 66-73.
24. Orsi GB, Franchi C, Giordano A, et al. Multi-drug resistant *Acinetobacter baumannii* in an Intensive Care Unit. *J Chemother* 2008; **20**: 219-224.
25. Cioffi P, Marotta V, Fanizza C, et al. Effectiveness and response predictive factors of erlotinib in a non-small cell lung cancer unselected European population previously treated: a retrospective, observational, multicentric study. *J Oncol Pharm Pract* 2013; **19**(3): 246-53. doi: 10.1177/1078155212465994.
26. Orsi GB, Franchi C, Marrone R, Giordano A, Rocco M, Venditti M. Laboratory confirmed bloodstream infection aetiology in an intensive care unit: eight years study. *Ann Ig* 2012; **24**: 269-78.
27. Orsi GB, Giuliano S, Franchi C, et al. Changed epidemiology of ICU acquired bloodstream infections over 12 years in an Italian teaching hospital. *Minerva Anestesiol* 2015; **81**(9): 980-8.
28. Nguyen CTT, Scuri S, Nguyen BT, Petrelli F, Grappasonni I. Levels of understanding of the rules of correct medical usage among Vietnamese pharmacy students: a cross-sectional study. *J Prev Med Hyg* 2018; **59**(4): E261-E266. doi: 10.15167/2421-4248/jpmh2018.59.4.925.
29. Grappasonni I, Petrelli F, Klusoňová H, Kračmarová L. Level of understanding of medical terms among Italian students. *Ceska Slov Farm Winter* 2016; **65**(6): 216-20.
30. Scuri S, Petrelli F, Tanzi E, Thi Thu CN, Grappasonni I. European university students of pharmacy: survey on the use of pharmaceutical drugs. *Acta Biomed* 2019; **90**(1): 83-91. doi: 10.23750/abm.v90i1.7572.
31. Messineo A, Marsella LT. Biological hazards and healthcare-associated infections in Italian healthcare facilities: some considerations on inspections and accountability. *Ann Ig* 2015; **27**(6): 799-807. doi: 10.7416/ai.2015.2073.
32. Traina F. Medical malpractice, the experience in Italy. *Clin Orthop Relat Res* 2009; **467**: 434-42. doi: 10.1007/s11999-008-0582-z
33. Pacella F, Collini S, Angelucci F, et al. Infections in hospital departments. What is hospital responsibility? *Clin Ter* 2017; **168**(4): e266-70. doi: 10.7417/T.2017.2018.
34. Epicentro. Infezioni correlate all'assistenza. Available on: <http://www.epicentro.iss.it/infezioni-correlate/> [Last accessed: 2019, June 25].
35. <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002150> [Last accessed: 2019, June 25].

36. Scarchillo G. La responsabilità medica: risarcimento o indennizzo? Riflessioni, evoluzioni e prospettive di diritto comparato. *Responsabilità Civile e Previdenza* 2017; **82**(5): 1490-520.
37. Moro ML, Nascetti S. Infezioni correlate all'assistenza sanitaria, il Progetto INF-OSS. *GIIO* 2006; **13**(4): 88-93.
38. Donelli FM, Gabbrielli M, eds. *Responsabilità medica nelle infezioni ospedaliere. Profili giuridici e medico-legali*. 2.ed. Maggioli, 2018: 94 ss.
39. Siracusa M, Grappasonni I, Petrelli F. The criminal liability of the hospital pharmacist vs the liability of the hospital. *Recenti Prog Med* 2016; **107**(1): 19-24. doi: 10.1701/2132.23100.
40. <https://www.penalecontemporaneo.it/upload/1351253564de%20simone%20definitivo.pdf> [Last accessed: 2019, June 25].
41. https://www.penalecontemporaneo.it/pdf-viewer/?file=%2fpdf-fascicoli%2fdpc_3_2018.pdf#page=246 [Last accessed: 2019, June 25].
42. Cass. Pen., 07/10/2014, n. 46336. *Guid. Dir.* 2014, 48, 45 (s.m).
43. Faccioli M. L'incidenza delle carenze strutturali e organizzative dell'ente sanitario sui doveri e sulle responsabilità individuali del medico. *Resp. Civ. e previd.* 2016; 6: 1851b ss.
44. Ronchi M. La responsabilità civile della struttura e del medico per le infezioni nosocomiali. *Resp. Civ. E previd.* 2007; 1527 ss.
45. Cass. Pen., 19/07/2018, n. 39733, in *Guid. Dir.*, 2018, 40, 79 e Cass. Civ., 29/01/2018, n. 2060, in *Rass. Dir. Farmaceutico*, 2018, 3, 552.
46. Cass. Pen., 15/11/2018, n. 53453, in *CedCass. Pen.* 2019. e Cass. Civ. sez. III 22 ottobre 2014 n. 22338. Available on: <http://www.appaltiesanita.it/wp-content/uploads/2014/12/cass-civ-sentenza-22-ottobre-2014-n.-22338.pdf> [Last accessed: 2019, June 25].
47. Donelli FM, Gabbrielli M, eds. *Responsabilità medica nelle infezioni ospedaliere. Profili giuridici e medico-legali*; cit. 150 ss.
48. Cass. Civ. sez. III, 19/07/2018, n. 19204, rep. biblioteca digitale www.dejure.it.
49. Cass. Sez. Un., 10/7/2002, Franzese, CED 222138, FI 2002 II, 620.
50. Cassazione penale sez. IV, - 03/05/2016, n. 25689, rep. banche dati on-line www.dejure.it.
51. Di Landro A. *Dalle linee guida ai protocolli all'individualizzazione della colpa nel settore sanitario. Misura oggettiva e soggettiva della "malpractice"*. Torino: Giappichelli, 2012.
52. Chinè G, Fratini M, Zoppini A. *Manuale di diritto civile. Nel diritto Ed*, 2018: 2064.
53. Donelli FM, Gabbrielli M, eds. *Responsabilità medica nelle infezioni ospedaliere. Profili giuridici e medico-legali*; cit. 108.
54. Cass., Sez. Un., 11 novembre 2008, n. 26972. *Resp. civ. prev.*; 2009:38 ss.

Corresponding author: Iolanda Grappasonni, School of Medicinal and Health Products Sciences, University of Camerino, Via Madonna delle Carceri 9, 62032 Camerino (MC) Italy
 e-mail: iolanda.grappasonni@unicam.it