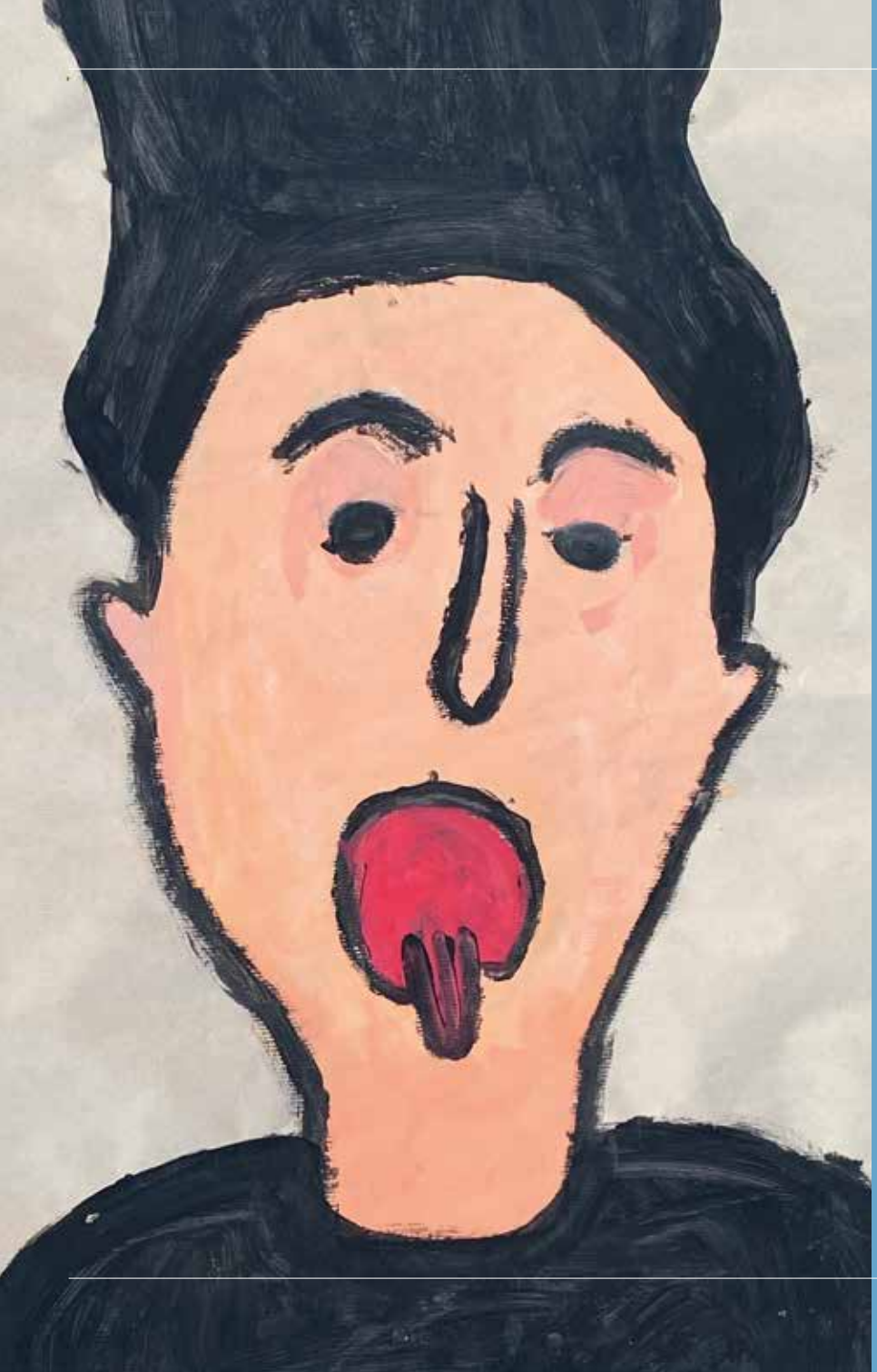

Patient profile and cost of acute poisonings

A comparative study of emergency department admissions versus poison centre consultations

ANNE-MARIE DESCAMPS

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Patient profile and cost of acute poisonings

A comparative study of emergency department admissions versus poison centre consultations.

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Thesis submitted to fulfill the requirements for the degree of "Doctor in Health Sciences" (Ghent University) and "Doctor in Biomedical Sciences" (Hasselt University)

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UNIVERSITEIT GENT

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Faculty of Medicine and Health Sciences

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HASSELT UNIVERSITY
Faculty of Medicine and Life Sciences

“Do what you love
Love what you do”

Opgedragen aan Toon, *dimidium animae meae*

Tijdens mijn doctoraatstraject heb ik kunnen rekenen op een stevig triumviraat: professor Vandijck, professor Buylaert en professor De Paepe, alias Dominique, Walter en Peter. Zoals het in een goed driemanschap past, nam elk lid een specifieke rol op zich. Dominique haalde me over de streep om dit doctoraatstraject aan te vatten en liet me mijn eigen ding doen. Hij schonk me een erg geapprecieerd vertrouwen om deze missie tot een goed einde te brengen en me op te tillen tot een hoger niveau. Walter was voor mij de leermeester waar je enkel kunt van dromen. Hij leerde me de kneepjes van het vak en deed me nog meer puntjes op de i plaatsen dan ik ooit had gedacht, zonder zijn eigen ideeën hierbij op te dringen. Peter zorgde op een bedachtzame en wijze manier voor de kritische reflectie en rake opmerkingen. Op elk moment kon ik op hem rekenen.

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Anne-Marie Descamps

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Chapter 1

General introduction

Abbreviations

AAPC: American Association of Poison Control Centers
BFM: Budget of Financial Resources (Budget Financiële Middelen)
BPC: Belgian Poison Centre
DALY: Disability Adjusted Life Year
ED: Emergency Department
ED-amb: Emergency Department-ambulatory care
ED-24h: Emergency Department-24-hours-observation unit
GDP: Gross Domestic Product
GUH: Ghent University Hospital
ICD-10: International Classification of Diseases, version 10
IFIC: Instituut voor FunctIeClassificatie
Hosp: Hospitalization unit
Hosp-watchful-wait: patients advised by the poison centre to go to the Hospital if symptoms appear or their condition worsens
Hosp-referral: patients advised by the poison centre to go to the Hospital
Hosp-urgent-referral: patients advised by the poison centre to go urgently to the Hospital
ICU: Intensive Care Unit
NPDS: National Poison Data System
NPIS: National Poisons Information Service
NVIC: National Poisons Information Centre
OECD: Organisation for Economic Co-operation and Development
PPP: Purchasing Power Parity
RIZIV: National Health and Disability Insurance Service
WHO: World Health Organisation

Poisoning : a significant global public health problem

Poisoning poses a significant global public health problem with medical, social and financial implications.

It is associated with high morbidity and mortality [1-4]. According to World Health Organisation (WHO) data, in 2012 an estimated 193,460 people died worldwide from unintentional poisoning. In the same year, unintentional poisoning caused the loss of over 10.7 million years of healthy life (disability adjusted life years, DALYs). The mortality rate attributed to unintentional poisoning in 2016 was 1.4 per 100,000 around the world and 0.2 in Belgium [5].

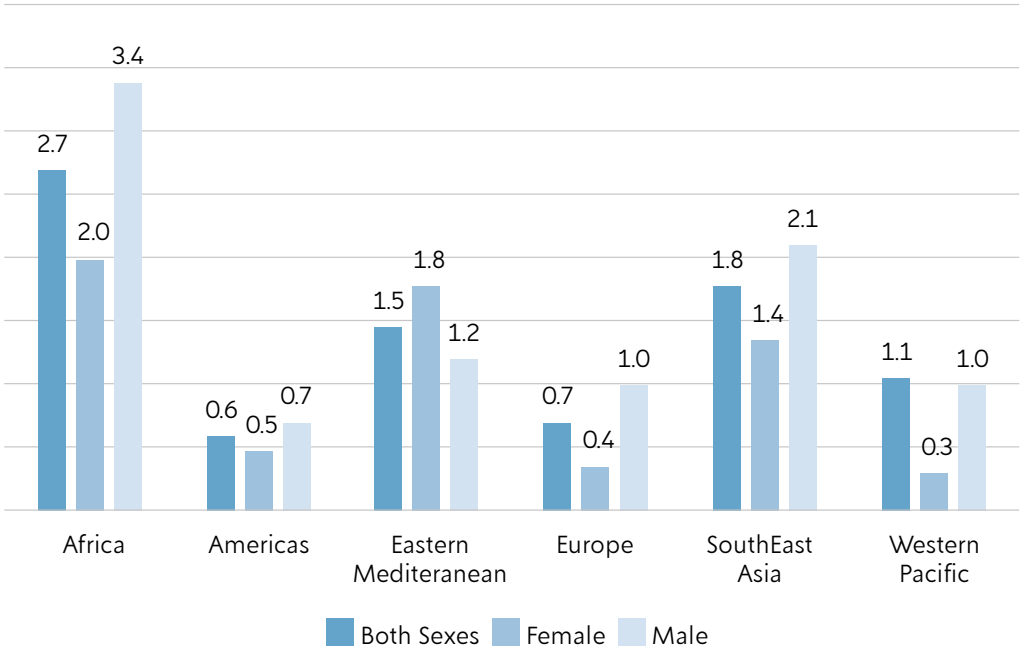

Figure 1 | Mortality rate attributed to unintentional poisoning per 100,000 population, 2016. Source : WHO

Definition of poisoning

Poisoning occurs « when people drink, eat, breathe, inject, or touch enough of a hazardous substance (poison) to cause illness or death.

Some poisons can cause illness or injury in very small amounts. Illness may occur very quickly after exposure to a poison, or it may develop over several years with long-term exposure » [6].

We distinguish between different types of intentionality: (1) accidental (unintentional) poisoning, (2) use of substances of abuse, (3) intentional self-harm or (4) undetermined intentionality of poisoning.

Poisoning is considered as accidental in case of "external causes of poisoning and accidents (e.g. taking the wrong medication) with the agent taken for neither self-harm nor intoxication purposes" [4]. Use of substances of abuse are defined as "recreational use of substances of abuse ». Intentional self-harm is defined as "purposely self-inflicted poisoning", as categorized in ICD-10, X60-X69 [7]. When the underlying reason is unclear, poisonings are categorized as undetermined poisoning.

Medical healthcare services in case of acute poisoning

Apart from doing nothing, calling ambulance services or going to the doctor, a large number of patients with suspected acute poisoning call a poison centre or go to the emergency department of a hospital.

In Norway, Oslo, poisonings related to drug abuse, especially heroin overdoses, are frequently discharged from the ambulance service and outpatient clinic without admission to the hospital. The majority of poisoned patients are treated at the Oslo Accident and Emergency Outpatient Clinic, a pre-hospital outpatient emergency clinic with limited diagnostic and treatment resources [8,9].

A considerable part of poisonings remain undetected and registered poisonings are generally regarded as the tip of an iceberg. Two-three times higher figures in everyday life are expected [10]. Some patients do even not realize they have a poisoning issue. Other patients are aware of the problem, but do not take any action to contact healthcare services. Some other patients go to their doctor or physician who may diagnose the poisoning and register it in the individual file of the patient. Patients who call a poison centre or go to the hospital with a suspected poisoning are at least registered in the statistics of the poison centre and the electronic patient files of the patient, respectively. At best, they are also registered in the national statistics of a country.

In this dissertation, we focus on two groups of patients with acute poisoning: those who call the poison centre and those who go to the hospital.

In what follows, we give a brief overview of the role of poison centres in the US and Europe, and of emergency department admissions in hospitals in case of suspected poisoning. Then, we give a global insight into the financing of healthcare systems in the Organisation for Economic Co-operation and Development (OECD) countries and into the financing of the Belgian healthcare system. Next, we focus on the financing of the Belgian hospitals and the Belgian Poison Centre (BPC), and we address the problems and challenges which hospitals and the BPC are confronted with.

To conclude the introduction, we discuss the existing evidence and the aims and main research questions of this dissertation.

Role of poison centres and hospitals in case of suspected poisoning

Poison centre

One of the most important missions of a poison centre is to guide patients confronted with (suspected) poisoning to the most appropriate level of medical care. Poison centres assess whether a particular exposure is hazardous, and give information on the need for treatment and the type of treatment that should be given. They promote the evidence-based, cost-effective management of poisoning and ensure that unnecessary or ineffective treatment is avoided.
In 2019, only 47% of WHO Member States have a poison centre. They can be found in most industrialized countries. In other parts of the world, poison centre services are less available. This is particularly true in Africa and in parts of the Eastern Mediterranean and Western Pacific regions [5].

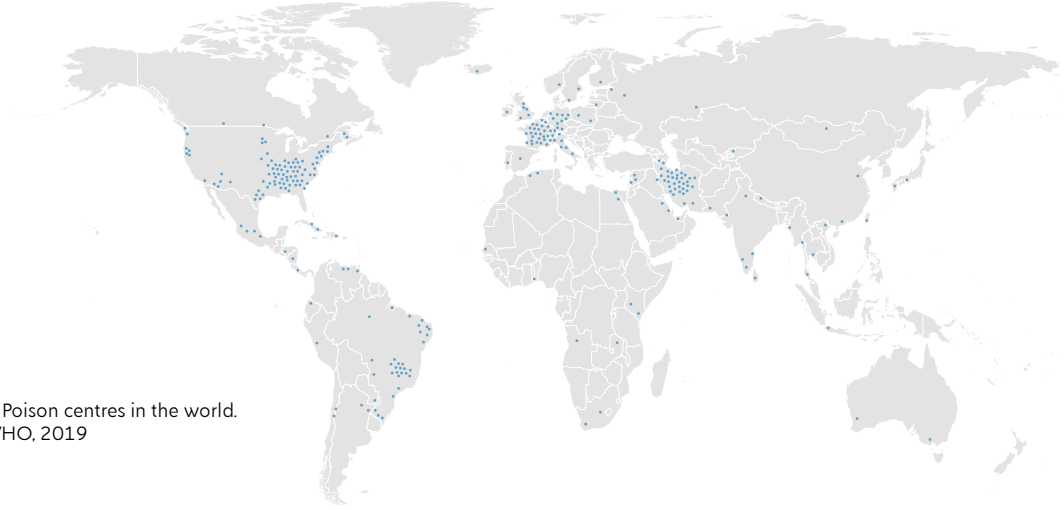

Figure 2 | Poison centres in the world.
Source : WHO, 2019

United States

In the United States, the American Association of Poison Control Centers (AAPCC) manages a 24-hour hotline (1-800-222-1222), which is continuously staffed by pharmacists, physicians, nurses, and poison information specialists who have received dedicated training in the field of toxicology. Calls to the number are automatically routed to the poison control centre that covers the territory from which the call is placed [20].

An online tool using algorithms to make the right recommendation is also available: https://triage.webpoisoncontrol.org/#/recommendation [21]. The app gives a warning to call 911 immediately if the individual collapses, has a seizure, has trouble breathing or cannot be awakened. It remains advisable to consult the poison centre if a larger number of substances is involved.

The AAPCC has a National Poison Data System (NPDS), which is a near real-time exposure management and information database and surveillance system for the nation's 55 poison control centers. Each poison control center submits de-identified case data to NPDS after providing necessary poison exposure management and information services to callers. NPDS provides a nationwide infrastructure for surveillance for all types of exposures (e.g. foreign body, infectious, venomous, chemical agent, or commercial product) and identifies and tracks significant public health events [22].

Europe

In *the Netherlands*, the National Poisons Information Centre (NVIC) of the University Medical Center Utrecht provides a 24/7 hotline service (030-2748888), staffed by poison information specialists . It is open to medical professionals only. Since 2011 the NVIC also provides a web-based exposure analysis and poison information system that enables medical professionals to quickly and efficiently assess the potential risks of (mixed) exposures, as well as their clinical signs and symptoms, and possible therapeutic interventions [23]. In *France*, 9 "Centres Antipoison et de Toxicovigilance"» provide telephone assistance in case of suspected poisonings to health professionals and the public in the diagnosis, management and treatment of poisonings. They are involved in toxicovigilance [24]. In *Germany*, there are 8 poison centres, 24/7 open for calls from the public and professionals. According to the German Chemicals Act the poison centres are run or substantially supported by the 16 federal states [25]. In *the United Kingdom*, the National Poisons Information Service (NPIS) provides toxicological information to health professionals to ensure patients receive appropriate treatment. They do not take calls from the general public, who are advised to contact the non-emergency 111 number for specific information on poisons, or 999 in an emergency [26].

In *Norway*, the Norwegian Poison Information Centre (22 59 13 00) serves the whole country, and takes enquiries from health care professionals, as well as the public [27].

In *Finland*, the Poison Information Centre (358 9 4711) serves the whole of Finland by telephone and provides guidance to the public and to healthcare professionals [28].

In *Belgium*, the Belgian Poison Centre (BPC) is open to the public and medical professionals and is 24/7 accessible by phone (070 245 245) for urgent cases and by mail and website for non-urgent cases. The BPC covers the country of Belgium and the Grand Duchy of Luxembourg as a single center and answers 60,000 calls per year. A poison information specialist (doctor or pharmacist) helps people with a poisoning issue to the appropriate care level and place. According to the risk assessment made, the advice given by the BPC is either (1) to stay at home and/or to follow the advice on first aid, (2) to consult a doctor, (3) to go to the hospital if symptoms appear or their condition worsens (Hosp-watchful-wait), (4) to go to the hospital (Hosp-referral), or (6) to go urgently to the hospital (Hosp-urgent-referral).

Hospital

Acute poisonings contribute to an important number of poisoning-related admissions to the emergency services worldwide [29, 30]. They represent a considerable workload in the hospitals and an important challenge for the management of the healthcare sector. Due to the lack of admission guidelines, hospital admission rates are high and vary considerably between hospitals [31]. In the Netherlands around 11,000 patients with an intentional poisoning are seen each year in accident and emergency departments [32].

In *the United Kingdom*, acute poisoning contributed to 15-20% of the workload in medical departments in 1999 [33] and self-poisoning accounted for 10% of the workload in the emergency department [34, 2]. In *Finland*, the annual incidence of hospitalized poisonings over 2 years (1987-1988) was 11.7 for a population of 10,000 [35].

In *Belgium*, patients who decide to go to the hospital are first assessed in the emergency department (ED) of the hospital, which is followed by (1) discharge home (ED-amb), (2) observation in the 24-hours-observation unit of the ED (ED-24h), (3) hospitalization (Hosp), or (4) admission to the intensive care unit (ICU).

In this dissertation, the cases of three hospitals of different size and region are analyzed: a university hospital, a regional hospital and two admission sites of a general hospital.

The university hospital is a tertiary care referral center in Belgium with more than 1,000 beds and about 35,000 ED admissions per year. The regional hospital has about 300 beds and 20,000 ED admissions per year. The general hospital is one of the large(st) non-university hospitals in Belgium with about 1,600 beds and 45,000 ED admissions. It has two ED's located in different cities.

Financing of the healthcare system in belgium and other oecd countries

In this chapter, we focus on the financing of the Organisation for Economic Co-operation and Development (OECD) countries and the Belgian healthcare system.

One of the main sources of information for this chapter is the report *Health at a Glance 2017* of the OECD [28]. *Health at a Glance 2017* compares key indicators for health and health system performance across the 35 OECD countries.

Financing of healthcare

In *OECD countries*, healthcare goods and services are paid by a mix of different sources i.e. (1) the government, (2) compulsory health insurance, usually financed by social contributions payable by employees and employers, (3) out-of-pocket payments by the patient, and/or (4) a voluntary private health insurance. In most OECD countries (not in the United States), the main sources of healthcare financing are the government and the compulsory health insurance.

In Belgium 18% of health expenditure is financed by government, 59% by the compulsory health insurance, 18% by out-of-pocket payments, and 5% by voluntary private health insurance. Belgian citizens have a compulsory insurance against disease and invalidity and must subscribe to one of seven health insurance funds.

These health insurance funds are among other things responsible for the payment of a substantial part of hospitalization costs, charged by the hospital to the government and the patient. The residual fraction of the cost has to be paid via a fee from the patient (out-of-pocket contribution, cost-sharing system) or in some cases by a supplementary private but non-obligatory insurance. The personal fee charged to the patient is determined by an agreement negotiated in a committee of the National Health and Disability Insurance Service (RIZIV) with representation of employers, employees, health insurance funds and representatives of care providers. The Minister of Public Health determines the cost and reimbursement rates for a list of medical acts on the basis of a proposal from the committee.

The degree of cost-sharing applied to healthcare services also affects access to care as out-of-pocket expenditures can create financial barriers to healthcare. In Belgium, the share of out-of-pocket expenditure is estimated at 3.2% of final household consumption

Health expenditure per capita and in relation to the Gross Domestic Product

The average health expenditure per capita in *OECD countries* in 2016 was $4,003, and $4,840 in Belgium. The United States outspend all other OECD countries by a wide margin, spending the equivalent of $9,892 for each resident, which is almost two-and-a-half-times the average of the 35 OECD countries and 25% above

Switzerland, the next highest spender (adjusted for the different Purchasing Power Parities (PPP)).

The health expenditure as a share of the Gross Domestic Product (GDP) was 10.4% in *Belgium*. Health spending was 9,0% of GDP on average in the OECD, ranging from 4.3% in Turkey to 17.2% in the United States.

Health expenditure by type of service

In *Belgium*, inpatient care amounts to 30% of health expenditure, outpatient care 24%, long-term-care 24%, medical goods (mainly pharmaceuticals) 16% and collective services (a.o. prevention, public health services) 5%, versus an average of 28%, 33%, 14%, 19% and 6% for the 35 OECD countries, respectively.

While the organization of healthcare services varies considerably across OECD countries, hospitals are the main healthcare provider in terms of health spending: they account for nearly 40% of overall health spending on average and represent the main spending category.

Financing of the Belgian hospitals

In Belgium, there are four sources of funding for the hospitals: the federal government, the health insurance funds, the out-of-pocket contribution by the patient, and the regional states. There are also different types of funding, e.g. funding of the infrastructure and the operational costs.

Financing of the infrastructure of the hospital

The financing of the hospital infrastructure is mainly covered by subventions from the federal government, and the regional states.

Financing of the operational costs of the hospital

The operational costs of the hospital are covered for approximately 36.5% within a closed federal budget, called 'Budget of Financial Resources' (Budget Financiële Middelen, BFM). Fees contribute for 40.9% (part of the physicians fees is withheld by the hospital for among other things the use of the hospital's infrastructure), revenues from rebates on pharmaceutical products for 17.2%, and lump sums and supplements (e.g. for the use of single rooms, cost charged to the patient and/or his private insurance) for 5.4%.

Hospitalization cost charged by the hospital to the government and the patient

The hospitalization cost is paid partly via an advance payment from the BFM-budget and partly via the invoice. This cost is composed of four parts: (1) costs for accommodation and nursing (not applicable for ambulatory patients who could leave the emergency department after care, (2) pharmaceuticals, (3)

physicians' fees, and (4) other items (for extra utilities, e.g. bottle of water).

The *cost for accommodation and nursing* comprises a fixed and a variable part and includes the cost for nursing staff, administration, maintenance, laundry, legal obligations with regard to the quality and safety of care, investment in medical equipment, the operational cost of the hospital pharmacy, and lump sums per day for clinical biology and pharmaceuticals. The fixed part is covered by the government via an advance payment from the BFM-budget. The variable part depends on the number of hospitalization days and is charged by the hospital via the invoice to two parties: a major contribution is charged to the government and paid via one of the health insurance funds, a smaller part being charged to and paid by the individual patient (personal fee).

For *pharmaceuticals and physician's fees*, a flat rate amount per admission to the hospital plus an amount that varies from patient to patient is charged to the government via the invoice and paid by one of the health insurance funds. The individual patient pays also a personal contribution via the invoice for pharmaceuticals and physician's fees and some small other costs for extra utilities to the hospital. The physicians' fees contain the lump sums per admission for clinical biology, medical imaging and medical 24 hour cover, together with the fees of the individual physicians involved in the patient care.

The fees in the Belgian system are fees for service based and are independent of physician status (consultant versus specialist-in-training). There is a national standard list of agreed tariffs, which are largely reimbursed by the social security system. Whether it is allowed to charge these costs depends on the physician discipline, not on the physician status.

Financing of the Belgian Poison Centre

The BPC is a royal foundation of public utility (Royal Decree of 10/03/1967). The BPC has been qualified as an emergency service in the Royal Decree of 9 October 2002. Each financial year, the minister of public health determines the amount of the subsidy granted to the BPC in the context of emergency medical assistance. The subsidy is paid by the National Lottery: a royal decree determines the distribution of the subsidies of the National Lottery for the financial year, including the part allocated to the BPC.

Other sources of income are sponsorships and research projects. A call to the BPC is free of charges for the caller.

Rationale for undertaking the research: problems and challenges

Hospitals under financial pressure

Belfius, a Belgian bank-assurer, provides each year an analysis of the financial situation of general hospitals, called MAHA study. For the financial year 2017, all Belgian general hospitals (private and public) participated in the study. This analysis gives a picture of the financial evolution that the sector has undergone in recent years.

The conclusion of the study is as follows: "In the coming years, the hospital sector will continue to face major challenges, with consequences both for its operation and for its organization and financing. In addition to social developments (ageing, digitalization of the economy, changes in medical techniques, etc.), the hospital sector will have to successfully face up to the implementation of reforms introduced by both the federal (creation of networks, system of financing by cluster, classification of functions in the healthcare sector with a corresponding wage model (IFIC), etc.) and the regional authorities (financing of infrastructure), and all this within a tight budgetary framework. The increasing financial vulnerability of the sector raises questions about its ability to meet these challenges successfully, at least in a number of institutions. »

Emergency Departments of hospitals under pressure

EDs ensure efficient and high-quality response for patients with urgent needs. These facilities are worldwide under high pressure because of increasing number of patients. In 21 OECD countries, the number of ED visits increased by nearly 5,2%: from 29.3 visits per 100 inhabitants in 2001 to 30.8 visits per 100 inhabitants in 2011 [37]. The same evolution can be noticed in Belgium where the number of ED contacts increased by nearly 3.6% between 2009 and 2012: from 28 visits per 100 inhabitants to 29 visits per 100 inhabitants in 2012, especially due to the increase of ambulatory care visits [38].

The Belgian Poison Centre under pressure

The BPC is a service organization where personnel costs account for more than 80% of the costs. Since 2014, the subvention by the government (and paid by the National Lottery) has not been increased and has not even been indexed. As a result, the investment margin is decreasing year after year. However, investments in informatics, especially in the context of an increasing influence of Europe and European rules, are more critical than ever. The number of calls is also rising year after year (54,206 calls in 2014 and 60,616 in 2019) and has to be taken by a declining workforce.

The issue of cost-effectiveness

In addition to this problem of high and even augmenting pressure on EDs, hospitals and the BPC, cost-effectiveness has always been an important issue in care management. Governments try to create care systems that combine quality, affordability and accessibility of care in an effective but cost-efficient way. This focus on cost-effectiveness implicates that alternative healthcare systems are receiving increased attention to obtain more health benefit at reduced costs. The access to and organization of primary care services, especially in urgent situations, is an important topic in this respect.

Existing evidence

In this chapter, we focus on the existing evidence in literature. It is possible that parts of this text show some overlap with the introductions of the peer reviewed articles 1, 2 and 3.

Hospital

Characteristics of acute poisonings

Studies on the characteristics of acute poisonings have been conducted in a number of countries. Some of them focused on cases in EDs [10,32,39-47], while others on cases in hospitals [4,35,48-50]. They give an idea of the demographic characteristics of the patients, the time of admission, the substances involved, the therapeutic measures taken and the outcome of the patients. With regard to cost studies, some include only ED-costs [51-53], while others also hospitalization costs [55] or ICU costs [56,57]. Other studies are limited to the financial burden of poisoning by drugs, medicaments and biological substances [58], illicit drugs [59], opioids [60], alcohol and drug overdoses [61] or self-poisoning cases [62-64].

In Belgium, studies of acute poisonings are scarce and limited to the analysis of cases treated in the ED [65] or focus on alcohol intoxications [52] or deliberate self-poisonings [53].

Costs of acute poisonings

Cost studies have been conducted in a number of countries regarding acute poisoning. To make international comparison easier, we expressed all costs in international dollars 2017. In Spain, Muñoz et al. [51] calculated a total cost of $2,716,034 for 3,195 patients (period of 30 months). They analyzed the healthcare costs for the Spanish National Health System for inpatients and outpatients using the corresponding hospital discharge reports. In the United States, Krajewski et al. [55] estimated a cost of $8.9 billion for 425,491 patients based on the charges imposed by Illinois hospitals among outpatients and inpatients. In Japan, Okumara et al. [58] estimated a cost of $67.2 million for 37,200 patients using total hospital charges based on a standardized fee-for-service payment system. In the United Kingdom, Tsiachristas et al. [66] investigated the association between hospital costs and methods of self-harm. They found that costs were mainly associated with the type of healthcare service contact, and estimated an overall annual cost of general hospital management of self-harm of $222.3 million per year. In Australia, Mathers et al. estimated a total expenditure of $3.2 billion for injury and poisoning [67].

Other studies limited the analysis either to (1) Emergency Department (ED) visits [54], (2) cases of self-poisoning [57,62-64,67], (3) poisonings with specific agents [59-61,69] or studied only (4) intensive care units [56,57,70-72] or (5) costs on changes in management guidelines (e.g. paracetamol poisoning) [73].

In Belgium, only a few studies attempted to analyze the cost for poisoned patients. Verelst [52] assessed the cost of ED visits due to alcohol intoxication in patients 16 years or older using billing data, while Hendrix [53] focused on the pattern and cost restricted to deliberate self-poisoning and its impact on the ED using invoices. Senterre et al. [74] analyzed a.o. the epidemiology and cost of self-injuries, of which 91% were poisonings by medicinal and non-medicinal substances.

Poison centres

Financial impact of a poison centre

The financial impact of PCCs has been demonstrated in many studies dealing with the financial impact of PCCs. A number of these studies investigated how many people with poisonings calling the PCC without need for further medical treatment would have used the Emergency Healthcare System in the absence of a PCC and what effect this would have had on the healthcare costs [15-19,75-76]. Some studies focused on the reduction of the length of stay with assistance of a PCC [11,12]. Other studies mentioned a reduction of unnecessary visits to emergency departments (ED) and associated hospital charges, and improved patient management [11,13-14,77].

In the USA, cost-benefit-ratios ranged from 1.4 to 36.0 in the presence versus absence of a PCC in poisoning cases not needing further medical treatment after PCC consultation [15-18, 74,75]. The Lewin Group [78] calculated a return on investment running up to 13.39US$/case with 41.3% due to avoided medical utilization, 24.2% to reduced length of hospital stay, 1.3% to education and community outreach and 33.1% due to reduced work-loss days.

In Europe, Anell [79] (Sweden) calculated a cost-benefit-ratio of 1.05, while Toverud [80] (Norway) concluded that the PCC did not save money (cost-benefit-ratio 0.76) but provided safety.

Acute poisonings in poison centres versus in hospitals

The interaction between poison centres and hospitals in acute poisoning cases is documented in the literature. Some studies mentioned a reduction of unnecessary visits to emergency departments and associated hospital charges, and improved patient management [11-14]. Other studies focused on the reduction of the length of stay with assistance of a poison centre [11,12]. A number of studies investigated how many people with poisonings who called the poison centre without need for further medical treatment would have used the Emergency Healthcare System in the absence of a poison centre, and what effect this would have on the healthcare costs [15-19].

As far as we know, there are no studies focusing on the degree of similarity between 1) the group of patients who called the poison centre and was advised to go to a hospital, and 2) the group of patients admitted to the ED of a hospital.

Aims of the thesis and main research questions

In the present dissertation we want to gain more insight into the profile and cost of patients with acute poisoning for whom the Belgian Poison Centre (BPC) is called upon and/or who present to the ED. The ultimate question is to what extent both services offer a complementary service and serve a different population. In case of an overlap between the two services, an optimized referral strategy may result in an equally high-quality service at a lower cost.

The outline of the dissertation will start with a general introduction **(Chapter 1)** and end with the general discussion in **Chapter 7. Chapters 2, 3, 4, 5 and 6** are written as separate articles and can be read independently. Inevitably, the content of the chapters may show some overlap.

Chapter 2 and Chapter 3 focus on patients admitted to the Emergency Department of a hospital with acute poisoning. The following research questions will be addressed:

RQ1. What are the characteristics of patients admitted with acute poisoning to the emergency department of Ghent University Hospital (GUH)? What are the factors associated with the hospitalization type? What are the general costs charged to the government and the patient? (article 1)

RQ2. What are the more detailed costs and cost components charged to the government and the patients in case of acute poisoning for all types of hospitalization? What are the factors associated with the cost? Are the costs charged by GUH in line with the costs as available in national data? (article 2)

Chapter 4 and 5 focus on the patients who called the Belgian Poison Centre with (suspected) acute poisoning. The following research questions will be addressed:
RQ3. What is the cost-benefit of the BPC? (article 3)

RQ4. What are the characteristics and associated factors of patients with acute poisoning who were advised by the Belgian Poison Centre (BPC) to go to the hospital? Can we assess the compliance and potential health-economic impact of referral advice? (article 4)

Chapter 6 focuses on the Belgian Poison Centre and three hospitals. The following research question will be addressed:
RQ5. Can we find similarities and differences in characteristics, involved agents and costs between patients who called the BPC and were referred to a hospital, and patients who were admitted to the ED of a hospital? (article 5)

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Chapter 2 Article 1

Characteristics and costs in adults with acute poisoning admitted to the emergency department of a university hospital in Belgium

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Abbreviations

ED: Emergency Department
ED-amb: Emergency Department- ambulatory care
ED-24h: Emergency Department-24-hours-observation unit
Hosp: Hospitalization unit
EPD: Electronic Patient File
ICD-10: International Classification of Diseases, version 10
ICU: Intensive Care Unit
EPD: Electronic Patient File
FPS Health: Federal Public Service Health
GCS: Glasgow Coma Score
GUH: Ghent University Hospital
GUHED: Ghent University Hospital Emergency Department
IQR: InterQuartile Range
MZG: Minimal hospital data (Minimale Ziekenhuis Gegevens)
MICU: Mobile Intensive Care Unit
NICE: National Institute for Health and Care Excellence
NSAIDs: Non-Steroidal Anti-Inflammatory Drugs
OECD: Organisation for Economic Cooperation and Development
RIZIV: National Health and Disability Insurance Service (Rijksdienst voor Ziekte- en Invaliditeitsverzekering)
SD: Standard Deviation
STROBE: Strengthening the Reporting of Observational Studies in Epidemiology Statement
UREG: Official Emergency Registration System at Emergency Departments (Urgentie REGistratiesysteem).

Introduction

Poisoning poses a significant global public health problem. According to WHO data, in 2012 an estimated 193,460 people die worldwide from unintentional poisoning [1]. Hospitals, and in particular emergency departments (ED), are faced with a considerable number of admissions leading to a substantial number of hospitalizations and costs.

Studies on the characteristics of acute poisonings have been conducted in a number of countries. Some of them focused on cases in EDs [2-12], while others on cases in hospitals [13-17]. They give an idea of the demographic characteristics of the patients, the time of admission, the substances involved, the therapeutic measures taken and the outcome of the patients. With regard to cost studies, some include only ED-costs [18-21], while others also hospitalization costs [22] or ICU costs [23,24]. Other studies are limited to the financial burden of poisoning by drugs, medicaments and biological substances [25], illicit drugs [26], opioids [27], alcohol and drug overdoses [28] or self-poisoning cases [29-31].

In Belgium, studies of acute poisonings are scarce and limited to the analysis of cases treated in the ED [32] or focus on alcohol intoxications [19] or deliberate self-poisonings [20].

The monitoring of poisoning trends and costs is important to evaluate the appropriateness and quality of care, to identify factors associated with the type of hospitalization and to give an idea of the costs involved. In this context, it may also be clear that the development of a uniform data reporting tool would facilitate comparison of studies. Therefore, the aims of the present study are (1) to inventarize the characteristics of acute poisoning admissions to the ED of a Belgian university hospital, (2) to identify risk factors for hospitalization type, and (3) to calculate general direct medical costs of acute poisonings.

Materials and methods

We used the "Strengthening the Reporting of Observational Studies in Epidemiology Statement" STROBE as a guideline for reporting [33].

Study design and setting

This study is a retrospective analysis of data considering patient records of all poisoning-related admissions of patients aged 14 years or older admitted to the ED of the Ghent University Hospital (GUH). GUH is a 1,062-

beds tertiary care referral center in Belgium with about 34,000 ED admissions per year and where more severe cases are admitted. It is serving an urban area with many students and covering to a lesser extent a rural area. This should be kept in mind when comparing our results with other studies. Data were collected from 1 January 2017 to 31 December 2017.

Inclusion criteria

To avoid overlooking patients who came in with a different chief complaint but were also poisoned, all ED patients with the codes for intoxication, carbon monoxide intoxication, suicide attempt, social, mental or psychological reason, were screened for poisoning. They were included when the reason for admission could be encoded in T36-T50 (poisoning by drugs, medicaments and biological substances) or in T51-T65 (toxic effects of substances chiefly nonmedicinal as to source) of the International Classification of Diseases (ICD-10) [34]. For each admission included, the first author (AMD) and another researcher (KL) considered independently if inclusion was justified. The cases without agreement were discussed with the department head of GUHED (PDP) and were included after consensus.

Variables

All admitted patients were triaged according to the Manchester Triage Scale [35]. After treatment, ambulatory patients (ED-amb) were discharged home, while patients requiring observation were admitted to the ED-24-hours-observation-unit (ED-24h). Some patients had to be admitted to the hospital ward (Hosp) or transferred to the intensive care unit (ICU) for further monitoring.

The cases were categorized according to (1) accidental (unintentional) poisoning, (2) use of substances of abuse, (3) intentional self-harm or (4) undetermined cause of poisoning. Poisoning was considered as accidental in case of "external causes of poisoning and accidents (e.g. taking the wrong medication) with the agent taken for neither self-harm nor intoxication purposes" [17]. A substance of abuse was defined as "recreational use of substance of abuse" [36]. Intentional self-harm was defined as "purposely self-inflicted poisoning", as categorized in ICD-10, X60-X69 [34]. The term undetermined poisoning was used when the underlying reason was unclear.

Tables 1 to 3 present the analysis of the characteristics and agents for all admissions, including those of patients readmitted during the study period. Since some patients were admitted more than once, we performed also a separate analysis in which readmissions were accounted for by considering all patients who presented only once as well as patients with readmissions; for the latter only their first admission was taken into account. These data can be consulted in Supplementary Files S1-S5 of the published article.
For the multilevel analysis of the factors associated with the type of hospitalization, the group of patients who were admitted only once were considered as well as the group of patients who were admitted more than once.

Data collection

We used the minimum-hospital-data (MZG) as a first source of information. This obligatory registration system contains administrative, medical and nursing data of hospitalized patients such as diagnoses, treatments provided, intentionality and discharge status. For patients hospitalized, the ICD-10 codes were used, available in the section "diagnosis" of the minimum-hospital-data (MZG). The before last digit of the ICD-10-codes gives an indication of the intentionality.

The emergency registration system for hospital EDs, named UREG, was used as the second source. According to a Royal Decree, each Belgian hospital with a specialized ED has to register administrative and medical data on all ED patients and to transmit them to the Federal Public Service Health (FPS Health). UREG provides demographic data (age, gender, marital status, nationality, type of insurance), admission and discharge times, location prior to admission and type of transport to the hospital. Data about the reason for admission, symptoms, type of agent(s), diagnosis, degree of severity, type of discharge, destination after discharge, were also collected. This registration system also provides data on intentionality by mentioning either intake of a substance of abuse, suicide and/or self-harm.

The third source of information was the electronic patient file (EPD), available for both ambulatory and hospitalized patients. We used data such as the Glasgow Coma Score (GCS), intentionality, agents involved and consultations for psychiatric care. Data on intentionality from MZG and UREG, were verified in the EPD. If the intentionality was not clear from data of the different sources, the case was categorized as 'undetermined'.

Financial data on direct medical costs were obtained from the hospital's financial department. They were abstracted from the invoices of the individual patients and expressed in EUR (1 EUR = 1.17 USD, December 2017). Cost was defined as the payer's cost.
In case of an admission to the hospital, the payer is (1) on the one hand the government, through contributions from the health and disability insurance, obligatory for people in Belgium, and (2) on the other hand the individual patient.

The financing of Belgian hospitals is complex. A part of the hospital budget is fixed and is paid monthly to the hospitals (system of budgetary twelfths) by the government via seven Belgian insurance institutions. Another part is variable and consists of an amount per admission and per hospitalization day. This variable cost is charged by the hospital to two parties: a major part is paid by the government via the seven insurance institutions, a smaller part is paid by the individual patient via the hospital's invoice to the patient (usually between 18 and 20% of the variable cost). The invoice contains four parts: accommodation and nursing, physicians' fees, use of pharmaceuticals and other costs (e.g. bottle of drinking water, use of refrigerator and/or television). The payer's hospital cost presented in this study is the cost paid by the government (fixed and variable part, paid via the insurance companies) plus the cost paid by the individual patient. Cost is calculated on the patients with an obligatory insurance.

Statistical analysis

A descriptive study was performed on the variables using Pearson Chi-Square test and Fisher's Exact Test to compare categorical data between groups.

A multilevel multinomial logistic regression with generalized logit link function was used to analyze the factors associated with the type of hospitalization. Univariate analysis was used calculating the unadjusted odds ratios to assess the predicting variables related to the hospital admission type.

In the multivariate analysis, the step-by-step method was used with the variables which in the univariate analysis achieved a statistically significant association ($p<0.05$) or had a clear clinical and/or biological significance. The predictors of the final model were selected based on the Akaike Information Criterion (AIC). The discriminatory power of the model was assessed through the determination of the area under the ROC curve (AUC). To avoid overoptimistic areas under the ROC curve and to validate the model, k-fold cross-validation (k=10) was applied. A multilevel multinomial logistic regression was applied on a dataset containing one record per patient. The sample of data was partitioned at random into 10 complementary subsets. For each subset, the predicted probabilities were estimated on the sample data excluding that particular subset. All analyses were performed using SPSS 25.0 (IBM®).

Ethical considerations

The study protocol was approved by the Ethical Committee of the Ghent University Hospital (approval number B670201732651).

Results

Demographics and characteristics of the patients on admission

In total, 1,214/34,000 (3.6%) admissions were included, of whom 62.2% were male (Table 1). Of these admissions, 54.5% received ambulatory care, 24.6% had to stay for 24-hours (or less) in the ED, 20.9% were hospitalized or admitted to the intensive care unit (ICU). Mean age was 37 years (SD 15.56y), with 43.0% between 21-40y and the age group >60y being less represented. Of all patients, 90.9% was admitted once, 5.8% twice and 3.4% three times or more.

The majority was unmarried, widow(er) or divorced and 1,175 had a Belgian obligatory insurance. Forty-nine percent presented on Fridays or during the weekend. Sixty percent came from home and 26.5% from a public place. In the group of hospitalized patients, 80.3% came from home, 12.2% from a public place and 40.2% were transported by ambulance.

Table 1. | Demographic data and characteristics of admissions for poisoning to the Ghent University Hospital according to hospitalization type.

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Gender					**0.017**
Male	755 (62.2)	435 (65.8)	171 (57.2)	149 (58.7)	
Female	459 (37.8)	226 (34.2)	128 (42.8)	105 (41.3)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Age					**<0.001**
14-20y	213 (17.5)	169 (25.6)	29 (9.7)	15 (5.9)	
21-40y	522 (43.0)	295 (44.6)	119 (39.8)	108 (42.5)	
41-60y	387 (31.9)	161 (24.4)	118 (39.5)	108 (42.5)	
>60y	92 (7.6)	36 (5.4)	33 (11.0)	23 (9.1)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Marital status					**0.099**
Unmarried/ widow(er)/divorced	834 (83.6)	417 (86.2)	223 (81.1)	194 (81.2)	
Married/cohabiting	164 (16.4)	67 (13.8)	52 (18.9)	45 (18.8)	
Total	*998 (100.0)*	*484 (100.0)*	*275 (100.0)*	*239 (100.0)*	
Residence					**0.63**
Ghent	475 (39.1)	253 (38.3)	124 (41.5)	98 (38.6)	
Outside Ghent	739 (60.9)	408 (61.7)	175 (58.5)	156 (61.4)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value1
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Day of the week admission					**<0.001**
Monday	141 (11.6)	60 (9.1)	42 (14.0)	39 (15.4)	
Tuesday	171 (14.1)	85 (12.9)	54 (18.1)	32 (12.6)	
Wednesday	143 (11.8)	78 (11.8)	32 (10.7)	33 (13.0)	
Thursday	159 (13.1)	73 (11.0)	55 (18.4)	31 (12.2)	
Friday	199 (16.4)	124 (18.8)	31 (10.4)	44 (17.3)	
Saturday	194 (16.0)	121 (18.3)	38 (12.7)	35 (13.8)	
Sunday	207 (17.1)	120 (18.2)	47 (15.7)	40 (15.7)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Time of admission					**<0.001**
8am-12pm	103 (8.5)	50 (7.6)	20 (6.7)	33 (13.0)	
12pm-4pm	176 (14.5)	69 (10.4)	45 (15.1)	62 (24.4)	
4pm-8pm	245 (20.2)	96 (14.5)	86 (28.8)	63 (24.8)	
8pm-12am	275 (22.7)	103 (15.6)	111 (37.1)	61 (24.0)	
12am-4am	272 (22.4)	226 (34.2)	23 (7.7)	23 (9.1)	
4am-8am	143 (11.8)	117 (17.7)	14 (4.7)	12 (4.7)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Victim location					**<0.001**
Home	727 (59.9)	323 (48.9)	200 (66.9)	204 (80.3)	
Public place	322 (26.5)	243 (36.8)	48 (16.1)	31 (12.2)	
Other	165 (13.6)	95 (14.4)	51 (17.1)	19 (7.5)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value1
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Referred by					**<0.001**
On its own initiative	657 (54.1)	357 (54.0)	153 (51.2)	147 (57.9)	
Externals, no patient participation	472 (38.9)	273(41.3)	126 (42.1)	73 (28.7)	
General practitioner/ physician	77 (6.3)	26 (3.9)	18 (6.0)	33 (13.0)	
Other	8 (0.7)	5 (0.8)	2 (0.7)	1 (0.4)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Transport					**<0.001**
By own means	357 (29.4)	167 (25.3)	79 (26.4)	111 (43.7)	
Ambulance	659 (54.3)	386 (58.4)	171 (57.2)	102 (40.2)	
Mobile Intensive Care Unit	198 (16.3)	108 (16.3)	49 (16.4)	41 (16.1)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	

[1] Chi-square and Fisher's exact test

Characteristics of hospitalized patients, examinations, treatment and follow-up

As shown in Table 2, 21.2% of the patients showed changes in consciousness and 16.8% behavioural and emotional disorders. The number of patients with a GCS score lower than 15 was higher (24.3% versus 21.2%) than the number of patients with changes in consciousness. This may be explained by the fact that consciousness was registered as a UREG-parameter by the nurse during the admission process. The GCS, which is more accurate, was noted by the doctor in a later stage in the electronic file (EPD) of the patient. Some patients may have evolved to a lower level of consciousness. However, we should also keep in mind that a decrease in consciousness is not a rigorous, but subjective interpretation.

According to the Manchester Triage Scale, 11.8%

were evaluated as not urgent but were nevertheless hospitalized. The mean length of hospital stay was 1.12 days (SD 3.12) and the median length was 0.00 days (IQR 0.00-1.00). Subtracting the 661 ambulatory patients who stayed less than 1 day (the ED-amb-patients), we obtained a mean of 2.46 (SD 4.26) and a median of 1.00 (IQR 1.00-3.00) days for the remaining 553 patients.

N-acetylcysteine was administered in 3.4% and naloxone in 0.8% of admissions assessed as intentional self-harm. Thiamine was given to 32.1% of admissions involving ethanol. Psychiatric consultations were performed in 59.6% of all admissions and in 95.0% of admissions for intentional self-harm. Most patients (80.9%) could return home after discharge from the hospital and 8.8% were referred to a psychiatric hospital. One patient died in the intensive care unit (mortality of 0.1%). Monitoring of vital parameters and administration of medication and/or an intravenous drip were the most common treatments.

Table 2. | Characteristics, examinations and treatment of admissions for poisoning to the Ghent University Hospital in 2017 according to hospitalization.

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Symptoms on admission					
Changes in consciousness	257 (21.2)	153 (23.1)	57 (19.1)	47 (18.5)	
Behavioural/ emotional disorders	204 (16.8)	92 (13.9)	57 (19.1)	55 (21.7)	
Other	144 (11.9)	81 (12.3)	36 (12.0)	27 (10.6)	
Non-specific symptoms	131 (10.8)	89 (13.5)	20 (6.7)	22 (8.7)	
Nausea, vomiting	70 (5.8)	26 (3.9)	20 (6.7)	24 (9.4)	
General malaise	58 (4.8)	27 (4.1)	17 (5.7)	14 (5.5)	
Headache	22 (1.8)	11 (1.7)	9 (3.0)	2 (0.8)	
Wounds, swelling, fracture	20 (1.6)	10 (1.5)	7 (2.3)	3 (1.2)	
External signs of bleeding or bleeding	11 (0.9)	8 (1.2)	3 (1.0)	0 (0.0)	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Dermatological, ophthalmic, nose throat ear problems	8 (0.7)	5 (0.8)	2 (0.7)	1 (0.4)	
Signs of neurological failure	6 (0.5)	0 (0.0)	2 (0.7)	4 (1.6)	
Abdominal pain	5 (0.4)	4 (0.6)	1 (0.3)	0 (0.0)	
Retrosternal and thoracic pain	3 (0.2)	1 (0.2)	2 (0.7)	0 (0.0)	
Pain in limbs, neck, shoulder, pelvic region	3 (0.2)	2 (0.3)	0 (0.0)	1 (0.4)	
Palpitations	3 (0.2)	1 (0.2)	1 (0.3)	1 (0.4)	
Dizziness and syncopal feeling	3 (0.2)	2 (0.3)	1 (0.3)	0 (0.0)	
Tremor, coordination disorders	3 (0.2)	0 (0.0)	0 (0.0)	3 (1.2)	
Respiratory problems	2 (0.2)	2 (0.3)	0 (0.0)	0 (0.0)	
Fever and convulsion	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	
Diarrhoea	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	
Unknown	259 (21.3)	145 (21.9)	64 (21.4)	50 (19.7)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Route of exposure					**0.024**
Oral/oromucosal	1,047 (86.2)	566 (85.6)	264 (88.3)	217 (85.4)	
Inhalation	65 (5.4)	45 (6.8)	9 (3.0)	11 (4.3)	
>1 way	91 (7.5)	48 (7.3)	23 (7.7)	20 (7.9)	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Other or unknown	11 (0.9)	2 (0.3)	3 (1.0)	6 (2.4)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Manchester Triage Score					**<0.001**
Not urgent	222 (18.3)	156 (23.6)	36 (12.0)	30 (11.8)	
Less urgent	748 (61.6)	409 (61.9)	195 (65.2)	144 (56.7)	
(Very) urgent evaluation	226 (18.6)	88 (13.3)	64 (21.4)	74 (29.1)	
Unknown	18 (1.5)	8 (1.2)	4 (1.3)	6 (2.4)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Glasgow coma score					**0.003**
<8	30 (2.5)	19 (2.9)	2 (0.7)	9 (3.5)	
8-14	265 (21.8)	141 (21.3)	79 (26.4)	45 (17.7)	
15	644 (53.0)	363 (54.9)	157 (52.5)	124 (48.8)	
Unknown	275 (22.7)	138 (20.9)	61 (20.4)	76 (29.9)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Number of days hospitalization					**<0.001**
0	661 (54.4)	662 (100.0)	0 (0.0)	0 (0.0)	
1	313 (25.8)	0 (0.0)	299 (100.0)	14 (5.5)	
2	87 (7.2)	0 (0.0)	0 (0.0)	87 (34.3)	
>=3	153 (12.6)	0 (0.0)	0 (0.0)	153 (60.2)	
Total	*1,214 (100.0)*	*662 (100.0)*	*299 (100.0)*	*254 (100.0)*	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Number of agents involved					**<0.001**
1	910 (75.0)	535 (80.9)	205 (68.6)	170 (66.9)	
2	190 (15.7)	84 (12.7)	62 (20.7)	44 (17.3)	
>=3	114 (9.4)	42 (6.4)	32 (10.7)	40 (15.7)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Type of agents involved					**<0.001**
T36-T50 & T51-T65	166 (13.7)	80 (9.8)	51 (12.7)	35 (10.8)	
T36-T50[2]	268 (22.1)	107 (22.9)	76 (31.7)	85 (37.0)	
T51-T65[3]	776 (64.1)	470 (67.3)	172 (55.6)	134 (52.2)	
Total	*1,210 (100.0)*	*657 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Intentionality					
Accidental (unintentional)	40 (3.3)	34 (5.1)	6 (2.0)	0 (0.0)	
Use of substances of abuse	790 (65.1)	555 (84.0)	162 (54.2)	73 (28.7)	
Intentional self-harm	261 (21.5)	67 (10.1)	97 (32.4)	97 (38.2)	
Undetermined intentionality	123 (10.1)	5 (0.8)	34 (11.4)	84 (33.1)	<0.001
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Monitoring vital parameters					**<0.001**
Yes	772 (63.6)	401 (60.7)	227 (75.9)	144 (56.7)	
No	442 (36.4)	260 (39.3)	72 (24.1)	110 (43.3)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Laboratory testing					**<0.001**
Yes	703 (57.9)	315 (47.7)	216 (72.2)	172 (67.7)	
No	511 (42.1)	346 (52.3)	83 (27.8)	82 (32.3)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Medical imaging					**<0.001**
Yes	276 (22.7)	103 (15.6)	81 (27.1)	92 (36.2)	
No	938 77.3)	558 (84.4)	218 (72.9)	162 (63.8)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Intravenous drip / medication					
Yes	763 (62.9)	393 (59.5)	220 (73.6)	150 (59.1)	<0.001
No	451 (37.1)	268 (40.5)	79 (26.4)	104 (40.9)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Wound, catheter, ostomy care/ minor surgical intervention					
Yes	109 (9.0)	57 (8.6)	27 (9.0)	25 (9.8)	0.85
No	1,105 (91.0)	604 (91.4)	272 (91.0)	229 (90.2)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Invasive techniques					**<0.001**
Yes	685 (56.4)	257 (38.9)	224 (74.9)	204 (80.3)	
No	529 (43.6)	404 (61.1)	75 (25.1)	50 (19.7)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Patient restraint					**<0.001**
Yes	86 (7.1)	27 (4.1)	38 (12.7)	21 (8.3)	
No	1,128 (92.9)	634 (95.9)	261 (87.3)	233 (91.7)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Other treatment					**0.15**
Yes	1,167 (96.1)	629 (95.2)	291 (97.3)	247 (97.2)	
No	47 (4.9)	32 (4.8)	8 (2.7)	7 (2.7)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Use of antidotes					**<0.001**
Yes	27 (2.2)	5 (0.8)	9 (3.0)	13 (5.1)	
No	1,187 (97.8)	656 (99.2)	290 (97.0)	241 (94.9)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	
Psychiatric care					**<0.001**
No psychiatric consultation	490 (40.4)	405 (61.3)	64 (21.4)	21 (8.3)	
Psychiatric consultation	399 (32.9)	224 (33.9)	136 (45.5)	39 (15.4)	
Admission to psychiatry	288 (23.7)	11 (1.7)	89 (29.8)	188 (74.0)	
Compulsory admission to psychiatry	37 (3.0)	21 (3.2)	10 (3.3)	6 (2.4)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	

	Total	ED-ambulatory care	ED-24-hours-observation	Hospitalization/ICU	p-value[1]
	1,214	661	299	254	
	n (%)	n (%)	n (%)	n (%)	
Fate of the patient after discharge hospital					**<0.001**
Home	982 (80.9)	558 (84.4)	246 (82.3)	178 (70.1)	
Another, non-university hospital	52 (4.3)	5 (0.8)	12 (4.0)	35 (13.8)	
Psychiatric hospital	107 (8.8)	39 (5.9)	33 (11.0)	35 (13.8)	
Home for the elderly	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	
Deceased	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.4)	
Other	17 (1.4)	6 (0.9)	7 (2.3)	4 (1.6)	
Unknown	54 (4.4)	52 (7.9)	1 (0.3)	1 (0.4)	
Total	*1,214 (100.0)*	*661 (100.0)*	*299 (100.0)*	*254 (100.0)*	

[1] Chi-square and Fisher's exact test
[2] T36-T50: Drugs, medicaments and biological substances
[3] T51-T65: Substances chiefly non-medicinal as to source

Agents involved

A total number of 1,701 agents were involved (Table 3). Substances most commonly involved were ethanol (52.9%), benzodiazepines (9.7%), cocaine (4.9%), cannabis (4.6%), antidepressants (4.6%) and psychostimulants (4.6%).

In 75.0% of admissions only one agent was taken. Most popular combinations were ethanol with benzodiazepines (36 admissions), ethanol with cannabis (24), ethanol with cocaine (18), benzodiazepines with antidepressants (14) and ethanol with amphetamines (13 admissions).

Table 3 gives an overview of the agents used by men and women separately. Women used more frequently benzodiazepines, antidepressants, paracetamol and NSAIDs, while men used more ethanol, cocaine, cannabis, psychostimulants, heroin and anaesthetics (ketamine and procaine).

Table 3. | Agents used by patients admitted for poisoning to the emergency department of the Ghent University Hospital in 2017, classified by all agents, single or combined use, and by gender.

ICD-10	Agents[1]	Total	1 agent	>1 agent	Male	Female	p-value[2]
			n = 1,701	n = 910	n = 791	n = 1,024	n = 677
T51	**Alcohol**	**901 (53.0)**	**730 (80.2)**	**171 (21.6)**	**597 (58.3)**	**304 (44.9)**	
T51.0	Ethanol	899 (52.9)	729 (80.1)	170 (21.5)	596 (58.2)	303 (44.8)	<0.001
T40	**Narcotics and psychodysleptics (hallucinogens)**	**229 (13.5)**	**47 (5.2)**	**182 (23.0)**	**176 (17.2)**	**53 (7.8)**	
T40.2	Other opioids	30 (1.8)	6 (0.7)	24 (3.0)	17 (1.7)	13 (1.9)	0.632
T40.5	Cocaine	83 (4.9)	17 (1.9)	66 (8.3)	63 (6.2)	20 (3.0)	0.008
T40.7	Cannabis (derivatives)	79 (4.6)	15 (1.6)	64 (8.1)	65 (6.3)	14 (2.1)	<0.001
T40.1	Heroin	14 (0.8)	5 (0.5)	9 (1.1)	13 (1.3)	1 (0.1)	
T43	**Psychotropic drugs, NEC[3]**	**199 (11.7)**	**39 (4.3)**	**160 (20.2)**	**99 (9.7)**	**100 (14.8)**	
	Antidepressants	78 (4.6)	13 (1.4)	65 (8.2)	21 (2.1)	57 (8.4)	<0.001
	Antipyschotics	43 (2.5)	10 (1.1)	33 (4.2)	17 (1.7)	26 (3.8)	0.003
	Psychostimulants	78 (4.6)	16 (1.8)	62 (7.8)	61 (6.0)	17 (2.5)	0.006
T42	**Anti-epileptic, sedative-hypnotic, antiparkinsonism drugs**	**179 (10.5)**	**23 (2.5)**	**156 (19.7)**	**77 (7.5)**	**102 (15.1)**	
T42.4	Benzodiazepines	165 (9.7)	21 (2.3)	144 (18.2)	68 (6.6)	97 (14.3)	<0.001
	Anti-epileptics	5 (0.3)	1 (0.1)	4 (0.5)	3 (0.3)	2 (0.3)	
T39	**Nonopioid analgesics, antipyretics, antirheumatics**	**70 (4.1)**	**21 (2.3)**	**49 (6.2)**	**13 (1.3)**	**57 (8.4)**	
T39.1	Paracetamol	42 (2.5)	14 (1.5)	28 (3.5)	11 (11)	31 (4.6)	<0.001

ICD-10	Agents[1]	Total	1 agent n = 1,701	>1 agent n = 910	Male n = 791	Female n = 1,024	p-value[2] n = 677
T39.3	Other nonsteroidal anti-inflammatory drugs [NSAIDs]	27 (1.6)	6 (0.7)	21 (2.7)	2 (0.2)	25 (3.7)	<0.001
T46	Agents primarily affecting the cardiovascular system	28 (1.6)	1 (0.1)	27 (3.4)	9 (0.9)	19 (2.8)	
	Beta-blockers	11 (0.6)	0 (0.0)	11 (1.4)	0 (0.2)	9 (1.3)	
T58	Carbon monoxide	20 (1.2)	17 (1.9)	3 (0.4)	15 (1.5)	5 (0.7)	0.234
T59	Other gases, fumes and vapours	13 (0.8)	12 (1.3)	1 (0.1)	8 (0.8)	5 (0.7)	
T41	Anaesthetics and therapeutic gases	11 (0.6)	2 (0.2)	9 (1.1)	9 (0.9)	2 (0.3)	
T47	Agents primarily affecting the gastrointestinal system	9 (0.5)	0 (0.0)	9 (1.1)	3 (0.3)	6 (0.9)	
T54	Corrosive substances	7 (0.4)	5 (0.5)	2 (0.3)	4 (0.4)	3 (0.4)	
T45	Primarily systemic and haematological agents, NEC[3]	7 (0.4)	2 (0.2)	5 (0.6)	2 (0.2)	5 (0.7)	
T7003	Other[4]	6 (0.4)	4 (0.4)	2 (0.3)	2 (0.2)	4 (0.6)	
T36	Systemic antibiotics	3 (0.2)	0 (0.0)	3 (0.4)	2 (0.2)	1 (0.1)	
T38	Hormones and their synthetic substitutes and antagonists, NEC	4 (0.2)	0 (0.0)	4 (0.5)	1 (0.1)	3 (0.4)	
T50	Diuretics and unspecified drugs, medicaments and biological substances	4 (0.2)	1 (0.1)	3 (0.4)	3 (0.3)	1 (0.1)	

ICD-10	Agents[1]	Total	1 agent n = 1,701	>1 agent n = 910	Male n = 791	Female n = 1,024	p-value[2] n = 677
T55	Soaps and detergents	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	
T65	Other and unspecified substances	2 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)	2 (0.3)	
T49	Agents primarily affecting skin, mucous membrane and ophthalmological, otorhinolaryngological and dental drugs	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	
T60	Pesticides	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	
T52	Organic solvents	2 (0.1)	0 (0.0)	2 (0.3)	2 (0.2)	0 (0.0)	
T44	Drugs primarily affecting the autonomic nervous system	2 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	
T37	Other systemic anti-infectives and antiparasitics	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)	
T56	Metals	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	
		1,701 (100.0)	910 (100.0)	791 (100.0)	1,024 (100)	677 (100.0)	

[1] The main ICD-10-groups are listed and the most important agents of those main groups.
[2] Chi-square and Fisher's exact test
[3] NEC = Not Elsewhere Classified
[4] Other: pushpin, absorbent granules, tinplate, toothbrush, lighter, plasticine.

Factors associated with hospitalization type

Table 4 shows the results of the univariate (unadjusted OR) and multivariate (adjusted OR) analysis performed to identify the factors associated with hospitalization type using the ED-amb population as the reference. In the univariate analysis, the odds ratios of the following variables were calculated to assess the predicting variables related to the hospital admission type: gender, age, marital status, residence, day of the week of admission, time of admission, victim location, referral, transport, route of exposure, degree of severity, Glasgow Coma Score, number of agents involved, type of agents involved, use of antidotes, involvement of ethanol, antidepressants, antipsychotics, psychostimulants, benzodiazepines, cocaine, cannabis, paracetamol and NSAIDs. In the final model (multivariate analysis), age, time of admission, victim location, degree of severity, use of antidotes, involvement of ethanol, antidepressants, antipsychotics, psychostimulants and benzodiazepines were associated with the hospitalization type. After cross-validation, the estimated AUCs were 81.3% (95%CI: 78.7%-83.8%) for ED-amb, 78.4% (95%CI: 75.5%-81.3%) for ED-24h and 80.2% (95%CI: 77.4%-83.1%) for Hosp.

The estimated odds for ED-24h or Hosp versus ED-amb increased with age. The estimated odds for ED-24h and Hosp versus ED-amb were much higher for day and evening hours between 8am and 12am (midnight) than for night hours between 12am (midnight) and 8am. Patients triaged as urgent or very urgent by the Manchester triage scores were associated with higher estimated odds of being admitted to ED-24h or Hosp. Needing antidotes and involvement of antidepressants and benzodiazepines were also factors associated with a greater risk of ED-24h or Hosp as opposed to ED-amb. Ethanol was significantly associated with a greater risk of ED-24h and psychostimulants with a greater risk of Hosp.

Table 4. | Univariate and multivariate analysis of factors associated with hospitalization type of patients admitted for poisoning to the Ghent University Hospital in 2017.

	ED-24h (ref: ED-amb)		Hosp (ref: ED-amb)	
	Unadjusted OR[1] (CI[2])	Adjusted OR[1] (CI[2])	Unadjusted OR[1] (CI[2])	Adjusted OR[1] (CI[2])
Age				
>60y	5.29 (2.82-9.90)*	3.58 (1.74-7.33)*	7.08 (3.27-15.30)*	5.13 (2.12-12.41)*
41-60y	4.22 (2.64-6.74)*	2.56 (1.48-4.44)*	7.55 (4.15-13.72)*	4.78 (2.37-9.64)*
21-40y	2.31 (1.47-3.65)*	1.79 (1.07-3.02)*	4.05 (2.25-7.28)*	2.80 (1.43-5.49)*
14-20y	REF	REF	REF	REF
Hour of admission				
8am - 12pm	3.31 (1.53-7.12)*	2.77 (1.23-6.24)*	6.41 (2.98-13.81)*	5.17 (2.20-12.17)*
12pm - 4pm	5.40 (2.75-10.61)*	3.72 (1.79-7.74)*	8.73 (4.30-17.73)*	6.01 (2.69-13.39)*
4pm - 8pm	7.36 (3.91-13.85)*	5.28 (2.65-10.52)*	6.33 (3.16-12.67)*	4.50 (2.04-9.94)*

	ED-24h (ref: ED-amb)		Hosp (ref: ED-amb)	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	OR[1] (CI[2])	OR[1] (CI[2])	OR[1] (CI[2])	OR[1] (CI[2])
8pm - 12am	8.94 (4.80-16.65)*	6.99 (3.58-13.64)*	5.73 (2.87-11.45)*	4.95 (2.27-10.77)*
12am - 4am	0.85 (0.42-1.72)	0.82 (0.39-1.72)	0.98 (0.46-2.07)	1.03 (0.45-2.36)
4am - 8am	REF	REF	REF	REF
Victim location				
Other	0.87 (0.59-1.29)	1.90 (1.09-3.32)*	0.32 (0.18-0.54)*	0.86 (0.41-1.79)
Public place	0.32 (0.22-0.46)*	1.75 (1.15-2.67)*	0.21 (0.13-0.31)*	2.39 (1.46-3.93)*
Home	REF	REF	REF	REF
Manchester Triage score				
Urgent or very urgent	3.16 (1.92-5.19)*	2.67 (1.54-4.64)*	4.37 (2.60-7.34)*	3.87 (2.13-7.03)*
Less urgent	2.06 (1.37-3.10)*	1.96 (1.26-3.06)*	1.80 (1.15-2.83)*	1.78 (1.08-2.93)*
Not urgent	REF	REF	REF	REF
Use of antidotes				
Yes	4.05 (1.32-12.44)*	7.35 (2.12-25.47)**	7.12 (2.41-21.02)*	13.07 (3.80-44.90)*
No	REF	REF	REF	REF
Antidepressants				
Yes	3.20 (1.63-6.27)*	2.40 (1.09-5.26)*	5.63 (2.94-10.82)*	4.10 (1.85-9.08)*
No	REF	REF	REF	REF
Antipsychotics				
Yes	2.44 (1.08-5.51)*	1.33 (0.52-3.36)	3.96 (1.78-8.81)*	2.06 (0.80-5.29)
No	REF	REF	REF	REF
Psychostimulants				
Yes	0.84 (0.44-1.59)	1.62 (0.75-3.50)	1.50 (0.83-2.72)	2.72 (1.28-5.81)*
No	REF	REF	REF	REF
Benzodiazepines				
Yes	3.54 (2.27-5.52)*	2.59 (1.56-4.31)*	3.44 (2.14-5.55)*	1.92 (1.10-3.37)*
No	REF	REF	REF	REF
Ethanol				
Yes	0.72 (0.52-1.00)*	1.68 (1.08-2.61)*	0.55 (0.44-0.76)*	1.52 (0.94-2.47)
No	REF	REF	REF	REF

[1] OR= Odds Ratio
[2] CI = Confidence Interval
* significant, p<0.05
REF= Reference category

Cost

Table 5 shows the total, mean and median costs for the 1,175/1,214 admissions (including readmissions) for patients with an obligatory insurance. Total direct costs were €1,512,346: €125,326 for 637 ED-amb patients, €389,539 for 290 ED-24h patients and €997,481 for 248 Hosp patients. The total cost for the initial care in the ambulatory ward of the ED accounted for €198,677 (with inclusion of the cost for the ED-amb patients, the ED-24h patients and the Hosp patients). The total cost for ED-amb patients who were discharged home after their care was €125,326 or a mean of €197 per patient. The total cost for both ED-24h patients and Hosp patients (with inclusion of the cost of the initial care in the ED-amb ward) was €1,387,020 representing a mean cost of €2,578 per patient.

The age groups 15-20y, 21-40y, 41-60y and the group older than 60y represented 17.9%, 42.1%, 32.2% and 7.7% of the total study group and accounted for 8.6%, 37.8% and 44.0% and 9.6% of total costs respectively.

The mean cost per admission amounting to €1,287 (SD 2,653), was covered by the government for 95.7% via the obligatory insurance and for 4.3% by the fee for the patient. The median cost was €423 (IQR €154-1,471).

Table 5. | Total, mean and median cost in EUROs of patients admitted for poisoning to the Ghent University Hospital, 2017

Type of hospitalization[1]	Total cost[5], €	Cost in the ED unit	Cost in the hospitalization unit
Total (all types of hospitalization)	**1,512,346**	198,677	1,313,669
ED-amb[2]	**125,326**	125,326	0.0
ED-24h[3]	**389,539**	38,383	351,156
Hosp[4]	**997,481**	34,968	962,513
Type of hospitalization[1]	**Mean cost[6], € (SD)**	**Cost in the ED unit**	**Cost in the hospitalization unit**
Total (all types of hospitalization)	**1,287 (2,653)**	169	1,118
ED-amb[2]	**197(147)**	197	0.0
ED-24h[3]	**1,343 (292)**	132	1,211
Hosp[4]	**4,022 (4,766)**	141	3,881
Type of hospitalization[1]	**Median cost[7], € (Q1-Q3)**	**Cost in the ED unit**	**Cost in the hospitalization unit**
Total	**423 (154-1,472)**	140 (82-216)	0.1 (0.1-0.1)
ED-amb[2]	**164 (93-253)**	164 (93-253)	0.0 (0-0)
ED-24h[3]	**1,301 (1,237-1,396)**	118 (72-173)	1,170 (1,109-1,261)
Hosp[4]	**2,854 (2,157-3,768)**	117 (60-189)	2,745 (2,024-3,5878)

[1] Costs are categorized into type of admission and are presented in EUROs
[2] ED-amb: ambulatory patients discharged home after treatment in the emergency department
[3] ED-24h: patients requiring 24-hours-observation at maximum in the emergency department
[4] Hosp: patients admitted to a hospital ward/ intensive care unit
[5] Total cost, categorized by emergency department (ED) cost and hospitalization cost
[6] Mean cost, categorized by emergency department (ED) and hospitalization cost; SD = standard deviation
[7] Median cost, categorized by emergency department (ED) cost and hospitalization cost; Q1-Q3 = Interquartile range.

When excluding the readmissions, the mean cost for the 1,042 patients was €1,264 (SD 2,692), of which 95.5% was covered by the government via the obligatory insurance and 4.5% by a fee to the patient. The mean cost was €199 for ED-amb patients, €1,359 for ED-24h patients and €4,146 for hospitalized patients. The median cost was €372 (IQR €152-1,440).

In cases of ethanol poisoning (whether or not in combination with other agents, the mean cost per admission was €1,216 (SD €2,691) for the 1,175 admissions (including readmissions), with a median cost of €376 (IQR 154-1,389). In cases of poisoning without involvement of ethanol, the mean cost per admission was €1,490 (SD 2,533), with a median cost of €376 (IQR €154-2,036).

When medicinal agents were involved (T36-T50, poisoning by drugs, medicaments and biological substances), the median cost for hospitalized poisoned patients (including readmissions) was €1,983 (IQR €1,310-2,036). When non-medicinal agents were involved (T51-T65, toxic effects of substances chiefly nonmedicinal as to source), the median cost was €1,534 (IQR €1,272-2,782).

Discussion

This study analyzed data of 2017 of all poisoning cases in a university hospital, with analysis of the factors associated with hospitalization type and cost calculation based on the individual invoices. As far as we know, this study is the first to combine these aspects, which may prove to be valuable for healthcare professionals and policy makers.

Patients with acute poisoning represented 3.6% of total patient population. Figures from other countries are lower (range 0.3-1.7%) [3,6,11,12,18]. Verstraete & Buylaert [32], who analyzed poisonings between 1983 and 1990 in the same hospital, but with exclusion of single poisonings with ethanol, reported 3.2%.

The mean age average of 37 years in our study was within the range of most studies (33-40y) [3,4,10,11,14,17,18,32] although some studies found a lower mean age (range 23-28y) [2,5,12].

Men accounted for 62.2% of the admissions, compared to 44.0% [32] between 1983-1990. This can be due to the inclusion in our study of single poisonings with only ethanol, as men accounted for 66.3% of these cases.

In our study, patients were most likely to consult the ED between 8pm and 12 am and between 12 am and 4 am (22.4%). Other healthcare services are often not available at these times and psychosocial problems are then probably more prevalent. The higher consumption of ethanol at these hours is possibly another contributing factor.

The socially accepted drug ethanol was used in 52.9%

(74.0% of cases): in 80.1% of the admissions as a single agent and in 21.5% as concomitant substance. In a recent study of Muňoz et al.[18] in Spain, ethanol was involved in 44.7% of cases, which is close to our result (52.9%).

In the Netherlands, Duineveld et al. [4] analyzed acute intoxications in six hospitals. They reported the use of ethanol whether or not in combination with other drugs in 318/1,183 patients. In cases of drugs of abuse (DOA), ethanol was involved in 73.5%, of which 60.7% mono-intoxications and 39.3% in combination with (illicit) drugs. In the 735/1.183 suicide attempts in the study of Duineveld et al. [4], seven cases of mono-intoxications with ethanol with the intention of self-harm were recorded. It is not clear if ethanol was involved in other cases of intentional self-harm which may to some extent explain the low percentage of cases with ethanol involved.

The percentages of ethanol mentioned in the studies on poisoning in Oslo hospitals of Hovda [14] and Lund [17] (17% and 18% respectively) are lower than in our study, but one should keep in mind that there is one ambulance service and a large outpatient clinic and four public emergency hospitals in Oslo. The majority of ethanol poisonings are referred to the outpatient clinic [37,38]. In the hospitals, pharmaceuticals are most frequently involved. Data from the hospitals and the outpatient clinic must be seen together.

The ten most frequently used agents are comparable in most studies, although their ranking could vary [3,4,14,18,20,25].

In our study, benzodiazepines were mentioned in 9.7% (13.5% of cases)., cocaine was used in 4.9% (6.8% of cases) and psychostimulants in 4.6% (6.4% of cases). In the study of Duineveld et al. [4], cocaine was involved in 27.3% of drugs of abuse cases and psychostimulants in 21.0%. The more liberal drug policy in the Netherlands may be one of the factors explaining this higher percentage.

Carbon monoxide was involved in 1.2% (1.6% of cases), versus in 11.7% during the period 1983-1990 in our hospital [32]. A possible explanation may be found in the regulatory measures on technical appliances by the government. Antidotes were given in 2.2% of admissions, with naloxone in 0.5% and N-acetylcysteine in 1.1%. In Oslo [17], naloxone was given in 17% and N-acetylcysteine in 11%.

The overall percentage of patients receiving psychiatric care was high, presumably because of the psychiatric nature of many poisoning admissions and the 24/7 availability of a psychiatrist in GUHED. For intentional poisonings, it amounted to even 95.0% compared with 67.0% and 90.0% in the studies of Lund [17] and Hendrix [20]. Providing psychiatric help with a low threshold is in accordance with the current National Institute for Health and Care Excellence (NICE) guidelines [39], as intentional self-harm in the past is the strongest known predictor of a later successful suicide attempt.

Following the care in the ED, 54.4% patients were discharged home and 24.6% left the ED within 24 hours. Only 20.9% of patients were hospitalized. In the earlier study from GUHED, Verstraete & Buylaert [32] reported 27.8% of patients being discharged home from ED. The exclusion of ethanol cases when it was the sole agent in this previous study probably explains this difference in the discharge rate.

With regard to the factors influencing the hospitalization type, we found that, among other criteria, antidepressants and benzodiazepines were significantly associated with a higher estimated odds for ED-24h or Hosp versus ED-amb. It is also not surprising that the odds for ED-24h or Hosp versus ED-amb is higher for urgent or very urgent Manchester Triage Scores than for patients with a non or less urgent scores. The need for antidotes is also a factor more frequently leading to hospitalization. The higher odds for ED-24h and Hosp during the day and evening hours compared with night hours was unexpected and requires further investigation.

When analyzing the cost, we found a mean cost of €1,287 per admission in our study: a mean of €197 per ED-amb patient and €1,118 hospitalization cost for ED-24h patients and Hosp patients. In Spain, Muñoz et al. [18] calculated a mean cost of €571 (indexed 2017: €586): €222 (indexed 2017: €228) per ED-amb patient and €4,121 (indexed 2017: €4,224) for hospitalized patients (both ED-patients who stayed longer than 6 hours and hospitalized patients). Compared with our total mean cost of €1,287, the cost calculated by Muñoz (€586) is lower. This may be due to the fact that our study comprises 54.2% of ambulatory patients and 45.8% of hospitalized patients versus 11.2% (359/3,159) ambulatory patients and 88.8% (2,836/3,195) hospitalized patients in the study of Muñoz. The cost for ED-amb patients in our study (€197) is indeed comparable to that in the study of Muñoz (€228) but is lower for hospitalized patients (€2,578 versus €4,224) which is difficult to explain. We suppose that, as more patients were ambulatory in Spain, the admission protocol to observe patients during more than 6 hours in the ED or to hospitalize them, was more selective than in our study. This could have led to a higher degree of severity in the Muñoz paper. It should however be mentioned that this hypothesis is not supported by the mean duration of the hospital stay. The mean hospital stay in the study in Spain is indeed very similar to ours (1.19 versus 1.12 days), with a mean stay for ED-24h and hospitalized patients that is even shorter in the Spain study (1.99 days) than in ours (2.46 days). Another hypothesis is that the type of poisonings included in the study of Muñoz is different from our study, as it is based on the information provided by the diagnosis-related groups (DRG), which could not be used in our study.

In our study, the median cost for hospitalized patients with medicinal agents involved (T36-T50, poisoning by drugs, medicaments and biological substances,) was €1,983. Okumara et al. [25] reported a median cost of $1,776 (indexed 2017: $2,134 or €1,824) for inpatients with drug poisoning (ICD-10, T36-T50,) which is close to our figure (€1,983). Okumara et al. also reported that the age group between 20-39y (19,200/37,200 patients, i.e. 51%) was responsible for 50% of the costs, which is in the same range of our results: the group 21-40y (495/1,175 or 42.1%) was responsible for 37.8% of the costs.

The costs in two studies available for Belgium [19,20], are comparable with our figures. Hendrix [20] calculated €828/patient (indexed January 2017: € 948.48) from admission until ED-discharge for deliberate self-poisoning cases (use of substances of abuse and intentional self-harm, excluding alcohol as single drug). The mean cost/admission in our study using the same inclusion criteria was in the same order of magnitude, i.e. €796 (SD 2,340). Verelst [19] mentioned an estimated ED-cost for ethanol poisoning of €541/patient (indexed January 2017: €620). In our

study, the mean ED-cost for alcohol poisoning (ED-amb and ED-24h) was in the same order of magnitude: €418/patient (SD 470).

The total consolidated Public Health Expenditure of the National Health System in Belgium in 2017 was US$ 4,774 (€ 4,224) per capita [40-42]. This represents US$ 53.9 billion (€ 47.7 billion) or 10% of the Gross Domestic Product (GDP). In 2015, Belgian hospitals accounted for nearly 33% (US$ 17.7 billion or € 15.6 billion) of health spending (versus 40% in Organisation for Economic Cooperation and Development (OECD) countries on average). In Ghent University Hospital, there were 575,000 hospital admissions in 2017 of which 1,214 (0.21%) for poisoning.

Strengths and weaknesses

As the present study was carried out in one university hospital, data cannot simply be extrapolated to other settings. It would be of interest to use the same methodology in other hospitals of other levels and with different settings. Because of the retrospective character and the fact that we had to rely on data collected by doctors, nurses and/or administrative staff during their routine work, it is likely that some admissions and information is missing in our database and/or that a number of cases were not correctly categorized (e.g. intentionality). Another limitation is that comorbidities were not registered in our study, which obviously may have had an impact on the type of hospitalization and on the duration of the stay in the hospital. Our study found multiple associations with hospitalization type, but obviously we should keep in mind that causal relationship cannot be derived from our data.

A strength of our study is that we used the WHO International Classification of Diseases 10th Revision (ICD-10). This use of a clear and international standard may be a first step in the development of a template for uniform data reporting and comparison between centers in order to facilitate international comparison.

Conclusion

Acute poisonings account for a considerable proportion of ED admissions representing a significant organizational and financial burden to hospitals and healthcare workers. We observe a high proportion of ethanol poisoning in our study which is of major concern. Our data may provide an incentive for the government to take the necessary preventive measures such as limiting availability by restricting points of sale, set strict age limits for purchase and consumption, increase the price via taxes and forbidding advertising which are proven to be effective [43].

It is difficult to compare results on admissions for poisoning between different EDs. This is due to

incompleteness of data on the one hand and the lack of uniformity in reporting on the other hand. A possible solution would be to recommend for epidemiological study purposes a uniform template aimed to report data on poisoning in a standardized way. This is in analogy with registration methods that appeared useful in other domains of emergency medicine like the Utstein template in patients with cardiopulmonary arrest [44] and the registration by the 'Deutsche Gemeinschaft für Unfallchirurgie' [45] of patients with severe trauma. Such registrations allow benchmarking of the care. With regard to poisoning cases admitted to the emergency department, a template would be very helpful, with a clear definition of the collected variables using a uniform definition of poisoning, involved agents, intentionality, charges versus cost together with information on country-specific health organizational structure which would be very valuable.

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Chapter 3

Article 2

Adults with acute poisoning admitted to a university hospital in Belgium in 2017: cost analysis benchmarked with national data

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Abbreviations

APR-DRG: All Patient Refined Diagnosis Related Group
BFM: Budget of Financial Resources (Budget Financiële Middelen)
DALY: Disability-Adjusted Life Years
ED: Emergency Department
ED-amb: Emergency Department- ambulatory care
ED-24h: Emergency Department-24-hours-observation unit
Hosp: Hospitalization Unit
EPD: Electronic Clinical Patient File
FPS Health: Federal Public Service
GUH: Ghent University Hospital
ICD-10: International Classification of Diseases, version 10
ICU: Intensive Care Unit
IQR: Interquartile Range
MICU: Mobile Intensive Care Unit
MZG: Minimal Clinical Data (Minimale Ziekenhuis Gegevens)
NSAID: Non-Steroidal Anti-Inflammatory Drugs
RIZIV: National Health and Disability Insurance Service
SD: Standard Deviation
SOA: Substances Of Abuse
STROB: Strengthening the Reporting of Observational Studies in Epidemiology
UREG: Emergency Registration System for hospital emergency departments (Urgentie REGistratiestysteem)

Introduction

Hopitalizations due to acute poisoning entail costs including direct medical costs such as for accommodation and nursing, pharmaceuticals and physicians' fees. Information on (inter)national poisoning trends and cost is an essential element for benchmarking the cost-benefit ratio and are important to assess efficiency of health care.

Cost studies have been conducted in a number of countries regarding acute poisoning. To make international comparison easier, we expressed all costs in international dollars 2017. In Spain, Muñoz et al. [1] (2017) calculated a total cost of $2,716,034 for 3,195 patients (period of 30 months). They analyzed the healthcare costs for the Spanish National Health System for inpatients and outpatients using the corresponding hospital discharge reports. In the United States, Krajewski et al. [2] (2015) estimated a cost of $8.9 billion for 425,491 patients based on the charges imposed by Illinois hospitals among outpatients and inpatients. In Japan, Okumara et al. [3] (2012) estimated a cost of $67.2 million for 37,200 patients using total hospital charges based on a standardized fee-for-service payment system. In the United Kingdom, Tsiachristas et al. (2017) investigated the association between hospital costs and methods of self-harm. They found that costs were mainly associated with the type of healthcare service contact, and estimated an overall annual cost of general hospital management of self-harm of $222.3 million per year [4]. In Australia, Mathers et al. (1999) estimated a total expenditure of $3.2 billion for injury and poisoning [5].

Other studies limited the analysis either to (1) Emergency Department (ED) visits [6], (2) cases of self-poisoning [7-11], (3) poisonings with specific agents [12-15] or studied only (4) intensive care units [8,16,17-19] or (5) costs on changes in management guidelines (e.g. paracetamol poisoning) [20].

In Belgium, only a few studies attempted to analyze the cost for poisoned patients. Verelst [21] (2012) assessed the cost of ED visits due to alcohol intoxication in patients 16 years or older using billing data, while Hendrix [22] (2013) focused on the pattern and cost restricted to deliberate self-poisoning and its impact on the ED using invoices. Senterre et al. [23] (2014) analyzed a.o. the epidemiology and cost of self-injuries, of which 91% were poisonings by medicinal and non-medicinal substances.

It is clear that cost studies are difficult to compare because of diverging inclusion criteria, different social security systems, and cost analyses from different points of view: from the perspective of the admitting hospital to the payer being either the government, the patient, or the insurance system.
As there are no comprehensive cost data for all types of acute poisoning cases in Belgium, aims were to (1) analyze the direct cost and cost components charged by a university hospital to the government and the patients in case of acute poisoning including all types of hospitalization, (2) identify the factors associated with the cost and (3) compare the hospitalization cost of the university hospital studied with national data.

Materials and methods

We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement as a guideline for reporting [24].

Study design and setting

This study is a retrospective analysis of the invoices of all poisoning-related episodes of patients 14 years or older admitted to the ED of Ghent University Hospital (GUH) from 1 January to 31 December 2017. GUH is a teaching hospital in Belgium with >1,000 beds and 33,600 ED admissions in 2017. Because of the small number of patients younger than 14 years old (i.e. 7 patients), they were excluded.

In order to benchmark the hospitalization costs of GUH with national data, we used the latest available data from the Technical Unit of the Federal Public Service (FPS) Health of 2016. Because the Technical Unit does not use ICD-10 codes, we selected a subset of GUH data and national data with the codes All Patient Refined Diagnosis Related Group (APR-DRG) 812 (poisoning by medicinal agents) and 816 (toxic effects by non-medicinal substances). We subsequently compared these with data from ICD-10 codes, more specifically T36-T50 (poisoning by drugs, medicaments and biological substances) and ICD-10, T51-T65 (toxic effects of substances chiefly non-medicinal as to source) [25].

Data sources/measurement

Demographic data and hospitalization characteristics of GUH were retrieved from the hospital's electronic patient databases: the minimal clinical data (MZG) with administrative, medical and nursing data of hospitalized patients, the emergency registration system for hospital EDs (UREG) with administrative and medical data on all ED patients, and the electronic clinical file of the patient (EPD) available for both ambulatory and hospitalized patients.

Financial data on direct medical costs for GUH admissions were obtained from the department of finances. These were retrieved from the invoices of the individual patients.

Data on APR-DRG 812 and 816 (concerning GUH 2016 and the national level 2016) were retrieved from the "National Database medical diagnosis/care and cost" website of the Technical Unit of FPS [26].

Inclusion criteria

All ED patients who received a code for admission due to intoxication in general, carbon monoxide intoxication, suicide attempt, social, mental or psychological reasons, were screened for the identification of cases of poisoning. This method was used in order to also include patients who came in with a different chief complaint but nevertheless also suffered from acute poisoning. They were included when the reason for admission could be encoded in T36-T50 (poisoning by drugs, medicaments and biological substances) or in T51-T65 (toxic effects of substances chiefly non-medicinal as to source) of the International Classification of Diseases (ICD-10) [27]. The validity for inclusion was independently assessed by one author (AMD) and a masterthesis student (KL) on the basis of the hospital's electronic patient files. Cases of disagreement were discussed with the head of the ED (PDP) and included only when consensus was reached.

Patients without a Belgian mandatory health and disability insurance were excluded.

Variables

Patients were categorized into four groups: (1) ambulatory patients (ED-amb) who were discharged home after treatment, (2) ED-24-hours patients (ED-24h) requiring 24-hours-observation at maximum in the ED, (3) patients admitted to the hospital ward (Hosp) and those (4) admitted to the intensive care unit (ICU).

Agents were classified according to the above mentioned ICD-10 categorization.

Cost is defined as the payer's cost, i.e. the direct cost charged to the government and the individual patient by the hospital, and is expressed in international dollars 2017. Neither ambulance services, community health services, health promotion and illness prevention nor indirect costs such as lost production due to sickness and premature death, or costs that have an impact outside the health care sector are included.

Cost is paid partly via an advance payment from the 'Budget of Financial Resources' (Budget Financiële Middelen, BFM) of the government and partly via the invoice. Cost is composed of four parts: (1) costs for accommodation and nursing (not for ED-amb patients), (2) pharmaceuticals, (3) physicians' fees, and (4) other items (for extra utilities, e.g. bottle of water). Accommodation and nursing costs include nursing staff, administration, maintenance, laundry, legal obligations regarding quality and safety of care, and lump sums per day for clinical biology and pharmaceuticals. The physicians' fees contain lump sums per hospital admission for clinical biology, medical imaging and medical 24 hour cover, together with the fees of the individual physicians who were involved in the care of the patient.

Median costs and 25th and 75th percentiles are given because of the skewness of the quantitative variables. Mean values are also given to allow comparison with literature data and national cost data of the Technical Unit of FPS Health.

Supplementary files S2.1 - S2.3 give more details about the Belgian healthcare system.

Statistical analysis

A descriptive analysis was carried out on the financial data for each type of hospitalization. A generalized linear model with gamma loglink [28,29] was applied to assess which variables were associated with the cost. In the univariate analysis, age, gender, marital status, time of admission, victim location prior to admission, referral type, means of transport, route of exposure, degree of severity, Glasgow Coma Scale, hospital length of stay, number of agents, intentionality, use of antidotes, involvement of ethanol, paracetamol, NSAIDs, opioids, benzodiazepines, antidepressants, antipsychotics and amphetamines were screened to identify the factors associated with the cost. Variables with a statistically significant association ($p<0.05$) or of special clinical interest were further studied in a multivariate generalized linear model. The step by step selection procedure was used to simplify the model, excluding the variables which did not significantly contribute to the model. The quality of the model was assessed by the Akaike Information Criterion (AIC). Statistics were performed using SPSS 25.0 (IBM®). Exponential coefficients of the unadjusted and adjusted model (95% CI) were reported.

Ethical considerations

The study protocol was approved by the Ethical Committee of the Ghent University Hospital on March 06, 2017 (B670201732651).

Results

A total of 1,214 patients were admitted in 2017 to the ED with a poisoning problem, of which 96.9% (1,175) had a Belgian mandatory health and disability insurance. Of all admitted patients, 54.2% received ambulatory care, 24.7% had to stay for 24 hours in the ED, 17.8% were hospitalized and 3.3% admitted to the ICU.

Total and median cost according to type of hospitalization

The total, mean and median costs according to hospitalization type are shown in Table 1. Costs are expressed in international dollars. Supplementary files S2.4 and S2.5 present the same cost data as in Table 1 and 3, but expressed in EUROs. The total direct costs for the treatment of all patients with poisoning in GUH amounted to $1,830,870 of which 13.1% for ED-costs and 86.9% for hospitalization costs. Physicians' fees represented 98.5% of ED-amb-cost in contrast with only 21.4% of hospitalization cost. The largest part of hospitalization cost consisted of accommodation (71.4%).

The median cost per episode was $199.1 (IQR $113-$306) for ED-amb patients, $1,574.8 (IQR $1,498-$1,691) for ED-24h patients, $3,398.2 (IQR $2,587-$4,391) for Hosp patients and $4,858.9 (IQR $2,931-$7,174) for ICU patients.

The patients' contribution was higher for ED-amb (9.7%) and ED-24h (4.9%) than for Hosp (3.3%) or ICU observation (3.7%).

Table 1. | Total, mean and median cost in international dollars of patients admitted for poisoning to Ghent University Hospital, 2017

Cost[1]	TOTAL	ED-amb[2]	ED-24h[3]	Hosp[4]	ICU[5]
	1,175 patients	**637 patients**	**290 patients**	**209 patients**	**39 patients**
	$ (%)	**$ (%)**	**$ (%)**	**$ (%)**	**$ (%)**
Total cost[6]	1,830,870.2 (100.0)	151,721.1 (100.0)	471,582.3 (100.0)	856,839.6 (100.0)	350,727.2 (100.0)
ED	240,521.7 (13.1)	151,721.1 (100.0)	46,467.7 (9.9)	32,130.5 (3.7)	10,202.5 (2.9)
Physicians' fees	236,973.3 (98.5)	148,622.1 (98.0)	46,157.9 (99.3)	32,068.5 (99.8)	10,124.7 (99.2)
Pharmaceuticals	2,308.2 (1.0)	2,277.2 (1.5)	19.1 (0.0)	8.1 (0.0)	3.8 (0.0)
Other	1,240.3 (0.5)	821.9 (0.5)	290.7 (0.6)	53.9 (0.2)	74.0 (0.7)
Hospitalization	1,590,348.4 (86.9)	0.0 (0.0)	425,114.6 (90.1)	824,709.1 (96.3)	340,524.6 (97.1)
Physicians' fees	339,892.3 (21.4)	0.0 (0.0)	130,497.8 (30.7)	142,365.3 (17.3)	67,029.2 (19.7)
Pharmaceuticals	103,500 (6.5)	0.0 (0.0)	48,064.5 (11.3)	40,799.9 (4.9)	14,635.6 (4.3)
Accommodation	1,134,879.2 (71.4)	0.0 (0.0)	244,983.2 (57.6)	637,558.3 (77.3)	252,337.7 (74.1)
Other	12,076.9 (0.8)	0.0 (0.0)	1,569.1 (0.4)	3,985.7 (0.5)	6,522.1 (1.9)
	$ (%)	**$ (%)**	**$ (%)**	**$ (%)**	**$ (%)**
Total cost[7]	1,830,870.2 (100.0)	151,721.1 (100.0)	471,582.3 (100.0)	856,839.6 (100.0)	350,727.2 (100.0)
Patient	79,560.9 (4.3)	14,641.8 (9.7)	23,264.5 (4.9)	28,664.1 (3.3)	12,9990.5 (3.7)
Insurance	1,751,309.3 (95.7)	137,079.3 (90.3)	448,317.7 (95.1)	828,175.5 (96.7)	337,736.7 (96.3)
	$ (SD)	**$ (SD)**	**$ (SD)**	**$ (SD)**	**$ (SD)**
Mean cost[8]	1,558.2 (3,212)	238.2 (179)	1,626.1 (353)	4,099.7 (3,755)	8,993.1 (10,888)
ED	204.7 (156)	238.2 (179)	160.3 (93)	153.7(111)	261.6 (188)

Cost[1]	TOTAL	ED-amb[2]	ED-24h[3]	Hosp[4]	ICU[5]
	1,175 patients	**637 patients**	**290 patients**	**209 patients**	**39 patients**
Hospitalization	1,353.5 (3,215)	0.0 (0)	1,465.8 (338)	3,946.0 (3,746)	8,731.4 (10,863)
	$ (SD)	**$ (SD)**	**$ (SD)**	**$ (SD)**	**$ (SD)**
Mean cost[9]	1,558.2 (3,212)	238.2 (179)	1,626.1 (353)	4,099.7 (3,755)	8,993.1 (10,888)
Patient	67.7 (144)	23.3 (27)	80.1 (148)	137.2 (188)	334.4 (372)
Insurance	1,490.5 (3,130)	214.9 (166)	1,546.0 (255)	3,962.6 (3,694)	8,658.7 (10,647)
	$ (Q1-Q3)	**$ (Q1-Q3)**	**$ (Q1-Q3)**	**$ (Q1-Q3)**	**$ (Q1-Q3)**
Median cost[10]	511.6 (187-1,782)	199.1 (113-306)	1,574.8 (1,498-1,691)	3,398.2 (2,587-4,391)	4,858.9 (2,931-7,174)
ED	169.5 (99-261)	199.1 (113-306)	142.6 (87-209)	135.6 (71-210)	224.9 (158-325)
Hospitalization	0.1 (0.1-0.1)	0.0 (0-0)	1,416.4 (1,342-1,527)	2,095.8 (1,238-4,206)	4,654.0 (2,790-6,995)
	$ (Q1-Q3)	**$ (Q1-Q3)**	**$ (Q1-Q3)**	**$ (Q1-Q3)**	**$ (Q1-Q3)**
Median cost[11]	511.6 (187-1,782)	199.1 (113-306)	1,574.8 (1,498-1,691)	3,398.2 (2,587-4,391)	4,858.9 (2,931-7,174)
Patient	29.8 (9-91)	14.0 (6-34)	69.4 (17-111)	115.6 (40-171)	186.2 (93-433)
Insurance	472.5 (161-1,692)	180.5 (97-279)	1,506.4 (1,431-1,609)	3,331.5 (2,521-4,231)	4,527.1 (2,749-6,365)

[1] Costs are categorized by type of admission and are presented in international dollars
[2] ED-amb: ambulatory patients discharged home after treatment in the emergency department
[3] ED-24h: patients requiring 24-hours-observation at maximum in the emergency department
[4] Hosp: patients admitted to a hospital ward
[5] ICU: patients admitted to the intensive care unit
[6] Total cost, categorized by emergency department (ED) cost and hospitalization cost
[7] Total cost, categorized by cost for the patient and cost for the government (via the insurance)
[8] Mean cost, categorized by emergency department (ED) and hospitalization cost; SD = standard deviation
[9] Mean cost, categorized by cost of the patient and the government (via the insurance); SD = standard deviation
[10] Median cost, categorized by emergency department (ED) cost and hospitalization cost; Q1-Q3 = Interquartile range.
[11] Median cost, categorized by cost for the patient and cost for the government (via the insurance); Q1-Q3 = Interquartile range

Five percent of the patients accounted for 15.1% ($276,472.7 out of $1,830,870) of costs and 10% of the patients for 22.4% ($410,689.3 out of $1,830,870) of costs.

Median cost for Hosp and ICU patients admitted because of the involvement of substances of abuse (SOA) or intentional self-harm was $3,455.9 (IQR $2,611-4,562) with a median hospital stay of 3 (IQR 2-4) days.

Paracetamol was involved in 42 patients, of which 14 were treated with N-acetylcysteine: 2 ED-amb, 6 ED-24h, 4 Hosp and 1 ICU patient. This treatment accounted for a median cost of $394.7, $1,609.1, $3,123.6 and $3,917.6 respectively.

Factors associated with costs

Table 2 gives the results of the univariate and multivariate analysis.

In the univariate analysis, all variables screened to identify the factors associated with the cost had a p-value of p<0.05, except for the Glasgow Coma Scale (0.913) and the involvement of opioids (p=0.894) or amphetamines (p=0.171). As we were interested in the association of involved agents with the cost, we nevertheless tested in the multivariate analysis also the association of the involvement of opioids and amphetamines with the cost.

In the adjusted model, gender, degree of severity, type of hospitalization, intentionality, and involvement of ethanol, paracetamol, antidepressants, and amphetamines were significantly associated with the cost (for each parameter: p<0.20).

In the adjusted model, male patients were associated with a 13% higher cost than females. Patients with a high degree of severity were associated with a 40% higher cost than patients who were assessed as not urgent. The treatment of intensive care patients was associated with a 34 times higher cost than ambulatory patients. With regard to the involvement of paracetamol and antidepressants, a 22% and 23% higher cost was found as compared to patients in whom these substances were not involved.

Table 2. | Univariate (unadjusted) and multivariate (adjusted) analysis of factors possibly associated with the cost of patients admitted with poisoning to Ghent University Hospital, 2017

	n= 1,158	UNADJUSTED		ADJUSTED	
	n (%)	Exp (B) (95% CI)		Exp (B) (95% CI)	p-value
Gender			**0.03**		**<0.001**
Male	717 (61.9)	0.85 (0.73-0.99)	0.73	1.13 (1.05-2.21)	<0.001
Female	441 (38.1)	REF		REF	
Degree of severity			**<0.001**		**<0.001**
(Very) high risk	216 (18.7)	2.23 (1.78-2.79)	<0.001	1.40 (1.24-1.58)	<0.001
Low risk	728 (62.9)	1.09(0.91-1.30)	<0.001	1.15 (1.05-1.26)	<0.001
No risk	214 (18.5)	REF		REF	

Type of hospitalization			**<0.001**		**<0.001**
ICU	38 (3.3)	37.72 (30.90-46.05)	<0.001	34.72 (28.34-42.53)	<0.001
Hosp	204 (17.6)	17.20 (15.62-18.94)	<0.001	18.41 (16.48-20.55)	<0.001
ED-24h	287 (24.8)	6.82 (6.26-7.43)	<0.001	7.18 (6.58-7.83)	<0.001
ED-ambulatory	629 (54.3)	REF		REF	
Intentionality			**<0.001**		**<0.001**
Intentional self-harm	253 (21.8)	6.18 (4.13-9.24)	<0.001	1.17 (0.94-1.45)	0.15
Use of substances of abuse	748 (64.6)	3.11 (2.12-4.58)	<0.001	1.44 (1.17-1.77)	<0.001
Undetermined intentionality	118 (10.2)	7.80 (5.06-12.01)	<0.001	1.15 (0.91-1.46)	0.33
Accidental (unintentional)	39 (3.4)	REF		REF	
Involvement of ethanol			**0.02**		**0.09**
Yes	860 (74.3)	0.82 (0.69-0.96)		1.09 (0.99-1.19)	
No	298 (25.7)	REF		REF	
Involvement of paracetamol			**<0.001**		**0.04**
Yes	40 (3.5)	2.35 (1.60-3.46)		1.22 (1.01-1.48)	
No	1,118 (96.5)	REF		REF	
Involvement of antidepressants		**<0.001**		**0.01**	
Yes	67 (5.8)	2.44 (1.80-3.30)		1.23 (1.05-1.45)	
No	1,091 (94.2)	REF		REF	
Involvement of amphetamines		**0.17**		**0.09**	
Yes	64 (5.5)	1.24 (0.91-1.70)		1.15 (0.98-1.34)	
No	1,094 (94.5)	REF		REF	

Comparison of the GUH data with data from FPS health

In Table 3, we compared the mean and median costs of our GUH dataset 2017 with the data of the Technical Unit of FPS Health: (1) APR-DRG 812 (poisoning by medicinal agents) with ICD-10 T36-T50 (poisoning by drugs, medicaments and biological substances) and (2) APR-DRG 816 (toxic effects by non-medicinal substances) with ICD-10 T51-T65 (toxic effects of substances chiefly nonmedicinal as to source). As the

Technical Unit provides solely figures on hospitalized patients, only the cost of ED-24h, Hosp and ICU of GUH 2017 were taken into account.

Total mean costs of GUH 2017 in case of medicinal agents were in the same order of magnitude of the FPS data from GUH 2016, but were 23.2% lower than national data 2016 ($3,280.7 versus $4,040.6) due to less hospitalization days in GUH 2017. The mean cost per day in case of medicinal agents (T36-T50, $1,236.1) in our GUH 2017 study was 62.9% higher than the national mean 2016 ($777.0).

The mean cost per day in case of non-medicinal agents (T51-T65, $1,259.6) in our study 2017 was 66.1% higher than the national mean 2016 ($832.7), while the total mean cost was in the same order of magnitude, presumably due to less hospitalization days. This can be confirmed by the median cost for both medicinal and non-medicinal agents: the median cost for a median hospitalization day of 1 day is 70.5% and 54.4% higher for GUH data 2017 than for national data 2016, respectively.

Table 3. | Comparison of the Ghent University Hospital data 2017 with data from the Technical Unit of the Federal Public Service Health: comparison with Ghent University Hospital data 2016 and with national data 2016, international dollars 2017, Belgium

	GUH 2017	FPS, data GUH 2016	FPS, national data 2016
Medicinal agents	**ICD-10, T36-T50[1]**	**APR-DRG 812[2]**	**APR-DRG 812[2]**
Number of cases	**153**	**97**	**10,946**
Mean age	**34**	**35**	**44**
Median age (IQR)	**32 (23-42)**	**33 (21-45)**	**44 (26-58)**
Mean hospitalization days	**2.7**	**3.0**	**5.2**
Median hospitalization days (IQR)	**1.0 (1.0-3.0)**	**1.0 (1.0-3.0)**	**1 (1.0-5.0)**
Total mean cost/case ($)	**3,280.7**	**3,430.7**	**4,040.6**
Physicians' fees ($)	801.1	934.8	997.0
Pharmaceuticals ($)	209.8	56.2	84.5
Accommodation ($)	2,269.8	2,439.7	2,959.1
Mean cost/day ($)	**1,236.1**	**1,143.6**	**777.0**
Physicians' fees ($)	301.8	311.6	191.7
Pharmaceuticals ($)	79.0	18.7	16.3
Accommodation ($)	855.2	813.2	569.1

	GUH 2017	FPS, data GUH 2016	FPS, national data 2016
Medicinal agents	**ICD-10, T36-T50[1]**	**APR-DRG 812[2]**	**APR-DRG 812[2]**
Median cost ($) (IQR)	**2,400.2 (1,586-3,720)**	**1,522.2 (1,192-3,448)**	**1407.2 (947-3,928)**
Physicians' fees ($)	NA	NA	NA
Pharmaceuticals ($) (IQR)	166.7 (162-183)	9.2 (4-39)	8.6 (2-41)
Accommodation ($) (IQR)	866.3 (843-2,529)	843.1 (799-2,397)	819.0 (547-2,705)
Non-medicinal agents	**ICD-10, T51-T65[3]**	**APR-DRG 816[4]**	**APR-DRG 816[4]**
Number of cases	**301**	**19**	**1,699**
Mean age	**47**	**43**	**39**
Median age (IQR)	**47 (38-57)**	**39 (28-54)**	**40 (17-57)**
Mean hospitalization days	**3**	**1.7**	**3.7**
Median hospitalization days (IQR)	**1.0 (1.0-3.0)**	**1.0 (1.0-3.0)**	**1 (1.0-2.0)**
Total mean cost/case ($)	**3,086.1**	**2,233.5**	**3,081.0**
Physicians' fees ($)	787.8	645.7	849.4
Pharmaceuticals ($)	189.4	27.7	69.6
Accommodation ($)	2,108.9	1,560.1	2,162.0
Mean cost/day ($)	**1,259.6**	**1,313.8**	**832.7**
Physicians' fees ($)	321.5	379.8	229.6
Pharmaceuticals ($)	77.3	16.2	18.8
Accommodation ($)	860.8	917.7	584.3
Median cost ($) (IQR)	**1856.6 (1,540-3,369)**	**1460.1 (1,144-3,612)**	**1,201.8 (943-2,138)**
Physicians' fees ($)	NA	NA	NA
Pharmaceuticals ($) (IQR)	234.8 (163-174)	12.8 (4-343)	6.2 (0-29)
Accommodation ($) (IQR)	866.5 (843-2,529)	843.1 (799-2,397)	684.7 (653-1,369)

[1] International Classification of Diseases ICD-10, T36-T50, poisoning by drugs, medicaments and biological substances
[2] All Patient Refined Diagnosis Related Group (APR-DRG) 812, poisoning by medicinal agents
[3] International Classification of Diseases ICD-10, T51-T65, toxic effects of substances chiefly nonmedicinal as to source
[4] All Patient Refined Diagnosis Related Group 816, toxic effects by non-medicinal substances

Discussion

The first aim of this study was to analyze the direct cost charged by GUH to the government and the patients in case of acute poisoning in 2017. This could be achieved by linking medical and financial records of 1,175 individual patients with poisoning in 2017, and to take into account the whole chain of hospital care, from ED to hospitalization. Furthermore, factors associated with the cost could be identified which was the second aim of our study. Finally, the third aim was achieved by putting a cost analysis in a broader perspective allowing comparison of the results of GUH 2017 with cost data of GUH 2016 and national data 2016 supplied by FPS Health.

Cost by type of hospitalization

		GUH	Muñoz	Krajewski	Okumara	Hendrix	Verelst	Senterre	national mean 2016
		Belgium	Spain	USA	Japan	Belgium	Belgium	Belgium	Belgium
		$	$	$	$	$	$	$	$
median	all types	511.6							
	ED-amb	199.1							
	ED-24h	574.8							
	Hosp	3,398.2							
	ICU	4,858.9							
	all types, T36-T50	2,400.2			1,803.3				
	Hosp, ICU, SOA & intentional self-harm	3,455.9						961.9	
mean	all types	1,588.2	850.2						
	ED-amb	238.2		3,819.7					
	ED-24h, Hosp, ICU	3,121.0	6,131.4	36,411.2					
	ED and ED-24h, self-poisoning	964.0				1,221.2			
	ED, ethanol	569.2				757.6			
	ED-24h, Hosp, ICU, T36-T50	1,236.1					777.0		777.0
	ED-24h, Hosp, ICU, T51-T65	1,259.6							832.7

Our study revealed a median and mean cost per episode of $511.6 and $1,588.2, respectively. The median cost was $199.1, $1,574.8, $3,398.2 and $4,858.9 for ED-amb, ED-24h, Hosp and ICU patients, respectively. The mean cost for an ED-amb patient was $238.2 (54.2% of patients) and $3,121.0 for a hospitalized patient (45.8% of patients: ED-24h, Hosp and ICU).

We made a comparison with international literature, as summarized in Table 4.

In Spain, Muñoz [1] found a lower mean cost per episode of $850.1, which may be due to a completely different proportion of hospitalization type: 88.8% ED-amb patients with a cost of $330.3 per case, and 11.2% hospitalized patients with a cost of $6,131.4 per case in the study of Muñoz. In the US (Illinois), Krajewski [2] mentioned hospital charges: a total mean charge for outpatients of $3,819.7 and $36,411.2 for inpatients. This much higher amount compared to our figures and those of Muñoz [1] may partly be explained by the fact that Krajewski estimated charges and not the payer's cost.

The median cost for hospitalized poisoned patients involving medicinal agents (T36-T50, poisoning by drugs, medicaments and biological substances) was $2,400.2 in our study. In Japan, Okumara [3] estimated direct medical cost for T36-T50 as the product of the annual number of discharged patients and median cost per episode, with results in the order of magnitude similar to ours: a median cost per episode of $1,808.3.

In Belgium, Verelst [21] estimated the mean ED-cost for ethanol poisoning at $757.6/patient. In our study, the mean cost of ED-amb and ED-24h visits was in the same order of magnitude: $505.8/patient (SD $569.2). Hendrix [22] calculated a mean ED-cost of $1,221.2 per patient for deliberate self-poisoning cases with inclusion of substances of abuse and intentional self-harm and with exclusion of alcohol as single drug. The mean cost/admission in our study was in the same order of magnitude, i.e. $964.0 (SD $2,832.4).

Based on MZG data of 13 Belgian hospitals for a self-inflicted injuries group, Senterre et al. [23] estimated a median cost borne by social security of $916.9 (IQR $772-1,423) for the hospital stay. In our study, median cost for SOA and intentional self-harm cases for inpatients (Hosp or ICU) was substantially higher i.e. $3,455.9 (IQR $2,611-4,562) with a median stay of 3 (IQR 2-4) days. This can possibly be explained by different factors. Senterre et al. used estimates instead of individual bills of patients as in our study. Also the median stay in their study was shorter than in ours (2 versus 3 days). Furthermore these authors only calculated the cost for the government while we also included the cost for the patient. Importantly and in contrast with our study, Senterre et al used the day lump sum for accommodation and nursing and did not take the fixed advanced financing of hospitals for accommodation and nursing into account while this amounts to 80% of the total sum which e.g. represents $842.6 in our study.

Factors associated with cost

It is evident that the type of hospitalization has a high impact on the cost. This is largely due to the cost related to the length of hospital stay: ED-amb patients could leave the ED after treatment and were not charged for

accommodation costs, ED-24h patients were charged for only one day, Hosp patients were staying for a mean of 3.6 and median of 3 (IQR) 2-4) days, and ICU patients for a mean of 7.6 and a median of 3 (IQR 2-6) days.

In the multivariate analysis, the cost for males is higher than the cost for females due to the fact that they had to stay more often in the hospital or the ICU than females. When looking at the degree of severity, it is not surprising that patients assessed with a very high degree of severity had a 40% higher cost than those assessed with a no risk profile. Indeed, 26 patients in the group with a very high degree of severity were admitted to the ICU, of which 17 had to stay for three or more days, with a mean cost of $8,974.8 per admission.

Comparison of the GUH data 2017 with guh data 2016 and national data 2016 from FPS Health

The mean cost per day in case of medicinal agents (T36-T50, $1,236.1) in our study is 59.1% higher than the national mean 2016 ($777.0). This is not surprising, as we know that the cost for accommodation and nursing accounts for 71.4% of total hospitalization cost. The accommodation and nursing amount is determined by the government according to the hospital pathology mix of Belgian hospitals. University hospitals have more highly specialized care. With a financed sum for accommodation and nursing of $842.6 per day, GUH belongs to the highest category of care weight mix. The mean amount fluctuates around $484 [30]. However, the total mean cost for medicinal agents is 23.2% lower, especially due to fewer hospitalization days in GUH 2017 (mean of 2.7 days) than in national data 2016 (5.2 days), and even fewer than in GUH 2016 (3.0 days). It is indeed well known that total cost is predominantly driven by length of stay [19]. One of the reasons could be that Ghent is a university city with many young patients generally recovering faster: the median age is 34 years (IQR 23-42) in GUH 2017 while the national median is 44 years (IQR 26-58). However, the median age in GUH 2017 for non-medicinal agents is 47 (IQR 38-57) versus 39 years (IQR 17-57). More data about the factor age are needed to draw conclusions, as these data were not confirmed by the GUH 2016 data, especially for non-medicinal agents. Another reason for shorter stays in GUH could be the presence of a team of experts in toxicology as has been argued by King [31] and by Legg [32] in their systematic review about inpatient toxicology services. Six of the seven reviewed papers demonstrated a reduction in overall hospital length of stay in the presence of a medical toxicology inpatient service.

Limitations and future perspective

This study provides only data and insight into the costs of poisoned patients in a university hospital, and may not be representative for all hospitals in Belgium.

We did not include pre- and post-hospital costs nor indirect costs of poisoned patients. The financial burden for patients, government and society is even

much larger when taking into account the loss of working days, disability-adjusted life years (DALYs), morbidity and mortality. Although great care was taken of completeness during the inclusion process, it is still possible that some patients admitted with poisoning were not identified.

Comparison of our figures with international cost data was hampered by the heterogeneity in inclusion criteria, other social security systems, and by the use of variable exchange rates, diverging purchasing power between different currencies, and the different costs of staff in other countries.

Use of a uniform template in future studies would facilitate comparison and allow better monitoring policies for cost-benefit analysis studies.

Conclusion

Poisonings consume a considerable cost charged by the hospital to the government and patients. It is evident that the type of hospitalization has a high impact on the cost, primarily due to the length of hospital stay, with accommodation accounting for a large proportion of the costs. It is important to compare individual hospital data with (inter)national data to evaluate one's own cost management but at present this proves difficult. In order to reach this goal it will be necessary (1) to do a meta-analysis of existing studies specifying the definition of cost and their method of cost calculation, and (2) to conduct a prospective study using a template in which all possible costs which can be charged are included.

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Supplementary files, data available in published article

S2.1 Text. Belgian system of the hospitalization cost charged by the hospital to the government and the patient, 2017.

S2.2 Figure. Structure of the payer's cost for patients admitted in the Emergency Department of the hospital with acute poisoning in Belgium, 2017.

S2.3 Figure. Structure of the payer's cost for hospitalized patients admitted with acute poisoning in Belgium, 2017.

S2.4 Table. Total, mean and median cost in EUROs of patients admitted for poisoning to Ghent University Hospital, 2017.

S2.5 Table. Comparison of the Ghent University Hospital data 2017 with Ghent University Hospital data 2016 and national data 2016 of the Technical Unit of FPS Health, in EUROs, Belgium, 2017.

Chapter 4 Article 3

Belgian Poison Centre impact on healthcare expenses of unintentional poisonings: a cost-benefit analysis

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Abbreviations

BPC: Belgian Poison Centre
ED: Emergency Department
ED-amb: Emergency Department-ambulatory-care
ED-24h: Emergency Department-24hours-observation
FPS: Federal Public Service
GP: General Practitioner
GUH: Ghent University Hospital
Hosp: Hospitalization
PCC: Poison Control Centre
US: United States.

Introduction

Cuts on public service

In difficult financial times, the public sector in general and poison control centers (PCC) in particular are often a target for budget cuts or stagnation of the allocated resources. PCCs in the US frequently underwent severe financial cuts with some centers even closing down [1-3] and others reducing the type and availability of their services [4].

Relevance of poison control centers

However, the relevance of PCCs has been demonstrated in many studies dealing with the financial impact of PCCs. A number of these studies investigated how many people with poisonings calling the PCC without need for further medical treatment would have used the Emergency Healthcare System in the absence of a PCC and what effect this would have had on the healthcare costs [5-11]. Some studies focused on the reduction of the length of stay with assistance of a PCC [12,13]. Other studies mentioned a reduction of unnecessary visits to emergency departments (ED) and associated hospital charges, and improved patient management [12, 14-16].

Economic evaluation consistently showing cost-saving results from poison control centers

In the USA, cost-benefit-ratios ranged from 1.40 to 36.00 in the presence versus absence of a PCC in poisoning cases not needing further medical treatment after PCC consultation [5-8, 10, 11]. The Lewin Group [4] calculated a return on investment running up to 13.39US$/case with 41.3% due to avoided medical utilization, 24.2% to reduced length of hospital stay, 1.3% to education and community outreach and 33.1% due to reduced work-loss days.

In Europe, Anell [17] (Sweden) calculated a cost-benefit-ratio of 1.05, while Toverud [18] (Norway) concluded that the PCC did not save money (cost-benefit-ratio 0.76) but provided safety.

Absence and need of a Belgian analysis of poison control centers

Probably because of the large variability between the structure and cost of healthcare systems in different countries, figures from PCCs are hardly interchangeable. Since studies in Europe are scarce and no cost-benefit data were available for Belgium, it seemed of interest to study the activities and financial impact of the BPC. Therefore, the aim of this study was to examine the cost-benefit of the Belgian Poison Centre (BPC) in the presence versus the hypothetical absence of the BPC.

Materials and methods

Target population and subgroups

A prospective telephone survey was carried out between February 23 and March 18, 2016. All calls to the BPC for unintentional poisonings coming from the general public were included. Calls from general practitioners (GP) and hospitals were excluded. Calls were also excluded if patients did not give informed consent to be called back, if physicians handling the calls felt it was inappropriate to call them back (e.g. for psychological reasons) or if the patients could not be reached after three attempts.

Setting and location

The BPC is a public foundation, funded by the Federal Public Service Health (FPS Health) in the context of emergency medical assistance. Physicians of the BPC give 24/7 toll-free telephone advice to lay persons and healthcare professionals in Belgium (approximately 11,303,528 inhabitants) [19] in cases of (suspected) toxic exposures. Thirteen physicians handled 57,400 calls in 2017, of which 7,685 were only requests for information. According to the risk assessment made by the physicians of the BPC, the advice given is either (1) to stay at home and/or advice on first aid, (2) to consult a GP (3) or to go to the hospital. Patients who were advised to go to the hospital were first assessed in the ED of the hospital.

During the survey period, seven 24-hour periods (8 am until 8 am) were randomly selected taking care that each day of a week was represented once. The advice given by the physician was registered at this initial call and patients were subsequently contacted during the days following the call, with a delay ranging between 2 and 8 days. During this follow-up contact, the person was asked (1) which action he/she had actually taken after having called the BPC and (2) what he/she would have done if the BPC would have been unavailable.

Study perspective

The hypothesis was that unavailability of the BPC would lead to substantial cost increases in case of calls from the public for unintentional poisonings as poisoning victims would unnecessarily use other, more expensive medical services.

Comparators

Two situations were compared in order to calculate the cost and benefit of both scenarios: (1) the flow of care of accidentally poisoned patients after having called the BPC, and (2) the estimated flow of care without availability of the BPC.

Time horizon

In order to ensure optimal comparability, data from 2017 were used to calculate the costs of the BPC, the GP and the hospital.

Choice of health outcomes

A cost-benefit analysis was performed as the measure of benefit (York Health Economics Consortium 2016).

Cost was defined as the payer's cost, i.e. the cost paid by the government and the patient. A call to the BPC is free of charges to the caller and is paid via the financial subvention of the BPC by the government. The cost charged by the GP and the hospital is partly paid by the government, through contributions from the mandatory Health and Disability Insurance, and partly paid by a personal fee by the individual patient.

The benefit was determined by the cost of the chosen strategy as a measure of the use of service. We did not use natural units of effects like avoided harm and injuries.

Measurement of effectiveness

The results of the survey were used (1) to check – in the presence of the BPC - whether the advice given by the experts of the BPC was actually followed (stay at home, consult a GP, go to the hospital), and (2) to estimate – in the absence of the BPC - the proportion of patients who declared to have done nothing, to consult a GP or to go to the hospital.

A retrospective record review involving all poisoning-related episodes of patients admitted to the ED of Ghent University Hospital (GUH) in 2017 was used to estimate the proportion of patients with unintentional poisoning (accidental poisoning and use of substances of abuse) being referred by a GP to the hospital.

The same source was used to estimate the proportion of patients who (1) were ambulatory (ED-amb), (2) who had to stay in the ED for observation (ED-24h) and (3) who were hospitalized (Hosp). More information can be found In Supplementary Files S3.1 and S3.2..

Estimating resources and costs

The cost/call to the BPC was calculated by taking 70% of the governmental subsidies divided by the total number of calls in 2017.

The cost of a GP's consultation was obtained from the National Health and Disability Insurance Service "Rijksdienst voor Ziekte- en Invaliditeitsverzekering" [20] taking into account extra fees for out-of-hours-consultations. The direct cost for ED-amb, ED-24h and Hosp was abstracted from the invoices of the patients admitted with unintentional poisoning or use of substances of abuse to the ED of GUH in 2017.

Currency, price date, and conversion

Costs were expressed in EUR (€1 = US$1.17, December 2017).

Choice of the model

A decision tree was used as a tool to identify a model of decisions and their related financial outcomes [21, 22]. Cost presented is given as about weighted averages, depending on the probabilities and pay-offs of the followed pathways in the decision tree.

Assumptions

The assumption was made – based on the information of the survey - that callers followed the advice given by the BPC, and that callers – in the absence of the BPC – would really do what they declared in the survey.

We also assumed that the probability of patients being referred by the GP to the ED was the same as in the poisoning data 2017 of GUH. Another assumption was that the proportion of ED-amb, ED-24h and Hosp was the same all over the country as in GUH.

Analytical methods

A first sensitivity analysis was conducted assuming the hypothetical situation in which GPs would not send a single patient to the hospital and in which all ED-patients would receive only ambulatory treatment. A second sensitivity analysis was made using the same assumptions but applying an even more conservative financial scenario, i.e. by using median cost values instead of average cost values.

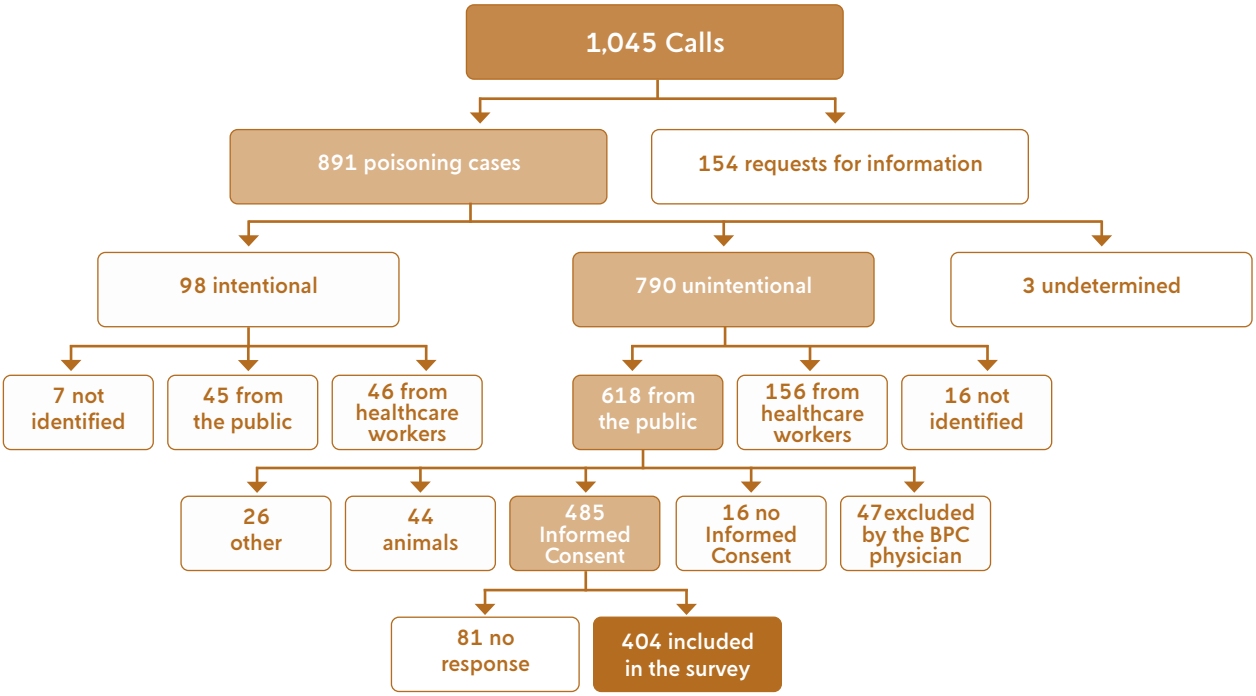
The study protocol was approved by the Ethical Committee of GUH on February 16, 2016. Data-analysis was performed using Microsoft Excel 2013 and SPSS 25.0 (IBM®).

Results

Study parameters

During the study period the BPC received 1,045 calls of which 891 (85.3%) were for actual poisoning cases and 154 (14.7%) only requests for information (Figure 1). Intentional and unintentional poisonings were involved in 98 (11.0%) and 790 (88.7%) cases respectively. In the latter group, 618 calls came from the general public. Informed consent for participating in the telephone survey was obtained from 485 callers, of which 404 (83.3%) could subsequently be contacted.

Fig 1. | Characteristics of calls to the Belgian Poison Centre and number of patients with unintentional poisoning included in the survey, Belgium, 2016



According to the initial BPC advice given during the first call, 90.1% should not have sought further medical help, 5.4% had to consult a GP and 4.5% had to go to a hospital (Table 1). From the subsequent telephone survey, it appeared that after having called the BPC 92.1% did not seek any other medical help, 4.2% consulted a GP and 3.7% went to the hospital. When confronted with a hypothetical absence of the BPC 13.8% of the callers would not have sought any help , 49.3% would have contacted the GP and 36.9% would have gone to the hospital. From the figures of GUH, we estimated that 3.5% of ED-patients were referred by the GP and that 71.0% of these patients would have left the ED after consultation, 20.1% would have had to stay in the ED for a 24h-observation and 8.9% would have been admitted to the hospital respectively.

Table 1. | Advice of the Belgian Poison Centre, patient's decision and further referral under circumstances of Belgian Poison Centre1 availability or hypothetical unavailability, Belgium, 23 Feb-18 March 2016

Medical help	Total	Estimated further referral[1]		
	n (%)		%	n (%)
Patients decision in the presence of the Belgian Poison Centre				
No further medical help	372 (92.1)	Home	100.0	372 (92.1)
General practitioner	17 (4.2)	General practitioner	96.5	16 (4.1)
		Hospitalization	3.5	1 (0.1)
Hospital	15 (3.7)	Emergency department ambulatory care	71.0	11 (2.6)
		Emergency department 24-hours observation	20.1	3 (0.7)
		Hospitalization	8.9	1 (0.3)
TOTAL	*404 (100.0)*			*404 (100.0)*
Patients decision in the hypothetical absence of the Belgian Poison Centre				
No further medical help	56 (13.9)	Home	100.0	56 (13.9)
General practitioner	199 (49.3)	General practitioner	96.5	192 (47.5)
		Hospitalization	3.5	7 (1.7)
Hospital	149 (36.9)	Emergency department ambulatory care	71.0	106 (26.2)
		Emergency department 24-hours observation	20.1	30 (7.4)
		Hospitalization	8.9	13 (3.3)
TOTAL	*404 (100.0)*			*404 (100.0)*

[1] The proportions of further referrals are derived from the invoices of poisoned (unintentional and SOA) patients in Ghent University Hospital, Belgium, 2017

Costs and outcomes

The BPC received a 2017 funding from the government of €2,044,930 per year, of which €1,431,451 was assigned to phone consulting. Considering 57,400 phone calls in 2017, the average cost per call was €24.94. The average cost for consulting a GP was €36.11 of which €30.28 was reimbursed by the government and €5.83 was paid by the patient (cost sharing).

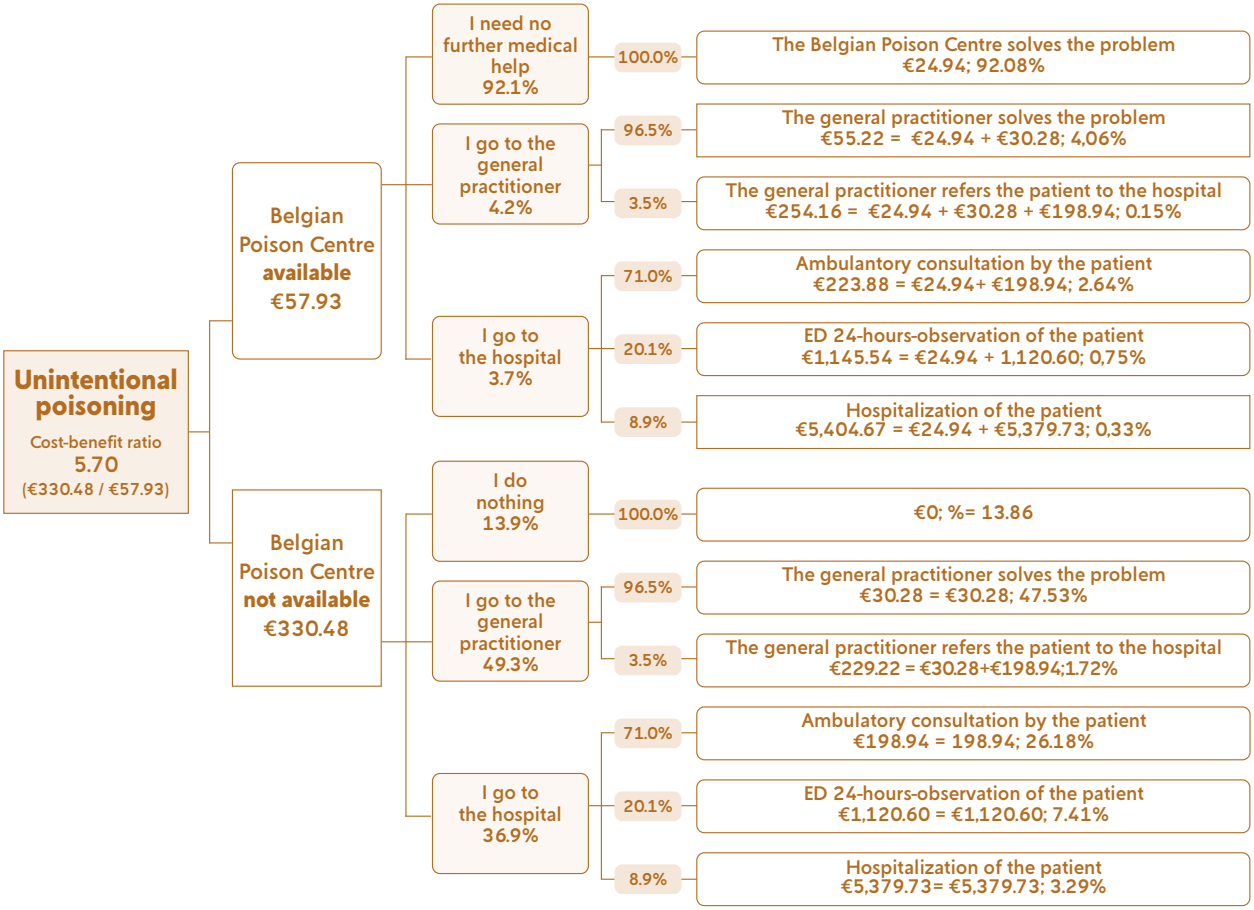
The average cost for the government in 2017 for GUH services, based on the analysis of 796 patients, was

€198.94 (CI 95%: €186.77-211.10) for ED-ambulatory-consultation, €1,120.60 (CI 95%: €1,060.06-1,181.15) for ED-24-hours-observation and €5,379.73 (CI 95%: €3,792.19-6,967.27) for hospitalization (total episode). GUH median cost was €166.19, €1,068.19 and €2,981.06 respectively.

Cost-benefit analysis

In the presence of the BPC, the estimated average weighted cost was €57.93 as compared with €330.48 without BPC (Figure 2).

Fig 2. | Decision tree for unintentional poisonings in the presence or hypothetical unavailability of the Belgian Poison Centre for calls from the public, Belgium, 2016



The cost-benefit-ratio amounts to 5.70 (€330.48/€57.93). Taking into account an average of 35,107 calls per year from the general public for unintentional poisoning to the BPC in 2017, this corresponds with an estimated saving for the government of €9,568,338.55/year.

CHARACTERISING UNCERTAINTY

In the hypothetical and unlikely situation in which not a single patient would be sent to the hospital by the GPs and in which all patients who went to the hospital would only receive ambulatory treatment, a cost-benefit-ratio of 2.55 (€88.29/€33.60) was found. In an even more conservative scenario using the same assumption as in the first analysis and using median values instead of average values, a cost-benefit-ratio of 2.34 (€75.57/€32.30) was estimated.

Discussion

Summary and interpretation of findings

The aim of this study was to make an economic evaluation of two alternatives in case of unintentional poisonings, i.e. in the presence or absence of the BPC. Our data indicate an estimated positive cost-benefit-ratio in the presence of the BPC of 5.70. Furthermore, we performed two sensitivity analyses. Even with these very conservative hypothetical situations which presumably underestimate the real cost savings, the estimated cost-benefit-ratios were still positive (2.55 and 2.34 respectively).

The proportion of ED-amb, ED-24h and Hosp were estimated based on the analysis of all patients with unintentional poisoning admitted to GUH in 2017.

Limitations

A first limitation is that, when considering the BPC ratio of 5.70, we should keep in mind that our ratio may lack accuracy as some assumptions have been made. It is difficult to extrapolate whether people, in real life confronted with poisoning in the absence of the BPC, would have taken the same decision as what they had answered in the survey.

Therefore, we performed two sensitivity analyses. The first hypothetically reduced to zero the number of patients sent by the GPs to the hospital and the number of ED-patients who had to go for an ED-24h or Hosp. The second sensitivity analysis applied an even more conservative financial scenario using median cost values instead of average cost values. Even with these very conservative hypothetical situations which

presumably underestimate the real cost savings, the cost-benefit-ratios were still positive (2.55 and 2.34 respectively).

A second limitation is that, although the response rate in our survey was high (83.3% i.e. 404/485), we should keep in mind that the study period was limited to seven days and restricted to winter time.
A third limitation is that we had to estimate the proportion of ED-patients being referred by the GP using admission data for poisoning of GUH. This proportion has to be checked with a larger number of hospitals and with data from GPs to validate these assumptions.
A fourth limitation is that the type of poisoning of patients calling the BPC and those consulting the GP or the ED were not analyzed. It is clear that further research is needed to have more detailed insight in the degree of similarity and differences between those patient groups and the related costs.

Research in context of current evidence

Many studies demonstrated that PCCs reduce healthcare expenses by avoiding inappropriate use of other medical services.

In our analysis, without BPC, 86.2% would have searched help from a healthcare professional (GP or hospital), which is in the same range as 79% of the study of Kearney [6] and 70% (37% Emergency Medical Services and 33% ED) in the study of LoVecchio [8]. It is also noteworthy that in our study an estimated 13.8% of the patients would not have sought any help in the absence of the BPC. Blizzard [5] and Kearney [6] mention figures of 21% and 63% respectively. Although not analyzed in detail and restricted by the limited number of patients in our survey, this indicates an increased risk of undertreatment in cases of serious poisoning when a low threshold consult of a PCC would not be available. It is clear that future research is needed to analyze the natural units of effects like harm of dangerous poisonings that are left untreated, morbidity and mortality.

Cost benefit-ratios reported in the literature vary between 0.76 and 36 [4-11]. When interpreting these ratios it should be kept in mind that there are important differences between these studies such as divergent types of economic evaluations, differences in the collection of data and heterogeneity of healthcare systems.

Some studies analyzed the costs and benefits in the presence versus absence of a PCC only in cases of poisoning *not needing further medical treatment* [5-8, 10, 11]. Our study, on the other hand, was not limited to unintentional poisonings not needing further medical treatment.

Three cost-benefit studies in the literature used, like in our study, *a telephone survey* [5, 6, 8], three other studies used only *data-analysis* without survey [4, 9, 11] and two set up an *experiment* by restricting public access to the PCC [7, 10]. Two of the three authors who conducted a telephone survey [5, 6] for poisoning cases without further medical treatment, calculated a cost-benefit-ratio of respectively 7.67 and 5.3. Although methodologically not entirely comparable with our study, the cost-benefit-ratio of 5.70 found by

us for BPC is in the same range (as reported by these authors). In contrast, LoVecchio et al. (2008) found a much higher ratio of 36. This difference can probably be explained by the calculated cost for an ED-visit used in his study which is much higher (US$1,152) than the average cost used in our study (€198.94).

In Norway in Europe, Anell [17] and Toverud [18] presented a *cost-benefit-ratio* of respectively 1.05 and 0.76, which is substantially lower than in our study. However, it should be noted that they included all calls to the PCC also including intentional poisonings, resulting in a higher proportion of patients sent to the hospital in the presence of the BPC.

It should be mentioned that the BPC contributes to avoiding the negative aspect of overcrowding in EDs resulting in less time left for high-quality care for the most severely ill patients. As in other countries in the world, Belgian EDs are under heavy public demand. A report of *The Belgian Healthcare Knowledge Centre* (KCE) [23] states that the number of ED contacts increased from 3,006,321 to 3,195,897 between 2009 and 2012, especially because of the increase of ambulatory care visits. Our study estimated that without BPC, an estimated shift of workload from the BPC to the GP (49.3%) and the ED (36.9%) would occur, thus adding to the burden and associated risks of overcrowding in those medical services.

Concisely answer the objective

The aim of the telephone triage by the physicians of the BPC is to guide patients to the appropriate care, and this in a qualitative and cost-efficient way. In the absence of the BPC, it seems that victims of unintentional poisoning would inappropriately use other, more expensive medical services, such as physician's consultations and hospital use. This represents an estimated cost-benefit-ratio of 5.70. In terms of avoided costs for the Belgian government this represents an estimated saving of €9,568,339 in 2017 for unintentional poisonings. All key parameters were validated by a telephone survey of 404 patients who called the BPC and by the cost analysis of the individual invoices of 796 patients with unintentional poisoning admitted with unintentional poisoning to a university hospital in 2017. Therefore, patients have to be sensitized by policy makers to first call the Poison Centre in case of unintentional poisoning.

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Supplementary files, data available in published article

S3.1 Figure. Flowchart of the proportion of poisoning cases referred by a general practitioner or physician among the poisoning cases that occurred in Ghent University Hospital in 2017.

S3.2 Figure. Flowchart of the proportion of ED-ambulatory cases, ED-24h cases and Hospitalizations among the poisoning cases that occurred in Ghent University Hospital in 2017.

Chapter 5

Article 4

Hospital referrals of patients with acute poisoning by the Belgian Poison Centre: analysis of characteristics, associated factors, compliance, and costs

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Abbreviations

AIC: Akaike Information Criterion
BPC: Belgian Poison Centre
ED: Emergency Department
FPS Health: Federal Public Service Health
GDPR: General Data Protection Regulation
GUH: Ghent University Hospital
Hosp-watchful-wait: watchful waiting, referral in case of deterioration
Hosp-referral: referral to a hospital
Hosp-urgent-referral: urgent referral to a hospital
ICD-10: International Classification of Diseases, version 10
ICU: Intensive Care Unit
NSAIDs: Non-Steroidal Anti-Inflammatory Drugs
OR: Odds Ratio
STROBE: Strengthening the Reporting of Observational Studies in Epidemiology
WHO: World Health Organization.

Introduction

Poisoning is an important social problem with a considerable impact on clinical workload and expenses. One can expect that an expertise centre in toxicology such as a poison centre will guide the patient confronted with suspected poisoning to the most appropriate level of care in an efficient and safe way. Speed, competence and appropriate triage are key factors in this process. In 2017, 19.3% of the patients for whom the Belgian Poison Centre (BPC) was called were given the advice to go (conditionally) to the hospital [1].

In 2018, the BPC switched from paper sheets to electronic data forms, used by the calltakers during a telephone call making it possible to distinguish between three types of hospital referral: (1) patients referred conditionally to the hospital, i.e. in case of appearance of symptoms or clinical deterioration, staying at home with watchful waiting (Hosp-watchful-wait), (2) patients immediately referred to the hospital (Hosp-referral), and (3) patients urgently referred to the hospital (Hosp-urgent-referral). Before 2018, all these cases were categorized as "hospitalization". A further specification of the type of referral to the hospital is important, as we want to investigate the characteristics and compliance with the BPC advice in each group. Compliance data are needed to estimate the health-economic impact of hospital referrals which can be substantial [2-13]. In order to estimate this cost, we only can take into account the cost of the patients who were compliant with the BPC advice, as this can give a more accurate indication of the cost charged to the government and the patient.

As far as we know, there are no studies focusing on the link between characteristics, associated factors, compliance and costs of patients with poisoning advised by a poison centre to go (conditionally) to the hospital. Therefore, aims of this study were (1) to assess the characteristics and associated factors of patients with acute poisoning advised by the BPC to go (conditionally) to the hospital, and (2) to assess the compliance and potential health-economic impact of referral advice.

Materials and methods

We used the "Strengthening the Reporting of Observational Studies in Epidemiology" STROBE Statement as a guideline for reporting [14].

Study design and setting

Medical doctors and pharmacists of the Belgian Poison Centre (BPC) provide 24/7 toll-free telephone advice in cases of suspected toxic exposures to both lay persons and healthcare professionals in Belgium and the Grand Duchy of Luxembourg. After risk assessment, the advice for patients who are not in the hospital

already is either (1) to stay at home and apply first aid when appropriate, (2) to consult a medical doctor, (3) to go to the hospital when symptoms appear or the condition worsens (Hosp-watchful-wait), (4) to go immediately to the hospital (Hosp-referral), or (5) to go urgently to the hospital (Hosp-urgent-referral).

Patients who are in the hospital already and for whom the BPC is called, are excluded from the analysis. The BPC advice on the type of referral is noted in a BPC electronic medical report and is a decision based on the calltaker's assessment having access to different toxicology databases. Strict protocols are used for some specific poisons like paracetamol and toxic alcohols. The BPC does not use the Poison Severity Score (PSS).

When in hospital, patients are assessed in the ED, and subsequently either (1) discharged home (ED-amb), (2) observed in the ED 24-hours-observation unit (ED-24h), (3) hospitalized (Hosp), or (4) admitted to the intensive care (ICU).

Participants

In the first part of the study, we included all calls to the BPC between 1 January and 30 June 2018 where patients were advised for Hosp-watchful wait, Hosp-referral or Hosp-urgent-referral. Calls for patients who were in the hospital already were excluded. Recalls to the BPC for the same patient were regarded as the same case and only counted once.

Between 1 March and 15 May 2019, we conducted the second part of the study which was a prospective telephone survey on patients who had received one of the three types of referral advice to estimate the compliance with the BPC advice to go (conditionally) to the hospital. The same inclusion criteria were used in analysis 1 and 2, except that calls for intentional self-harm, malicious behaviour and "intentional cases, not specified" were excluded in the telephone survey, as it was considered inappropriate to call back. We randomly selected 60% of the remaining calls for calling back in chronological order, with stratification by referral groups (distribution of Hosp-watchful-wait, Hosp-referral and Hosp-urgent-referral representative for the whole study population). Cases were excluded when three attempts for contact failed. The flowchart of the telephone survey is presented in Supplementary File S4.1.

In both analyses we included the Hosp-watchful-wait category because we wanted to investigate which proportion actually went to the hospital. If only a limited number went to the hospital, the inclusion of this category in the total number of patients advised to go to the hospital by the BPC, would lead to an overestimation of the number of effective hospital referrals.

Variables and data sources

In the first analysis, the electronic data forms filled in by the BPC medical doctor/pharmacist during or immediately after the call were used. These contained information on caller and victim, their location, symptoms, circumstances,

agent(s) involved, route of exposure, location, advice for examinations and treatment.

Patients included in the survey were asked if they were compliant with the BPC referral advice and what type of care they had received. When they went to the hospital, it was noted whether they were treated as ED-amb-, ED-24h-, Hosp- or ICU patients, as well as the length of their stay.

Cost was defined as the payer's cost charged by the hospital to the government and the patient. The cost per call to the BPC, the cost of a doctor's consultation and the cost per admission to the hospital was derived from previously published data [2, 15], where information on the financing of the Belgian healthcare cost can be found.

Study size

In analysis 1, the number of patients referred (conditionally) to the hospital by the BPC between 1 January and 30 June 2018 determined the sample size. In analysis 2, the number of patients reached during the survey period (1 March- 15 May 2019) determined the sample size. Our goal was to reach a representative sample of 500 callers.

Quantitative variables

Agents involved in the BPC cases were based on patients' electronic medical reports filled in by the BPC calltakers and grouped by a pharmacist (JVB) and one of the authors (AMD) according to the World Health Organisation (WHO) International Classification of Diseases ICD-10 [16]. Categories are T36-T50 (poisoning by drugs, medicaments and biological substances) and T51-T65 (toxic effects of substances chiefly nonmedicinal as to source) [17]. Symptoms were grouped according to the emergency registration system for hospital EDs [17].

Statistical methods

Chi-Square or Fisher's Exact Test were used to compare frequencies. Univariate analysis was used to identify variables possibly associated with the advice for the hospital referral type, followed by a multivariate logistic regression model for the variables achieving a statistically significant association and for variables considered as clinically relevant. The step by step procedure was used to retain the variables that significantly contributed to the model. We applied Bonferroni correction (n=9) by adjusting the alpha-level to 0.05/9 [18]. The Akaike Information Criterion (AIC) was used to compare the quality of the models. Analyses were performed using SPSS 25.0 (IBM®).

Ethical considerations

The anonymized BPC data was analyzed according to the General Data Protection Regulation (GDPR) guidelines of the BPC [19]. For the survey, informed consent was asked during the initial call.

Results

Demographics and characteristics of the patients

In analysis 1, 26,406 cases were handled of which 5,476 fulfilled the inclusion criteria. As shown in Figure 1, 43.2% were Hosp-watchful-wait cases, 48.9% Hosp-referrals and 7.9% Hosp-urgent-referrals.

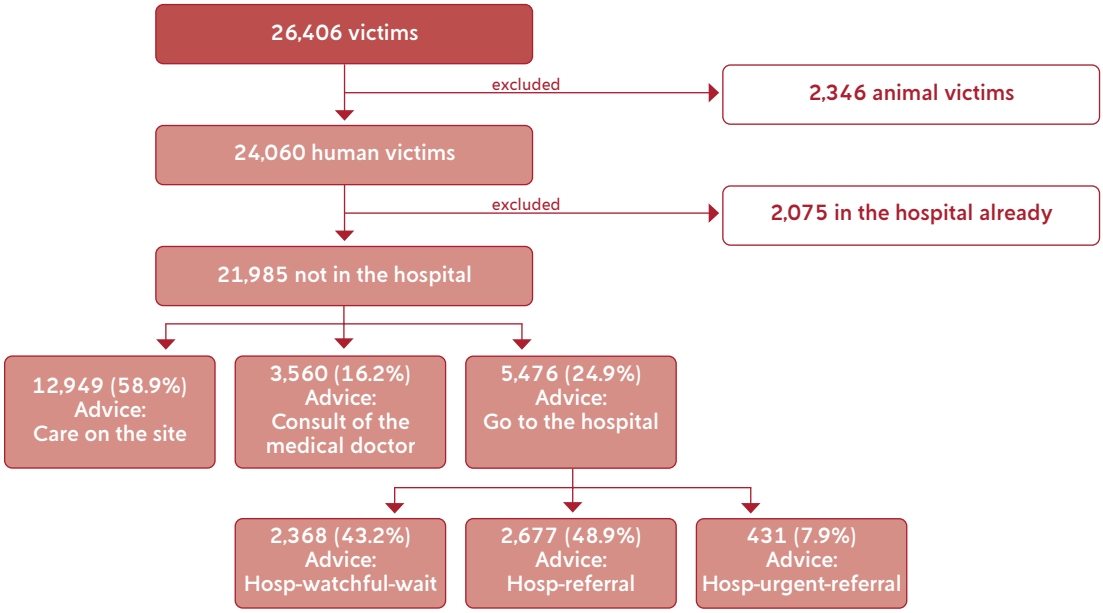

Fig 1. | Flowchart of the selection of Hosp-watchful-wait victims, Hosp-referral victims and Hosp-urgent referral victims collected between 1 January and 30 June 2018 in the Belgian Poison Centre.

Demographic data are presented in Table 1. Fifty-two percent came from family members and 16.0% from the victim (Table 1). In 20.2% the call was made by a medical professional. Almost half of the calls (49.8%) were received between 8am and 6pm. At the moment of the call, 86.4% of the victims were at home.

Table 1. | Demographic data and characteristics of patients advised to go (conditionally) to the hospital, categorized by hospital referral type.

	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value[2]
	n=5,476	n=2,368	n=2,677	n=431	
	%	%	%	%	
Gender					**<0.001**
Male	2,367 (45.8)	1,131 (50.3)	1,087 (43.2)	149 (37.0)	
Female	2,802 (54.2)	1,116 (49.7)	1,432 (56.8)	254 (63.0)	
Total	*5,169 (100.0)*	*2,247 (100.0)*	*2,519 (100.0)*	*403 (100.0)*	
Age					**<0.001**
Child <14y	2,360 (43.1)	1,444 (61.0)	822 (30.7)	94 (21.8)	
Adult >=14y	3,116 (56.9)	924 (39.0)	1,855 (69.3)	337 (78.2)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Time of the day					**<0.001**
8 am-6 pm	2,728 (49.8)	1,307 (55.2)	1,249 (46.7)	172 (39.9)	
6 pm- 12 am	2,407 (44.0)	989 (41.8)	1,201 (44.9)	217 (50.3)	
12 am- 8 am	341 (6.2)	72 (3.0)	227 (8.5)	42 (9.7)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Language					**<0.001**
French	3,259 (59.5)	1,287 (54.3)	1,678 (62.7)	294 (68.2)	
Dutch	2,200 (40.2)	1,071 (45.2)	993 (37.1)	136 (31.6)	
Other	17 (0.3)	10 (0.4)	6 (0.2)	1 (0.2)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Caller					**<0.001**
Family	2,862 (52.3)	1,601 (67.6)	1,097 (41.0)	164 (38.1)	
Victim	876 (16.0)	397 (16.8)	423 (15.8)	56 (13.0)	
General practitioner/ physician	480 (8.8)	54 (2.3)	368 (13.7)	58 (13.5)	
Other medical caregiver	422 (7.7)	105 (4.4)	265 (9.9)	52 (12.1)	

	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value[2]
	n=5,476	n=2,368	n=2,677	n=431	
	%	%	%	%	
Others	420 (7.7)	122 (5.2)	227 (8.5)	71 (16.5)	
Emergency medical dispatcher	202 (3.7)	14 (0.6)	165 (6.2)	23 (5.3)	
Profession other than medical	169 (3.1)	71 (3.0)	94 (3.5)	4 (0.9)	
Police/firefighter	45 (0.8)	4 (0.2)	38 (1.4)	3 (0.7)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Victim location					**<0.001**
Home	4,734 (86.4)	2,113 (89.2)	2,270 (84.8)	351 (81.4)	
Institute[1]	392 (7.2)	163 (6.9)	194 (7.2)	35 (8.1)	
Working place	136 (2.5)	46 (1.9)	83 (3.1)	7 (1.6)	
Physicians practice/ pharmacy	69 (1.3)	23 (1.0)	43 (1.6)	3 (0.7)	
Public place	49 (0.9)	12 (0.5)	26 (1.0)	11 (2.6)	
Other	52 (0.9)	8 (0.3)	36 (1.3)	8 (1.9)	
Mobile intervention unit	44 (0.8)	3 (0.1)	25 (0.9)	16 (3.7)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	

[1] Senior care facility, psychiatric care institution or school
[2] p-value: Chi-square and Fisher's exact test

Type of poisoning and advice given

As shown in table 2, 72.4% of calls were accidental, 25.3% intentional self-harm, 1.2% substance abuse and 1.1% of uncertain intentionality. In Hosp-watchful-wait cases, 93.9% were accidental of which 92.7% were single agent exposures. In 69.0% of these accidental cases, no symptoms were reported at the time of the call. In symptomatic cases, 39.6% concerned complaints of dermatological, ophthalmological or otorhinolaryngological nature.

In Hosp-referral cases, 58.5% were accidental and 38.5% intentional self-harm. The most common symptoms were dermatological, ophthalmological or otorhinolaryngological complaints (22.0%), a change in consciousness (18.6%), and nausea or vomiting (11.4%). The in-hospital administration of activated charcoal or an antidote was advised in 1.9%.

In Hosp-urgent-referral cases, 54.1% were for intentional

self-harm, 24.4% involved exposure to two or more agents and 28.3% suffered from a change in consciousness. Calling for a mobile intensive care unit was advised in 65.7% of these. Referral for antidote administration was advised in 3.2%.

Table 2. | Types of poisoning, presenting symptoms, diagnostic investigations and management advice of patients to go (conditionally) to the hospital, categorized by hospital by hospital referral type.

	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value[4]
	n=5,476	n=2,368	n=2,677	n=431	
	%	%	%	%	
Intentionality					**<0.001**
Accidental (unintentional)	3,964 (72.4)	2,224 (93.9)	1,567 (58.5)	173 (40.1)	
Intentional self-harm	1,384 (25.3)	121 (5.1)	1,030 (38.5)	233 (54.1)	
Use of substances of abuse	66 (1.2)	11 (0.5)	45 (1.7)	10 (2.3)	
Unclear intentionality	62 (1.1)	12 (0.5)	35 (1.3)	15 (3.5)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Number of agents involved					**<0.001**
1	4,675 (85.4)	2,195 (92.7)	2,154 (80.5)	326 (75.6)	
2	522 (9.5)	130 (5.5)	324 (12.1)	68 (15.8)	
>=3	279 (5.1)	43 (1.8)	199 (7.4)	37 (8.6)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Type of agents involved					**<0.001**
T51-T65	2,491 (45.5)	1,469 (62.0)	904 (33.8)	118 (27.4)	
T36-T50	2,641 (48.2)	784 (33.1)	1,581 (59.1)	276 (64.0)	
T36-T50 & T51-T65	344 (6.3)	115 (4.4)	192(7.2)	37 (8.6)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Patient transport					**<0.001**
Ambulance	264 (63.3)	18 (66.7)	237 (66.8)	9 (25.7)	
Mobile Intensive Care Unit	136 (32.6)	1 (3.7)	112 (31.5)	23 (65.7)	
By own means	17 (4.1)	8 (29.6)	6 (1.7)	3 (8.6)	
Total	*417 (100.0)*	*27 (100.0)*	*355 (100.0)*	*35 (100.0)*	

	Total n=5,476 %	Hosp-watchful-wait n=2,368 %	Hosp-referral n=2,677 %	Hosp-urgent-referral n=431 %	p-value[4]
Route of exposure					**<0.001**
Oral/oromucosal	4,334 (79.1)	1,829 (77.2)	2,125 (79.4)	380 (88.2)	
Cutaneous/eye	539 (9.8)	240 (10.1)	278 (10.4)	21 (4.9)	
Inhalation	344 (6.3)	154 (6.5)	170 (6.4)	20 (4.6)	
>1 route	138 (2.5)	94 (4.0)	41 (1.5)	3 (0.7)	
Other/unknown[1]	121 (2.2)	51 (2.2)	63 (2.4)	7 (1.6)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Presenting symptoms[2]					
Dermatological or, ophthalmic problems, otorhinolaryngological complaints	851 (25.6)	345 (39.6)	458 (22.0)	48 (13.1)	0.02
Changes in consciousness	549 (16.5)	57 (6.5)	388 (18.6)	104 (28.3)	<0.001
Nausea and/or vomiting	368 (11.1)	103 (11.8)	238 (11.4)	27 (7.4)	<0.001
Respiratory problems	276 (8.3)	109 (12.5)	140 (6.7)	27 (7.4)	0.105
General malaise	190 (5.7)	20 (2.3)	137 (6.6)	33 (9.0)	<0.001
Behavioural and emotional disorders	173 (5.2)	41 (4.7)	116 (5.6)	16 (4.4)	0.053
Other	157 (4.7)	38 (4.4)	86 (4.1)	33 (9.0)	0.287
Tremor, coordination disorders	129 (3.9)	15 (1.7)	89 (4.3)	25 (6.8)	<0.001
Abdominal pain	120 (3.6)	23 (2.6)	89 (4.3)	8 (2.2)	0.011
Dizziness, vertigo	89 (2.7)	19 (2.2)	63 (3.0)	7 (1.9)	<0.001
Headache	78 (2.3)	17 (1.9)	57 (2.7)	4 (1.1)	<0.001
Pain in limbs, neck, back shoulder and pelvic belt	62 (1.9)	28 (3.2)	32 (1.5)	2 (0.5)	0.003
Signs of neurological failure	44 (1.3)	8 (0.9)	30 (1.4)	6 (1.6)	<0.001

	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value[4]
	n=5,476	n=2,368	n=2,677	n=431	
	%	%	%	%	
Palpitations	39 (1.2)	3 (0.3)	30 (1.4)	6 (1.6)	<0.001
Diarrhoea	27 (0.8)	8 (0.9)	19 (0.9)	0 (0.0)	0.956
Wound, bite, sting	24 (0.7)	11 (1.3)	11 (0.5)	2 (0.5)	0.001
Fever and convulsion	23 (0.7)	5 (0.6)	16 (0.8)	2 (0.5)	0.104
Retrosternal and thoracic pain	17 (0.5)	3 (0.3)	14 (0.7)	0 (0.0)	<0.001
External signs of bleeding or bleeding	15 (0.5)	1 (0.1)	13 (0.6)	1 (0.3)	0.003
Life-threatening situation	8 (0.2)	0 (0.0)	5 (0.2)	3 (0.8)	<0.001
Urinary problems	5 (0.2)	0 (0.0)	4 (0.2)	1 (0.3)	<0.001
All kinds of non-specific, generalized symptoms	78 (2.3)	18 (2.1)	48 (2.3)	12 (3.3)	<0.001
Total	*3,322 (100.0)*	*872 (100.0)*	*2,083 (100.0)*	*367 (100.0)*	
Number of symptoms present					**<0.001**
0 symptoms	2,929 (53.5)	1,635 (69.0)	1,140 (42.6)	154 (35.7)	
1 symptom	1,933 (35.3)	610 (25.8)	1,115 (41.7)	208 (48.3)	
2 symptoms	483 (8.8)	110 (4.6)	321 (12.0)	52 (12.1)	
>= 3 symptoms	131 (2.4)	13 (0.5)	101 (3.8)	17 (3.9)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Laboratory testing advised					**<0.001**
No	5,145 (94.0)	2,343 (98.9)	2,439 (91.1)	363 (84.2)	
Yes	331 (6.0)	25 (1.1)	238 (8.9)	68 (15.8)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Medical imaging advised					**<0.001**
No	5,298 (96.7)	2,358 (99.6)	2,523 (94.2)	417 (96.8)	
Yes	178 (3.3)	10 (0.4)	154 (5.8)	14 (3.2)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	

	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value[4]
	n=5,476	n=2,368	n=2,677	n=431	
	%	%	%	%	
Monitoring vital signs advised					**<0.001**
No	5,085 (92.9)	2,326 (98.2)	2,396 (89.5)	363 (84.2)	
Yes	391 (7.1)	42 (1.8)	281 (10.5)	68 (15.8)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	
Antidotes advised[3]					**<0.001**
No	5,406 (98.7)	2,362 (99.7)	2,627 (98.1)	417 (96.8)	
Yes	70 (1.3)	6 (0.3)	50 (1.9)	14 (3.2)	
Total	*5,476 (100.0)*	*2,368 (100.0)*	*2,677 (100.0)*	*431 (100.0)*	

[1] Otic, rectal, subcutaneous
[2] Total number of 3,322 symptoms as mentioned by the caller
[3] N-acetylcysteine (47.1%), activated charcoal (14.3%), oxygen (11.4%), flumazenil (7.1%), glucagon (4.3%), atropine (2.9%), calcium gluconate (2.9%), ethanol (2.8%), deferoxamine (1.4%), digoxin fab fragments (1.4%), hydroxocobalamin (1.4%), naloxone (1.4%)
[4] p-value: Chi-square and Fisher's exact test

Agents involved

Among the 5,476 cases handled, 6,778 agents were involved (Table 3). Soaps and detergents (13.0%), benzodiazepines (11.6%), corrosive substances (8.1%), agents primarily affecting skin, mucous membranes and ophtalmological, otorhinolaryngological and dental drugs (7.4%), antidepressants (6.8%) and antipsychotics (5.9%) were most common, followed by alcohol (5.3%, of which 4.2% ethanol), pesticides (4.5%), and paracetamol (4.2%).

In Hosp-watchful-wait cases, soaps and detergents were represented most (22.8%), followed by agents primarily affecting the skin, mucous membranes or ophtalmological, otorhinolaryngological and dental drugs (9.0%) and by noxious substances eaten as food (8.3%). In Hosp-referral cases, benzodiazepines (16.9%), antidepressants (10.6%) and antipsychotics (8.9%) were most frequently involved. In Hosp-urgent-referral cases, benzodiazepines (20.6%), antidepressants (10.4%) and paracetamol (10.0%) were most common.

Table 3. | Agents involved in calls for acute poisoning to the BPC between 1 January and 30 June 2018, categorized by hospital referral type.

ICD-10	Agents[1]	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value
		n (%)	n (%)	n (%)	n (%)	
T42	**Anti-epileptic, sedative-hypnotic, antiparkinsonism drugs**	**789(14.4)**	**143(6.0)**	**535(20.0)**	**111(25.8)**	**<0.001**
T43	**Psychotropic drugs, NEC2**	**789(14.4)**	**113(4.8)**	**582(21.7)**	**94(21.8)**	**<0.001**
	Antidepressants	374(6.8)	46(1.9)	283(10.6)	45(10.4)	<0.001
	Antipsychotics	325(5.9)	46(1.9)	239(8.9)	40(9.3)	<0.001
	Psychostimulants	74(1.4)	17(0.7)	50(1.9)	7(1.6)	0.003
T55	**Soaps and detergents**	**714(13.0)**	**539(22.8)**	**165(6.2)**	**10(2.3)**	**<0.001**
T65	**Other and unspecified substances**	**515(9.4)**	**252(10.6)**	**234(8.7)**	**29(6.7)**	**0.001**
T65.2	Tobacco and nicotine	58(1.1)	25(1.1)	28(1.0)	5(1.2)	0.977
T65.6	Paints and dyes, not elsewhere classified	10(0.2)	7(0.3)	2(0.1)	1(0.2)	0.12
T39	**Nonopioid analgesics, antipyretics, antirheumatics**	**467(8.5)**	**77(3.3)**	**321(12.0)**	**69(16.0)**	**<0.001**
T39.1	Paracetamol	228(4.2)	20(0.8)	165(6.2)	43(10.0)	<0.001
T39.3	Other nonsteroidal anti-inflammatory drugs [NSAID]	198(3.6)	43(1.8)	134(5.0)	21(4.9)	<0.001
T54	**Corrosive substances**	**444(8.1)**	**188(7.9)**	**228(8.5)**	**28(6.5)**	**0.271**
T54.3	Corrosive alkalis and alkali-like substances	250(4.6)	108(4.6)	125(4.7)	17(3.9)	0.816
T54.2	Corrosive acids and acid-like substances	124(2.3)	55(2.3)	63(2.4)	6(1.4)	0.471
T49	**Agents primarily affecting skin, mucous membrane and ophthalmological, otorhinolaryngological and dental drugs**	**406(7.4)**	**213(9.0)**	**167(6.2)**	**26(6.0)**	**0.003**
T51	**Alcohol**	**290(5.3)**	**76(3.2)**	**172(6.4)**	**42(9.7)**	**<0.001**
T51.0	Ethanol	229(4.2)	38(1.6)	154(5.8)	37(8.6)	<0.001
T62	**Noxious substances eaten as food**	**287(4.2)**	**196(8.3)**	**82(3.1)**	**9(2.1)**	**<0.001**
T62.2	Ingested berries	177(3.2)	124(5.2)	47(1.8)	6(1.4)	<0.001
T62.0	Ingested mushrooms	28(0.5)	22(0.9)	6(0.2)	0(0.0)	0.001
T60	**Pesticides**	**248(4.5)**	**140(5.9)**	**91(3.4)**	**17(3.9)**	**0.04**
T40	**Narcotics and psychodysleptics (hallucinogens)**	**246(4.5)**	**39(1.6)**	**172(6.4)**	**35(8.1)**	**<0.001**
T40.2	Other opioids	169(3.1)	31(1.3)	113(4.2)	25(5.8)	<0.001

ICD-10	Agents[1]	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value
		n (%)	n (%)	n (%)	n (%)	
T40.5	Cocaine	19(0.3)	2(0.1)	15(0.6)	2(0.5)	0.015
T40.7	Cannabis (derivatives)	19(0.3)	5(0.2)	13(0.5)	1(0.2)	0.233
T40.8	Lysergic acid diethylamide [LSD]	3(0.1)	0(0.0)	3(0.1)	0(0.0)	0.416
T40.1	Heroin	1(0.02)	0(0.0)	1(0.04)	0(0.0)	1
T46	**Agents primarily affecting the cardiovascular system**	**245(4.5)**	**66(2.8)**	**152(5.7)**	**27(6.3)**	**<0.001**
	Beta-blockers	96(1.8)	23(1.0)	63(2.4)	10(2.3)	0.001
T52	**Organic solvents**	**189(3.5)**	**114(4.8)**	**68(2.5)**	**7(1.6)**	**<0.001**
T50	**Diuretics and unspecified drugs, medicaments and biological substances**	**184(3.4)**	**88(3.7)**	**80(3.0)**	**16(3.7)**	**0.238**
T47	**Agents primarily affecting the gastrointestinal system**	**162(3.0)**	**72(3.0)**	**78(2.9)**	**12(2.8)**	**0.091**
T45	**Primarily systemic and haematological agents, NEC**	**135(2.5)**	**32(1.4)**	**87(3.2)**	**16(3.7)**	**<0.001**
T48	**Drugs acting on smooth and skeletal muscles and respiratory system**	**137(2.5)**	**65(2.7)**	**67(2.5)**	**5(1.2)**	**0.113**
700 3	**Others**	**131(2.4)**	**91(3.8)**	**37(1.4)**	**3(0.7)**	**<0.001**
T36	**Systemic antibiotics**	**100(1.8)**	**22(0.9)**	**70(2.6)**	**8(1.9)**	**<0.001**
T38	**Hormones and their synthetic substitutes and antagonists, NEC**	**85(1.6)**	**26(1.1)**	**55(2.1)**	**4(0.9)**	**0.068**
T63	**Contact with venomous animals**	**46(0.8)**	**23(1.0)**	**20(0.7)**	**3(0.7)**	**0.646**
T59	**Other gases, fumes and vapours**	**41(0.7)**	**19(0.8)**	**15(0.6)**	**7(1.6)**	**0.055**
T44	**Drugs primarily affecting the autonomic nervous system**	**35(0.6)**	**9(0.4)**	**23(0.9)**	**3(0.7)**	**0.102**
T58	**Carbon monoxide**	**31(0.6)**	**5(0.2)**	**24(0.9)**	**2(0.5)**	**0.005**
T37	**Other systemic anti-infectives and antiparasitics**	**18(0.3)**	**4(0.2)**	**12(0.4)**	**2(0.5)**	**0.196**
T53	**Halogen derivative of aliphatic and aromatic hydrocarbons**	**16(0.3)**	**5(0.2)**	**11(0.4)**	**0(0.0)**	**0.213**
T61	**Noxious substances eaten as seafood**	**13(0.2)**	**5(0.2)**	**6(0.2)**	**2(0.5)**	**0.599**
T41	**Anaesthetics and therapeutic gases**	**9(0.2)**	**2(0.1)**	**5(0.2)**	**2(0.5)**	**0.196**
T56	**Metals**	**5(0.1)**	**4(0.2)**	**1(0.04)**	**0(0.0)**	**0.359**
T57	**Other inorganic substances**	**1(0.01)**	**0(0.0)**	**1(0.04)**	**0(0.0)**	**1**

ICD-10	Agents[1]	Total	Hosp-watchful-wait	Hosp-referral	Hosp-urgent-referral	p-value
		n (%)	n (%)	n (%)	n (%)	
TOTAL CASES		5,476(100)	2,368(100)	2,677(100)	431(100)	
TOTAL AGENTS		6,778	2,628	3,561	589	

Factors associated with type of referral

Table 4 shows the results of the univariate (unadjusted OR) and multivariate (adjusted OR) analysis performed to identify factors associated with the advised type of hospital referral. The Hosp-watchful-wait advice was used as the reference. In the univariate analysis, age, gender, time of the call, language of the caller, location of the victim, number of symptoms present, intentionality, type of transport, number of agents, number of symptoms, examinations, need for antidotes and type of agents were significantly associated with the referral type ($p<0.05$). In the multivariate analysis, number of symptoms present at the time of the call, intentionality, type of agents involved and advice for administration of antidotes were significantly associated with the referral type ($p<0.05$).

The estimated odds for Hosp-referral or Hosp-urgent-referral versus Hosp-watchful-wait was significantly higher with increasing number of symptoms, involvement of substances of abuse, unclear intentionality and intentional self-harm. In cases of self-harm, the estimated odds ratios for Hosp-urgent-referral versus Hosp-watchful-wait was substantially higher as compared with accidental cases. For the categories T36-T50 (medicinal agents) compared with the categories T51-T65 (non-medicinal agents), the estimated odds for Hosp-referral or Hosp-urgent-referral versus Hosp-watchful-wait was more than two times higher.

After Bonferroni correction ($\alpha=0.009$) the reported associations are still significant.

Table 4. | Univariate (unadjusted OR) and multivariate (adjusted OR) analysis of factors associated with BPC referral advice.

	Hosp-referral (REF: Hosp-watchful-wait)[1]				Hosp-urgent-referral (REF: Hosp-watchful-wait)[1]			
	UNIVARIATE		MULTIVARIATE		UNIVARIATE		MULTIVARIATE	
	OR[2] (CI[3])	p-value	OR[2] (CI[3])	p-value	OR[2] (CI[3])	p-value	OR[2] (CI[3])	p-value
Number of symptoms present								
>= 3 symptoms	11.14(6.22-19.95)	<0.001	13.82(7.59-25.18)	<0.001	13.88(6.62-29.12)	<0.001	18.28(8.45-39.56)	<0.001
2 symptoms	4.19(3.33-5.26)	<0.001	5.35(4.18-6.86)	<0.001	5.02(3.47-7.26)	<0.001	6.80(4.59-10.08)	<0.001

	Hosp-referral (REF: Hosp-watchful-wait)[1]				Hosp-urgent-referral (REF: Hosp-watchful-wait)[1]			
	UNIVARIATE		MULTIVARIATE		UNIVARIATE		MULTIVARIATE	
	OR[2] (CI[3])	p-value	OR[2] (CI[3])	p-value	OR[2] (CI[3])	p-value	OR[2] (CI[3])	p-value
1 symptom	2.62(2.32-2.97)	<0.001	3.23(2.80-3.73)	<0.001	3.62(2.88-4.55)	<0.001	4.56(3.56-5.85)	<0.001
0 symptoms	REF		REF		REF		REF	
Intentionality								
Intentional self-harm	12.08(9.90-14.74)	<0.001	9.81(7.90-12.17)	<0.001	24.76(18.92-32.38)	<0.001	20.54(15.17-27.81)	<0.001
Undetermined intentionality	4.14(2.14-8.00)	<0.001	3.92(1.97-7.82)	<0.001	16.07(7.41-34.87)	<0.001	15.37(6.84-34.57)	<0.001
Use of substances of abuse	5.81(2.99-11.26)	<0.001	2.74(1.37-5.49)	0.004	11.69(4.90-27.90)	<0.001	5.16(2.09-12.71)	<0.001
Accidental (unintentional)	REF		REF		REF		REF	
Type of agents								
T36-T50 & T51-T65	2.71(2.12-3.47)	<0.001	1.06(0.78-1.43)	0.714	4.01(2.64-6.07)	<0.001	0.97(0.60-1.58)	0.915
T36-T50	3.28(2.91-3.69)	<0.001	2.35(2.04-2.70)	<0.001	4.38(3.47-5.53)	<0.001	2.32(1.76-3.06)	<0.001
T51-T65	REF		REF		REF		REF	
Antidotes advised								
Yes	7.49(3.21-17.51)	<0.001	6.98(2.88-16.92)	<0.001	13.22(5.05-34.59)	<0.001	13.00(4.69-36.01)	<0.001
No	REF		REF		REF		REF	

[1] REF: Reference category = Hosp-watchful-wait
[2] OR: odds ratio
[3] CI: 95% Confidence Interval
[4] T36-T50: poisoning by drugs, medicaments and biological substances
[5] T51-T65: toxic effects of substances chiefly nonmedicinal as to source
[6] Predictors included in the multivariate model were Number of symptoms present, Intentionality, Type of agents, Antidotes advised

Survey of the patients' compliance with the BPC advice

During the second part of the study which was a prospective telephone survey, in total 2,237 victims were given the advice by the BPC to go (conditionally) to the hospital, of which 475 were excluded because of intentional self-harm, unknown intentionality or malicious behaviour (Supplementary File S4.1). The inclusion criteria were met in 1,762 cases and 561 of 1,057 (60%) could be contacted: 293 Hosp-watchful-wait,

211 Hosp-referral, and 57 Hosp-urgent-referral cases.

Table 5 shows the compliance of the patient with the advice of the BPC for referral to the hospital. Of the patients advised "Hosp-watchful-wait" 7.8% went to hospital, while 4.1% went to a medical doctor. Of the "Hospital-referral" cases 57.3% went to hospital and 59.6% of the "Hospital-urgent-referral" presented to hospital. In Supplementary File S4.2, the compliance of the caller with the advice given by the BPC for the group is presented, split into children and adults.

Table 5. | Compliance with the advice given by the BPC.

Patient's decision	**Advice given by the BPC during the first call to the BPC**			
	Total	Hosp-watchful-wait	Hospital-referral	Hospital-urgent-referral
	n(%)	**n(%)**	**n(%)**	**n(%)**
Total	**561 (100.0)**	**293 (100.0)**	**211 (100.0)**	**57 (100.0)**
Self-care at home	344 (61.3)	258 (88.1)	68 (32.2)	18 (31.6)
Went to a medical doctor	39 (7.0)	12 (4.1)	22 (10.4)	5 (8.8)
Went to the hospital	178 (31.7)	23 (7.8)	121 (57.3)	34 (59.6)
ED-amb[1]	109 (19.4)	18 (6.1)	76 (36.0)	15 (26.3)
ED-24h[2]	28 (5.0)	2 (0.7)	20 (9.5)	6 (10.5)
Hosp[3]	40 (7.1)	3 (1.0)	24 (11.4)	13 (22.8)
ICU[4]	1 (0.2)	0 (0.0)	1 (0.5)	0 (0.0)

[1] ED-amb: ambulatory patients discharged home after treatment in the emergency department
[2] ED-24h: patients requiring at maximum a 24-hours-observation in the emergency department
[3] Hosp: patients admitted to a hospital ward
[4] ICU: patients admitted to the intensive care unit

Cost

In previous work, the cost of the BPC and the cost of a visit to a medical doctor was estimated to be €24.9 and €36.1, respectively [17], and the mean hospitalization cost was calculated at €1,287.1 (SD €2,653) [2]. Table 6 presents the total cost according to the care chosen by the patients after having called the BPC. In case of Hosp-watchful-wait patients, 7.8% actually went to the hospital, while 4.1% went to the doctor, and 88.1% stayed at home. For Hosp-referral patients and Hosp-urgent-referral patients, 57.3% and 59.6% went to the hospital, 10.4% and 8.8% consulted a doctor, and 32.2% and 31.6% was treated on site, respectively. The cost was estimated to be €126.4, €767.8, and €794.4 for Hosp-watchful-wait patients, Hosp-referral patients and Hosp-urgent-referral patients, respectively, adding up to a total cost of €2,384,804. As previously shown, 12,949 patients were advised to

perform self-care at home, 3,560 were sent to a medical doctor and 5,476 (conditionally) to the hospital.

In Table 6, we apply the compliance proportions of the survey (article 5, Tables 4 and 5) to the 5,476 cases of this dataset. It is estimated that an additional 3,357 performed self-care at home, 383 went to a medical doctor, and 1,736 went to a hospital.

Based on the compliance data, it can be simulated that an additional 3,357 performed self-care at home, 383 went to a medical doctor, and 1,736 went to the hospital (Table 6).

Table 6. | Compliance proportions of the survey to the 5,476 BPC acute poisoning cases for adults and children

Action after BPC call	Total	Hosp-watchful wait	Hosp-referral	Hosp-urgent-referral
	n(%)	n(%)	n(%)	n(%)
Self-care at home	3,357(61.3)	2,519(88.1)	663(32.2)	175(31.6)
Went to the doctor	383(7.0)	119(4.1)	214(10.4)	50(8.8)
Went to the hospital	1,736(31.7)	222(7.8)	1,182(57.4)	331(59.6)
	5,476(100)	2,860(100)	2,060)(100)	556(100)

This represents an estimated cost of €83,589, €23,378, and €2,277,701, respectively (Table 7).

Table 7. | Assumed cost of care of victims from analysis 1, extrapolating compliance based on the survey results of analysis 2.

Advice		Action after BPC call		Cost/type of care				Total cost	Mean cost
				BPC	Doctor	Hospital	Total		
	n (%)		n (%)	€	€	€	€	€	€
Hosp-watchful-wait	2,860(52.2)	Self-care at home	2,519(88.1)	24.94	0	0	24.94	62,824	126.4
		Went to the doctor	119 (4.1)	24.94	36.1	0	61.04	7,264	
		Went to the hospital	222 (7.8)	24.94	0	1287	1312.04	291,273	
Hosp-referral	2,060(37.6)	Self-care at home	663 (32.2)	24.94	0	0	24.94	16,535	767.8
		Went to the doctor	214 (10.4)	24.94	36.1	0	61.04	13,063	
		Went to the hospital	1,183 (57.3)	24.94	0	1287	1312.04	1,552,143	
Hosp-urgent-referral	556(10.2)	Self-care at home	175 (31.6)	24.94	0	0	24.94	4,365	794.4
		Went to the doctor	50 (8.8)	24.94	36.1	0	61.04	3,052	
		Went to the hospital	331 (59.6)	24.94	0	1287	1312.04	434,285	
Total	*5,476 (100.0)*	*5,476*					*2,384,804*		

From these figures we can estimate that from the 21,985 non-hospitalized patients who called the BPC between 1 January and 30 June 2018 (see Figure 1), 74.2% (16,306 = 12,949 + 3,357) performed self-care at home, 17.9% (3,943 = 3,560 + 383) went to the doctor and 7.9% (1,736) went to the hospital, with an estimated total cost of €2,925,123. If all 5,476 patients had been hospitalized, the total estimated cost would be €7,184,731 or 2.5 times higher.

Discussion

Our study aimed to analyze the characteristics of patients calling the BPC in case of poisoning and who were advised to go (conditionally) to a hospital. Factors associated with the type of hospital referral recommendation were identified. Compliance of the patient with the BPC advice and its health-economic impact were estimated. Payer's cost was estimated on the basis of previously collected GUH data and taking into account the compliance of the patients with the BPC advice.

Factors found to be associated with the type of referral were number of symptoms, intentionality, type of agent(s) involved and advising antidotes.

The higher number of symptoms was associated with a higher estimated odds for Hosp-referral or Hosp-urgent-referral. The presence of multiple symptoms may indeed be an indication of severity but caution should be taken as some severe poisoning cases may exhibit a symptom free interval with a delayed time course.

Intentional self-harm also seems to increase the likelihood of hospital referral. This presumably reflects the fact that associated psychosocial problems with a risk for suicide result in the choice for hospitalization for psychiatric and social care. A similar trend is observed in cases of uncertainty with regard to intentionality, which may be explained by the fact that the calltaker chose to stay on the safe side when uncertain about the intentionality of the patient.

When agents T36-T50 (medicinal agents) were involved, a higher proportion of Hosp-referrals and Hosp-urgent-referrals is observed for benzodiazepines, antidepressants, antipsychotics, paracetamol, NSAIDs, and a lower proportion for soaps and detergents, food or skin products. These non-medicinal agents are more frequently present in the Hosp-watchful-wait category versus in Hosp-referrals and Hosp-urgent-referrals, respectively, which may be explained by their lower toxicity risk and less frequent association with self-harm compared to the medicinal agents. This observation corresponds with literature data on agents involved in patients seen at the hospital [17]. Cases from calls to the poison centres show a different profile: T51-T65 (non-medicinal) agents (household products, plants, cosmetics, food) are represented more often when compared with hospital admissions [1,20-24].

We estimate that the associated factors with hospital referral are consistent with appropriate toxicology

advice. However, less tangible elements which are not mentioned in the BPC electronic patient form may also influence the triage advice, such as mental status of the victim, family situation and comorbidity. The BPC has to consider to add some of these elements to the electronic patient form.

This study revealed a high percentage of non-compliance with the BPC advice, especially in the Hosp-referral and Hosp-urgent-referral categories. The 23.9% of patient's non-compliance for hospital referral cases in the study of Wattson et al. is lower, but lies in the same order of magnitude as our results [25].

A possible explanation from the patient's perspective may be that hospital referral by a poison centre signifies a burden to the patient with e.g. induction of anxiety, difficulties to reach a hospital, waiting time in the hospital, and fear for costs. Wezorek et al. cited motivation, concern, perceived threat posed by the exposure and perceived barriers as factors influencing the willingness to comply with a recommended behavior [26].

It is a cause for concern that more than 30% of Hosp-referrals and Hosp-urgent-referrals did not seek any medical help in view of the potentially serious consequences for morbidity or mortality. This was also cited by Watts et al. [25].

The triage process of the BPC and referral protocol should also be critically evaluated to see whether the use of extra protocols would be a good framework for more appropriate referral advice, taking also into account the objective and psychological condition of the patient. The use of qualitative research methods such as open-ended surveys or in-depth-interviews should also be considered.

A substantial insight into the financial impact of advice is an important element in the triage process. The low compliance rate for hospital attendance suggests on the one hand that the BPC advice to attend hospital may be overused by the BPC experts, with less financial cost to government and patient because of non-compliance, but on the other hand with a higher risk of harm to a number of patients not getting proper care, which could ultimately lead to higher costs due to delayed hospitalization . It underlines the fact that an appropriate but safe BPC triage could have considerable financial consequences and could be one of the reasons for non-compliance. However, we know from previous research that 95.7% of the total cost was charged by the hospital to the government and only 4.3% to the patient [17].

Limitations and generalisability

A first limitation is that we had to exclude the intentional cases from the survey. Self-harm is an important factor in the BPC decision to send a patient to the hospital, but we do not know which proportion of these patients effectively went to the hospital.

A second limitation is that we do not know if patients who went to the hospital received any intervention or could have been kept at home. This might help to refine the BPC referrals to the hospital.

A third limitation is that there may be bias in the results and the extrapolation of the survey results to the original analysis 1 as the survey was conducted at a different time.

Despite the fact that all patients were still alive when contacted in the survey, we cannot generalize about effectiveness of triage without a further in-depth follow-up.

Conclusion

This study identifies the differences in the characteristics, associated factors and costs of three types of referrals to the hospital: conditional referrals, referrals and urgent referrals. Only a proportion of patients follows the advice of the poison centre to go (conditionally) to the hospital. The reason why patients did not go to the hospital deserves further exploration.

A systematic follow-up of cases is recommended to examine whether the BPC referral advice can be improved . In addition to the “safety first” principle, a substantial insight into the financial impact of advice is also an important element in the triage process as non-compliance of patients with the advice of the poison centre has a substantial health-economic impact.

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Supplementary files

S4.1 Figure. Flowchart of the selection of the Hosp-watchful-wait victims, Hosp-referral victims and Hosp-urgent-referral victims that could be reached during the telephone survey between 1 March and 15 May 2019 in the Belgian Poison Centre.

S4.2 Table. Compliance of the caller with the advice given by the BPC. Results of a telephone follow-up survey between 1 March and 15 May 2019. Results, classified by children and adults.

Chapter 6 Article 5

Comparison of adults with acute poisoning advised by the Belgian Poison Centre to go to a hospital versus adults admitted to the emergency department of a hospital with acute poisoning

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Abbreviations

BPC: Belgian Poison Centre
DDD: Daily Defined Dose
ED: Emergency Department
ED-amb: Emergency Department-ambulatory care
ED-24h: Emergency Department-24-hours-observation unit
GDPR: General Data Protection Regulation
ICU: Intensive Care Unit
Hosp1: Hospital 1
Hosp2: Hospital 2
Hosp3: Hospital 3
Hosp3.1: Hospital 3, site 1
Hosp3.2: Hospital 3, site 2
Hosp-watchful-wait: Hospital watchful waiting, referral if deterioration of situation
Hosp-referral: referral to the Hospital
Hosp-urgent-referral: urgent referral to the Hospital
ICD-10: International Classification of Diseases, version 10
NSAID: Non-Steroidal Anti-Inflammatory Drugs
NHDI: National Health and Disability Insurance (RIZIV, RIjksdienst voor Ziekte- en InvaliditeitsVerzekering,)
UREG: Belgian emergency registration system for hospital emergency departments (Urgentie REGistratiesysteem)
WHO: World Health Organisation

Introduction

Acute poisoning is a significant healthcare problem across the world. Depending on the healthcare system of the country, people with suspected poisoning have different possibilities. They can decide not to contact any healthcare professional at all, or they can call a poison centre, consult a medical doctor, go to an emergency medical service or outpatient clinic or to the emergency department (ED) of a hospital.

In this study, we want to compare the characteristics of the patients calling a poison centre, and those admitted to the ED of a hospital.

In the literature, many articles examined the characteristics, involved agents and/or cost of patients who call the poison centre [1-9] while other articles investigated the profile of patients admitted to the ED [10-21]. These studies show that the characteristics of patients calling a poison centre differ from hospital cases. However, there is a lack of data on the degree of similarity between 1) the group of patients who called the poison centre and was advised to go to a hospital and 2) the group of patients admitted to the ED of a hospital.

Therefore, the aims of this study are (1) to compare the characteristics, involved agents and costs of patients with acute poisoning, advised to go to the hospital by a poison centre, with those of patients who went to three hospitals of different size and region: a university hospital, a regional hospital and a general hospital with two sites, and (2) to assess the compliance of the patients with the BPC advice to go to the hospital.

Materials and methods

We used the "Strengthening the Reporting of Observational Studies in Epidemiology Statement" STROBE as a guideline for reporting [22].

Study design and setting

The Belgian Poison Centre (BPC) covers the countries of Belgium and the Grand Duchy of Luxembourg receiving more than 60,000 calls per year either from the general public or healthcare professionals. It provides free telephone advice in case of (suspected) toxic exposures. As a 24/7 care service, a medical doctor or a pharmacist assists the callers by directing them to the appropriate level and place of care (either care at home, or referral to a medical doctor, hospital).

Hospital 1 (Hosp1) is a university hospital in Belgium with more than 1,000 beds and about 35,000 ED admissions per year. Hospital 2 (Hosp2) is a regional hospital with about 300 beds and 20,000 ED

admissions per year. Hospital 3 (Hosp3) is one of the large(st) non-university hospitals in Belgium with about 1,600 beds and 46,000 ED admissions which are spread over two sites: Hospital 3.1(Hosp3.1) and Hospital 3.2 (Hosp3.2).

Participants

Calls to the BPC between 1 January and 30 June 2018 either for or from adult victims of poisoning (>= 14 years) were included when the advice was to go to a hospital (Hosp-referral) or to go urgently to a hospital (Hosp-urgent-referral). Patients who were advised to go only to a hospital if symptoms appeared or if their situation would deteriorate (Hosp-watchful-wait) were excluded. The latter group was excluded as we know from previous research that only an estimated 7.8% of this group actually goes to the hospital [23]. Calls for patients who were in the hospital already were excluded. Patients admitted to an ED were screened for poisoning as described previously [24]. In Hosp1 and Hosp2, data between 1 January and 31 December 2017 were used, and in Hosp3.1 and Hosp3.2 data between 1 July 2016 and 30 June 2017. Cases were only included when consensus between data collectors. Patients without Belgian mandatory National Health and Disability Insurance (NHDI) were excluded from the cost analysis.

Variables

Symptoms were categorised according to the guidelines of the Belgian emergency registration system for hospital EDs, called UREG. Agents were grouped according to T36-T50 (poisoning by drugs, medicaments and biological substances) or T51-T65 (toxic effects of substances chiefly nonmedicinal as to source) of the International Classification of Diseases (ICD-10) [24] of the World Health Organization (WHO). Cases were categorized according to accidental (unintentional) poisoning, use of substances of abuse, intentional self-harm, or undetermined cause of poisoning [25].

Cost was defined as the direct payer's cost. In case of the BPC, calls to the BPC were free for the caller and cost was financed by the government via the BPC subvention [26]. In case of the hospital, the cost charged by the hospital to both the government and the patient was calculated. Cost was expressed in international dollars 2017.

Data sources

For the BPC, the electronic data form filled in by the expert during or immediately after the telephone call was used and cost per call was derived from the 2017 financial report of the BPC as described previously [27]. The compliance of the caller with the BPC advice was based on the results of a follow-up survey on patients for whom the BPC was called between 1 March and 15 May 2019 that was published earlier [23]. For Hosp1, data published in previous work were used [27,28]. For the data collection of Hosp2, Hosp3.1 and Hosp3.2, we used the same method as for Hosp1.

Study size

The sample size was determined by the number of cases in the study area during the study period.

Statistical methods

Pearson Chi-Square or Fisher's Exact Test (cell values <5) were used to compare frequencies. All analyses were performed using SPSS 25.0 (IBM®).

Ethical considerations

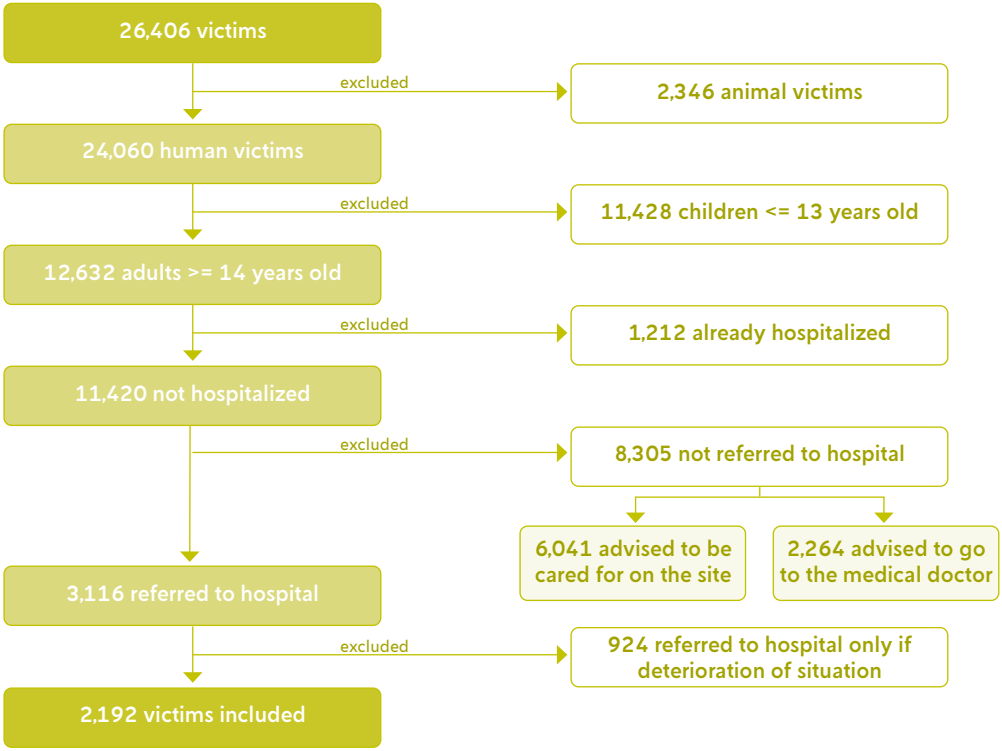
The study protocol was approved by the Ethical Committee of Hosp1, Hosp2 and Hosp3. The anonymous BPC data was analyzed according to the General Data Protection Regulation (GDPR) guidelines of the BPC [29].

Results

Participants

Fig 1 presents the BPC flowchart of inclusion. Of the 26,406 victims for whom was called to the BPC, 24,060 were human victims of which 12,632 adults. At the moment of the call, 11,420 victims were not already hospitalized, of which, 3,116 were advised by the BPC to go to the hospital (Hosp-watchful-wait, Hosp-referral, Hosp-urgent-referral). Excluding the 924 Hosp-watchful-wait victims, 2,192 patients were finally included.

Fig 1. | Flowchart of inclusion of the adult victims (aged >= 14 years) of suspected poisoning for whom was called to the Belgian Poison Centre between Jan-June 2018, Belgium



In Hosp1, Hosp2, Hosp3.1, and Hosp 3.2, a total of 1,214, 409, 414 and 259 ED admissions were included, respectively.

Characteristics

Table 1 compares the characteristics of victims who called the BPC and were referred to the hospital with those admitted to the hospitals. Only 39.7% of the victims in the BPC were males, in contrast with a range varying between 50.0% and 62.2% in the hospitals. With regard to time of referral and time of admission to the hospital, the BPC advised 14.5% of patients calling between 12am (midnight) and 8am to go to the hospital. Between these hours, there were between 16.2% and 34.2% hospital admissions. There was a marked difference between Hosp3.1 and Hosp3.2 with 16.2% and 30.9% night admissions respectively. Only

1.5% of victims were in a public place at the moment of the call to the BPC. A proportion between 11.6% and 26.5% of patients admitted to the ED came from a public place. In more than 50% of the cases, the patient (him(her)self) called the BPC and 41.7% to 68.9% of patients presented to the ED on their own initiative.

Table 1. | Characteristics of patients advised to go to a hospital by the Belgian Poison Centre and patients admitted to a hospital for acute poisoning in Belgium

Characteristics	BPC[1]	Hosp1 [2]		Hosp2 [3]		Hosp3.1 [4]		Hosp3.2 [5]	
n=	2,192	1,214		409		414		259	
	n(%)	n(%)	p-value [6]	n(%)	p-value [6]	n(%)	p-value [6]	n(%)	p-value [6]
Gender			<0.001		<0.001		<0.001		<0.001
Male	**839(39.7)**	755(62.2)		244(59.7)		207(50.0)		139(53.7)	
Female	**1,276(60.3)**	459(37.8)		165(40.3)		207(50.0)		120(46.3)	
Total	***2,115(100.0)***	*1,214(100.0)*		*409(100.0)*		*414(100.0)*		*259(100.0)*	
Age			<0.001		<0.001		<0.001		<0.001
14-20y	**74(15.5)**	213 (17.5)		44(10.8)		45(10.9)		24(9.3)	
21-40y	**154(32.4)**	522 (43.0)		124(30.3)		180(43.5)		103(39.8)	
41-60y	**198(41.6)**	387 (31.9)		189 (46.2)		158(38.2)		107(41.3)	
>60y	**50(10.5)**	92 (7.6)		52(12.7)		31(7.5)		25(9.7)	
Total	***476(100.0)***	*1,214 (100.0)*		*409(100.0)*		*414 (100.0)*		*259 (100.0)*	
Day of the week call/ admission			<0.001		<0.001				<0.001
Monday	**370(16.9)**	141(11.6)		59(14.4)		67(16.2)	0.019	42(16.2)	
Tuesday	**251(11.5)**	171(14.1)		68(16.6)		49(11.8)		29(11.2)	
Wednesday	**325(14.8)**	14 (11.8)		49(12.0)		71(17.1)		27(10.4)	
Thursday	**307(14.0)**	159(13.1)		42(10.3)		42(10.1)		33(12.7)	
Friday	**323(14.7)**	199(16.4)		53(13.0)		53(12.8)		31(12.0)	
Saturday	**347(15.8)**	194(16.0)		61(14.9)		58(14.0)		44(17.0)	
Sunday	**269(12.3)**	207(17.1)		77(18.8)		74(17.9)		53(20.5)	
Total	***2,192(100.0)***	*1,214(100.0)*		*409(100.0)*		*414(100.0)*		*259(100.0)*	
Time of call/ admission			<0.001		<0.001		0.015		<0.001
8am-12pm	**311(14.2)**	103(8.5)		27(6.6)		42(10.1)		17(6.6)	
12pm-4pm	**421(19.2)**	176(14.5)		73(17.8)		76(18.4)		34(13.1)	
4pm-8pm	**566(25.8)**	245(20.2)		99(24.2)		119(28.7)		53(20.5)	

Characteristics	BPC[1]	Hosp1 [2]		Hosp2 [3]		Hosp3.1 [4]		Hosp3.2 [5]	
n=	2,192	1,214		409		414		259	
	n(%)	n(%)	p-value [6]	n(%)	p-value [6]	n(%)	p-value [6]	n(%)	p-value [6]
8pm-12am	**576(26.3)**	275(22.7)		104(25.4)		110(26.6)		75(29.0)	
12am-4am	**221(10.1)**	272(22.4)		78(19.1)		35(8.5)		54(20.8)	
4am-8am	**97(4.4)**	143(11.8)		28(6.8)		32(7.7)		26(10.0)	
Total	***2,192(100.0)***	*1,214(100.0)*		*409(100.0)*		*414(100.0)*		*259(100.0)*	
Victim location			<0.001		<0.001		<0.001		<0.001
Home	**1,789(81.6)**	727(59.9)		299(73.8)		346(83.6)		175(67.6)	
Public place	**32(1.5)**	322(26.5)		79(19.5)		48(11.6)		39(15.1)	
Other	**371(16.9)**	165(13.6)		27(6.7)		20(4.8)		45(17.4)	
Total	***2,192(100.0)***	*1,214(100.0)*		*405(100.0)*		*414(100.0)*		*259(100.0)*	
Referred by/Called by			<0.001		<0.001		<0.001		<0.001
Own initiative (patient or family)	**1,104(50.4)**	657(54.1)		282(68.9)		177(42.8)		108(41.7)	
Externals, no patients participation	**282(12.9)**	472(38.9)		87(21.3)		165(39.9)		137(52.9)	
General practitioner/ physician	**547(25.0)**	77(6.3)		31(7.6)		72(17.4)		14(5.4)	
Other	**259(11.8)**	8(0.7)		9(2.2)		0(0.0)		0(0.0)	
Total	***2,192(100.0)***	*1,214(100.0)*		*409(100.0)*		*414(100.0)*		*259(100.0)*	
Transport			<0.001		<0.001		<0.001		<0.001
By own means	**5(1.4)**	357(29.4)		124(30.5)		198(47.8)		66(25.5)	
Ambulance	**233(63.5)**	659(54.3)		227(55.8)		184(44.4)		156(60.2)	
Mobile intensive care unit	***129(35.1)***	198(16.3)		56(13.8)		32(7.7)		37(14.3)	
Total	***367(100.0)***	*1,214(100.0)*		*407(100.0)*		*414(100.0)*		*259(100.0)*	

[1] BPC Belgian Poison Centre
[2] Hosp1: university hospital
[3] Hosp2: regional hospital
[4] Hosp3.1: site 1 of a general hospital, with an emergency department
[5] Hosp3.2: site 2 of a general hospital, with an emergency department
[6] p-value: chi-square test. Results of the comparison between the BPC and the hospital

As shown in Table 2, the calltakers of the BPC coded 42.1% as accidental, 2.4% as use of substances of abuse (SOA) and 53.6% as intentional self-harm, as opposed to a percentage ranging between 0.5%-6.1%, 51.2%-72.2%, and 21.5%-28.2% in the hospitals, respectively. Twenty-six percent of victims reported no symptoms at the time of the call to the BPC. Sixteen percent showed changes in consciousness, and 13.8% had dermatologic, ophtalmological or nose-throat-ear complaints. In cases of ED admissions, changes in consciousness ranged from 10.6% to 22.8%, and behavioural and emotional disorders from 16.8% to 57.7%. Less than one percent in hospital had dermatological, ophtalmological or nose-throat-ear complaints. In 74.2% of BPC cases, only one agent was involved in contrast with the hospitals where the figure ranged between 60.6% and 75.0%. The use of medicinal agents and non-medicinal agents were mentioned in 60.5% and 30% of calls to the BPC and between 22.1% and 31.6% and between 49.8% and 64.1% of admissions to the hospital, respectively.

Table 2. | Characteristics of patients advised to go to a hospital by the Belgian Poison Centre (January until June 2018) and patients who were seen at a hospital (2016-2017), Belgium

Characteristics	**BPC**[1]	Hosp1 [2]		Hosp2 [3]		Hosp3.1 [4]		Hosp3.2 [5]	
n=	**2,192**	1,214		409		414		259	
	n(%)	n(%)	p-value[8]	n(%)	p-value[8]	n(%)	p-value[8]	n(%)	p-value[8]
Symptoms			**<0.001**		**<0.001**		**<0.001**		**<0.001**
No/unknown symptoms	**718(25.9)**	259(21.3)		0(0.0)		11(2.7)		8(3.1)	
Changes in consciousness	**433(15.6)**	257(21.2)		50(10.6)		76(18.4)		59(22.8)	
Dermatological, ophtalmological, nose throat ear problems	**383(13.8)**	8(0.7)		1(0.2)		0(0.0)		0(0.0)	
Nausea, vomiting	**220(7.9)**	70(5.8)		14(3.0)		3(0.7)		6(2.3)	
General malaise	**155(5.6)**	58(4.8)		44(9.4)		7(1.7)		0(0.0)	
Respiratory problems	**131(4.7)**	2(0.2)		10(2.1)		4(1.0)		6(2.3)	
Other	**109(3.9)**	144(11.9)		107(22.8)		47(11.4)		13(5.0)	
Behavioural/ emotional disorders	**93(3.3)**	204(16.8)		150(31.9)		239(57.7)		143(55.2)	
Tremor, coordination disorders	**91(3.3)**	3(0.2)		0(0.0)		1(0.2)		0(0.0)	

Characteristics	BPC[1]	Hosp1 [2]		Hosp2 [3]		Hosp3.1 [4]		Hosp3.2 [5]	
n=	2,192	1,214		409		414		259	
	n(%)	n(%)	p-value[8]	n(%)	p-value[8]	n(%)	p-value[8]	n(%)	p-value[8]
Abdominal pain	**77(2.8)**	5(0.4)		5(1.1)		0(0.0)		1(0.4)	
Dizziness and syncopic feeling	**69(2.5)**	3(0.2)		7(1.5)		0(0.0)		4(1.5)	
Headache	**62(2.2)**	22(1.8)		2(0.4)		5(1.2)		2(0.8)	
Non-specific symptoms	**53(1.9)**	131(10.8)		29(6.2)		4(1.0)		1(0.4)	
Palpitations	**40(1.4)**	3(0.2)		2(0.4)		0(0.0)		2(0.8)	
Signs of neurological failure	**34(1.2)**	6(0.5)		3(0.6)		1(0.2)		0(0.0)	
Pain in limbs, neck, shoulder, pelvic region	**25(0.9)**	3(0.2)		16(3.4)		1(0.2)		2(0.8)	
Retrosternal and thoracic pain	**19(0.7)**	3(0.2)		2(0.4)		0(0.0)		1(0.4)	
External signs of bleeding or bleeding	**15(0.5)**	11(0.9)		0(0.0)		1(0.2)		0(0.0)	
Fever and convulsion	**15(0.5)**	1(0.1)		2(0.4)		1(0.2)		0(0.0)	
Diarrhoea	**13(0.5)**	1(0.1)		1(0.2)		0(0.0)		0(0.0)	
Wounds, swelling, fracture	**10(0.4)**	20(1.6)		25(5.3)		9(2.2)		8(3.1)	
Life-threatening situation	**7(0.3)**	0(0.0)		0(0.0)		3(0.7)		2(0.8)	
Pee problems	**5(0.2)**	0(0.0)		0(0.0)		1(0.2)		1(0.4)	
Total	*2,777(100.0)*	1,214(100.0)		470(100.0)		414(100.0)		259(100.0)	
Route of exposure			**<0.001**		**<0.001**		**<.001**		**<0.001**
Oral	**1,722(78.6)**	1,047(86.2)		343(83.9)		355(85.7)		234(90.3)	
Inhalation	**167(7.6)**	65(5.4)		23(5.6)		20(4.8)		8(3.1)	
>1way	**16(0.7)**	91(7.5)		27(6.6)		23(5.6)		6(2.3)	
Other or unknown	**287(13.1)**	11(0.9)		16(3.9)		16(3.9)		11(4.2)	
Total	*2,192(100.0)*	1,214(100.0)		409(100.0)		414(100.0)		259(100.0)	

Characteristics	BPC[1]	Hosp1 [2]		Hosp2 [3]		Hosp3.1 [4]		Hosp3.2 [5]	
n=	2,192	1,214		409		414		259	
	n(%)	n(%)	p-value[8]	n(%)	p-value[8]	n(%)	p-value[8]	n(%)	p-value[8]
Number of agents involved			**<0.001**		**<0.001**		**<0.001**		**0.023**
1	**1,627(74.2)**	910(75.0)		246(60.6)		268(64.7)		173(66.8)	
2	**350(16.0)**	190(15.7)		98(24.1)		82(19.8)		49(18.9)	
>=3	**215(9.8)**	114(9.4)		62(15.3)		64(15.5)		37(14.3)	
Total	*2,192(100.0)*	1,214(100.0)		406(100.0)		414(100.0)		259(100.0)	
Type of agents involved			**<0.001**		**<0.001**		**<0.001**		**<0.001**
T36-T50 & T51-T65	**207(9.4)**	166(13.7)		83(20.4)		77(18.6)		59(22.8)	
T36-T506	**1,327(60.5)**	268(22.1)		116(28.6)		131(31.6)		59(22.8)	
T51-T657	**658(30.0)**	776(64.1)		207(51.0)		206(49.8)		141(54.4)	
Total	*2,192(100.0)*	1,210(100.0)		406(100.0)		414(100.0)		259(100.0)	
Intentionality			**<0.001**		**<0.001**		**<0.001**		**<0.001**
Undetermined intentionality	**40(1.8)**	123(10.1)		59(14.5)		9(2.2)		2(0.8)	
Intentional self-harm	**1,176(53.6)**	261(21.5)		115(28.2)		104(25.1)		66(25.5)	
Use of substances of abuse	**53(2.4)**	790(65.1)		209(51.2)		299(72.2)		186(71.8)	
Accidental (unintentional)	**923(42.1)**	40(3.3)		25(6.1)		2(0.5)		5(1.9)	
Total	*2,192(100.0)*	1,214(100.0)		408(100.0)		414(100.0)		259(100.0)	
Use of antidotes (recommended)			**0.541**		**0.536**		**0.321**		**0.226**
Yes	**42(1.9)**	27(2.2)		6(1.5)		5(1.2)		2(0.8)	
No	**2,150(98.1)**	1,187(97.8)		403(98.5)		409(98.8)		257(99.2)	
Total	*2,192(100.0)*	1,214(100.0)		409(100.0)		414(100.0)		259(100.0)	

[1] BPC Belgian Poison Centre
[2] Hosp1: university hospital
[3] Hosp2: regional hospital
[4] Hosp3.1: site 1 of a general hospital, with an emergency department
[5] Hosp3.2: site 2 of a general hospital, with an emergency department
[6] T36-T50: drugs, medicaments and biological substances
[7] T51-T56: substances chiefly nonmedicinal as to source
[8] p-value: chi-square test. Results of the comparison between the BPC and the hospital

Table 3. | Characteristics of adults admitted to the ED of three hospitals (of which one with two sites) with acute poisoning

Characteristics	Hosp1 [1]	Hosp2 [2]	Hosp3.1 [3]	Hosp3.2 [4]	Hosp3 [5]	
n=	1.214	409	414	259		
	n(%)	n(%)	n(%)	n(%)		p-value[6]
Type of hospitalization						**<0.001**
ED-ambulatory	661(54.4)	219(53.9)	198(47.8)	166(64.1)	364(54.1)	
ED-24-hours	299(24.6)	90(22.2)	67(16.2)	69(26.6)	136(20.2)	
Hospitalization	214(17.6)	82(20.2)	131(31.6)	12(4.6)	143(21.2)	
Intensive care unit	40(3.3)	15(3.7)	18(4.3)	12(4.6)	30(4.5)	
Total	*1,214(100.0)*	*406(100.0)*	*414(100.0)*	*259(100.0)*	*673(100.0)*	
Glasgow coma score						**<0.001**
Unknown	275(22.7)	30(7.3)	39(9.4)	26(10.0)	65(9.7)	
Coma (<8)	30(2.5)	19(4.6)	15(3.6)	11(4.2)	26(3.9)	
Somnolent (8-14)	265(21.8)	84(20.5)	58(14.0)	49(18.9)	107(15.9)	
Awake (15)	644(53.0)	276(67.5)	302(72.9)	173(66.8)	475(70.6)	
Total	*1,214(100.0)*	*409(100.0)*	*414(100.0)*	*259(100.0)*	*673(100.0)*	
Number of days hospitalization					**<0.001**	
0	661(54.4)	219(53.5)	198(47.8)	166(64.1)	364(54.1)	
1	313(25.8)	104(25.4)	77(18.6)	79(30.5)	156(23.2)	
2	87(7.2)	11(2.7)	23(5.6)	2(0.8)	25(3.7)	
>= 3	153(12.6)	75(18.3)	116(28.0)	12(4.6)	128(19.0)	
Total	*1,214(100.0)*	*409(100.0)*	*414(100.0)*	*259(100.0)*	*673(100.0)*	
Examinations and treatments						
Monitoring vital parameters	772(16.9)	188(21.4)	398(36.3)	246(34.3)	644(35.5)	<0.001
Laboratory testing	703(15.4)	238(27.1)	340(31.1)	233(32.5)	573(31.6)	<0.001
Medical imaging	276(6.1)	103(11.7)	90(8.2)	59(8.2)	149(8.2)	0.676
Intravenous drip/ medication	763(16.7)	184(21.0)	185(16.9)	151(21.0)	336(18.5)	<0.001
Wound, catheter, ostomy care/ minor surgical intervention	109(2.4)	0(0.0)	34(3.1)	14(1.9)	48(2.6)	0.168

Characteristics	Hosp1 [1]	Hosp2 [2]	Hosp3.1 [3]	Hosp3.2 [4]	Hosp3 [5]	
n=	1.214	409	414	259		
	n(%)	n(%)	n(%)	n(%)		p-value[6]
Invasive techniques	685(15.0)	0(0.0)	8(0.7)	2(0.3)	10(0.6)	<0.001
Patient restraint	86(1.9)	50(5.7)	14(1.3)	6(0.8)	20(1.1)	<0.001
Other treatment	1,167(25.6)	115(13.1)	26(2.4)	7(1.0)	33(1.8)	<0.001
Total cases	*1,214*	*409*	*414*	*259*	*673*	
Total treatments	*4,561(100.0)*	*878(100.0)*	*1,095(100.0)*	*718(100.0)*	*1,813(100.0)*	
Fate of the patient after discharge hospital						**<0.001**
Home	982(80.9)	344(84.1)	369(89.1)	190(73.4)	559(83.1)	
Another non-university hospital	52(4.3)	2(0.5)	8(1.9)	3(1.2)	11(1.6)	
Psychiatric hospital	107(8.8)	32(7.8)	9(2.2)	63(24.3)	72(10.7)	
Home for the elderly	1(0.1)	2(0.5)	0(0.0)	1(0.4)	1(0.1)	
Deceased	1(0.1)	1(0.2)	3(0.7)	0(0.0)	3(0.4)	
Other	17(1.4)	23(5.6)	21(5.1)	2(0.8)	23(3.4)	
Unknown	54(4.4)	5(1.2)	4(1.0)	0(0.0)	4(0.6)	
Total	*1,214(100.0)*	*409(100.0)*	*414(100.0)*	*259(100.0)*	*673(100.0)*	

[1] Hosp1: university hospital
[2] Hosp2: regional hospital
[3] Hosp3.1: site 1 of Hosp3, general hospital
[4] Hosp3.2: site 2 of Hosp3, general hospital
[5] Hosp3: sum of Hosp3.1 and Hosp3.2
[6] p-value: chi-square test. Results of the comparison between the Hosp1, Hosp2 and Hosp3

Agents involved

The agents most often involved in the total number of BPC cases were benzodiazepines (22.7%), followed by antidepressants (14.1%), antipsychotics (10.4%), ethanol (8.4%), paracetamol (6.8%) and other opioids (5.2%). In the hospitals, ethanol was most frequently involved ranging between 65.5%-75.3% followed by benzodiazepines (range between 13.6%-26.7%). Cocaine, cannabis, antidepressants, antipsychotics, psychostimulants and paracetamol are also commonly seen in the hospitals, although not always in the same order of frequency.

Table 4. | Agents involved in calls to the Belgian Poison Centre for adults advised to go to a hospital with acute poisoning and adults who were seen at a hospital with acute poisoning. Percentages are calculated as percentages of the total number of cases.

ICD-10	Agents[1]	BPC[2]	Hosp1 [3]	Hosp2 [4]	Hosp3.1 [5]	Hosp3.2 [6]
			n (%)8	n (%)	n (%)	n (%)
T51	**Alcohol**	**200(9.1)**	**901(74.2)**	**268(65.5)**	**278(67.1)**	**195(75.3)**
T51.0	Ethanol	184(8.4)	899(74.1)	268(65.5)	278(67.1)	195(75.3)
T40	**Narcotics and psychodysleptics (hallucinogens)**	**167(7.6)**	**229(18.9)**	**82(20.0)**	**91(22.0)**	**39(15.1)**
T40.2	Other opioids	115(5.2)	30(2.5)	26(6.4)	19(4.6)	7(2.7)
T40.5	Cocaine	17(0.8)	83(6.8)	16(3.9)	14(3.4)	14(5.4)
T40.7	Cannabis (derivatives)	11(0.5)	79(6.5)	33(8.1)	56(13.5)	16(6.2)
T40.1	Heroin	1(0.0)	14(1.2)	2(0.5)	1(0.2)	2(0.8)
T43	**Psychotropic drugs, NEC**	**580(26.5)**	**199(16.4)**	**76(18.6)**	**81(19.6)**	**50(19.3)**
	Antidepressants	309(14.1)	78(6.4)	28(6.8)	31(7.5)	25(9.7)
	Antipyschotics	229(10.4)	43(3.5)	26(6.4)	28(6.8)	16(6.2)
	Psychostimulants	42(1.9)	78(6.4)	22(5.4)	22(5.3)	9(3.5)
T42	**Anti-epileptic, sedative-hypnotic, antiparkinsonism drugs**	**579(26.4)**	**179(14.7)**	**134(32.8)**	**123(29.7)**	**75(29.0)**
T42.4	Benzodiazepines	497(22.7)	165(13.6)	109(26.7)	109(26.3)	66(25.5)
	Anti-epileptics	48(2.2)	5(0.4)	6(1.5)	4(1.0)	4(1.5)
T39	**Nonopioid analgesics, antipyretics, antirheumatics**	**277(12.6)**	**70(5.8)**	**36(8.8)**	**36(8.7)**	**24(9.3)**
T39.1	Paracetamol	150(6.8)	42(3.5)	23(5.6)	21(5.1)	14(5.4)
T39.3	Other nonsteroidal anti-inflammatory drugs [NSAID]	110(5.0)	27(2.2)	11(2.7)	13(3.1)	8(3.1)
T46	**Agents primarily affecting the cardiovascular system**	**146(6.7)**	**28(2.3)**	**8(2.0)**	**8(1.9)**	**6(2.3)**
	Not beta-blockers	**85(3.9)**	**17(1.4)**	**4(1.0)**	**3(0.7)**	**2(0.8)**
	Beta-blockers	**61(2.8)**	**11(0.9)**	**4(1.0)**	**5(1.2)**	**4(1.5)**
T58	**Carbon monoxide**	**34(1.6)**	**20(1.6)**	**18 (4.4)**	**1(0.2)**	**3(1.2)**
T59	**Other gases, fumes and vapours**	**13(0.6)**	**13(1.1)**	**18(4.4)**	**0(0.0)**	**0(0.0)**
T41	**Anaesthetics and therapeutic gases**	**2(0.1)**	**11(0.9)**	**1(0.2)**	**1(0.2)**	**0(0.0)**
T47	**Agents primarily affecting the gastrointestinal system**	**56(2.6)**	**9(0.7)**	**6(1.5)**	**6(1.4)**	**2(0.8)**

ICD-10	Agents[1]	BPC[2]	Hosp1 [3] n (%)8	Hosp2 [4] n (%)	Hosp3.1 [5] n (%)	Hosp3.2 [6] n (%)
T54	Corrosive substances	60(2.7)	7(0.6)	2(0.5)	2(0.5)	1(0.4)
T45	Primarily systemic and haematological agents, NEC[7]	77(3.5)	7(0.6)	3(0.7)	4(1.0)	2(0.8)
700 [8]	Other	5(0.2)	6(0.5)	0(0.0)	0(0.0)	0(0.0)
T36	Systemic antibiotics	63(2.9)	3(0.2)	1(0.2)	2(0.5)	1 (0.4)
T38	Hormones and their synthetic substitutes and antagonists, NEC	38(1.7)	4(0.3)	4(1.0)	5(1.2)	2(0.8)
T50	Diuretics and unspecified drugs, medicaments and biological substances	17(0.8)	4(0.3)	2(0.5)	2(0.5)	2(0.8)
T55	Soaps and detergents	74(3.4)	1(0.1)	0(0.0)	1(0.2)	2(0.8)
T65	Other and unspecified substances	0(0.0)	2(0.2)	5(1.2)	0(0.0)	1(0.4)
T49	Agents primarily affecting skin, mucous membrane and ophthalmological, otorhinolaryngological and dental drugs	50(2.3)	1(0.1)	0(0.0)	2(0.5)	0(0.0)
T60	Pesticides	1(0.0)	1(0.1)	1(0.2)	0(0.0)	0(0.0)
T52	Organic solvents	26(1.2)	2(0.2)	0(0.0)	0(0.0)	0(0.0)
T44	Drugs primarily affecting the autonomic nervous system	17(0.8)	2(0.2)	1(0.2)	0(0.0)	0(0.0)
T37	Other systemic anti-infectives and antiparasitics	12(0.5)	1(0.1)	0(0.0)	0(0.0)	0(0.0)
T56	Metals	0(0.0)	1(0.1)	0(0.0)	0(0.0)	0(0.0)
T48	Poisoning by agents primarily acting on smooth and skeletal muscles and the respiratory system	18(0.8)	0(0.0)	0(0.0)	0(0.0)	1(0.4)
TOTAL CASES		2,192(100)	1,214(100)	409(100)	414(100)	259(100)
TOTAL AGENTS		2,512	1,701	666	643	406
TOTAL AGENTS NO ETHANOL		2,312	800	398	365	211

[1] ICD-10: International Classification of Diseases of the World Health Organization (WHO)
[2] BPC Belgian Poison Centre
[3] Hosp1: university hospital
[4] Hosp2: regional hospital
[5] Hosp3.1: site 1 of a general hospital
[6] Hosp3.2: site 2 of a general hospital
[7] NEC: Not Elsewhere Classified
[8] 700: agents that cannot be coded in T36-T65
[9] n(%): number and percentages of agents divided by the total cases

Cost

The mean cost for a call to the BPC was $30 which was entirely financed by the government.

Mean cost for a patient admitted to the hospital was $1,558, $2,522, $3,491 and $1,169 in Hosp, 2, 3.1 and 3.2, respectively (mean cost Hosp3: $2,616).

Median cost was $512 ($187-$1,782) in Hosp1, $513 ($153-$1,161) in Hosp2, $1,090 ($136-$4,000) in Hosp3.1 and $222 ($126-$1,168) in Hosp3.2 (median cost Hosp3: $428 ($132-$1,930)).

The mean proportion of the cost charged by the hospitals to the patient and the insurance was 4.4% and 95.6% respectively. These figures are in the same range in the different hospitals: 4.3% and 95.7% in Hosp1, 5.2% and 94.8% in Hosp2, 3.8% and 96.2% in Hosp3.1, 4.9% and 95.1% in Hosp3.2 (4.0% and 96.0% in Hosp3).

The proportion of cost charged for the ambulatory ED versus the cost of care for which at least one day of accommodation was charged (ED-24h, Hosp-referral and Hosp-urgent-referral) was 9.1% and 90.9%. In Supplementary File S5.1, we present Table 5 expressed in EUROs.

Table 5. | Total cost, mean cost and median cost of patients admitted with poisoning to Belgian hospitals, international dollars

	Hosp1 [1]	Hosp2 [2]	Hosp3.1 [3]	Hosp3.2 [4]	Hosp3 [5]
Cost	n=1,175	n=404	n=407	n=246	n=653
	$ (%)	$ (%)	$ (%)	$ (%)	$ (%)
Total cost	**1,830,870(100.0)**	**1,018,831(100.0)**	**1,420,923(100.0)**	**287,627(100.0)**	**1,708,549(100.0)**
ED	**240,522(13.1)**	**75,266(7.4)**	**59,214(4.2)**	**39,218(13.6)**	**98,431(5.8)**
Physicians' Fees	236,973(98.5)	69,617(92.5)	58,604(99.0)	38,487(98.1)	97,091(98.6)
Pharmaceuticals	2,308(1.0)	5,600(7.4)	560(0.9)	701(1.8)	1,261(1.3)
Other	1,240(0.5)	49(0.1)	49(0.1)	30(0.1)	79(0.1)
Hospitalization	**1,590,348(86.9)**	**943,565(92.6)**	**1,361,709(95.8)**	**248,409(86.4)**	**1,610,118(94.2)**
Physicans' Fees	339,892(21.4)	144,696(15.3)	227,654(16.7)	62,060(25.0)	289,714(18.0)
Pharmaceuticals	103,500(6.5)	23,680(2.5)	34,962(2.6)	18,131(7.3)	53,093(3.3)
Accommodation	1,134,902(71.4)	773,565(82.0)	1,096,489(80.5)	167,986(67.6)	1,264,475(78.5)
Other	12,054(0.8)	1,624(0.2)	2,604(0.2)	231(0.1)	2,835(0.2)
	$ (%)	$ (%)	$ (%)	$ (%)	$ (%)

Cost	Hosp1 [1] n=1,175	Hosp2 [2] n=404	Hosp3.1 [3] n=407	Hosp3.2 [4] n=246	Hosp3 [5] n=653
	$ (%)	$ (%)	$ (%)	$ (%)	$ (%)
Total cost	**1,830,870(100.0)**	**1,018,831(100.0)**	**1,420,923(100.0)**	**287,627(100.0)**	**1,708,549(100.0)**
Patient	79,561(4.3)	53,045(5.2)	53,926(3.8)	14,201(4.9).1026287308	68,127(4.0)
Insurance	1,751,309(95.7)	965,786(94.8)	1,366,997(96.2)	273,426(95.1)	1,640,422(96.0)
	$ (SD)	$ (SD)	$ (SD)	$ (SD)	$ (SD)
Mean cost/episode	**1,558(3,212)**	**2,522(5.917)**	**3,491(6,042)**	**1,169(3,228)**	**2,616(5,284)**
ED	205(156)	131(160)	145(110)	159(130)	151(118)
Hospitalization	1,353(3,215)	2,391(5,925)	3,346(6,038)	1,010(3,110)	2,466(5,281)
	$ (SD)	$ (SD)	$ (SD)	$ (SD)	$ (SD)
Mean cost/episode	**1,558(3,212)**	**2,522(5.917)**	**3,491(6,042)**	**1,169(3,228)**	**2,616(5,284)**
Patient	56(119)	171(335)	132(311)	58(128)	104(261)
Insurance	1,231(2,585)	2,351(5,611)	3,359(5,828)	1,111(3,110)	2,512(5,099)
	$ (IQR)	$ (IQR)	$ (IQR)	$ (IQR)	$ (IQR)
Median cost/episode	**512(187-1,782)**	**513(153-1,161)**	**1,090(136-4,000)**	**222(126-1,168)**	**428(132-1,930)**
ED	169(98-261)	147(97-203)	123(79-171)	122(81-185)	123(81-177)
Hospitalization	0 (0-1,557)	0(0-998)	1,003(0-3,810)	0(0-1,025)	0(0-1,786)
	$ (IQR)	$ (IQR)	$ (IQR)	$ (IQR)	$ (IQR)
Median cost/episode	**512(187-1,782)**	**513(153-1,161)**	**1,090(136-4,000)**	**222(126-1,168)**	**428(132-1,930)**
Patient	30(9-91)	36(17-105)	37(18-117)	25(13-68)	33(16-99)
Insurance	472(131-1,692)	450(127-6,566)	1,029(113-3,898)	200(108-1,093)	393(109-1,874)

[1] Hosp1: university hospital
[2] Hosp2: regional hospital
[3] Hosp3.1: site 1 of Hosp3, general hospital
[4] Hosp3.2: site 2 of Hosp3, general hospital
[5] Hosp3: general hospital

Compliance of the patients with the BPC advice

We know from a follow-up survey conducted in previous research [23] that 31.7% of Hosp-referrals and Hosp-urgent-referrals were cared for on site, 10.3% went to the doctor, and 58.0% went to the hospital. Extrapolating this proportions to our dataset of 2,192 calls for acute poisoning in Hosp-referral and Hosp-urgent-referral adults, 1,270/2,192 (58.0%) were compliant with the advice and went to the hospital, 695 (31.7%) performed self-care at home, and 227 (10.3%) went to the doctor.

As shown in Table 6, this represents an estimated total cost of $2,054,738 when using the mean hospitalization cost of Hosp1 and $3,278,597, $4,509,058 or $1,522,174 when using the mean hospitalization cost of Hosp2, Hosp3.1 and Hosp 3.2, respectively.

If all 2,192 patients had been hospitalized, the total estimated cost would have been $3,415,574 using the mean hospitalization cost of Hosp 1, or 1.6 times higher.

Table 6. | Proportion of patients compliance with the BPC advice extrapolated from the results of a follow-up survey conducted between 1 March and 15 May 2019 and expressed in international dollars

Advice	Action after BPC call		Cost/type of care				Total cost	Mean cost
			BPC	Doctor	Hospital	Total		
n (%)		n (%)	$	$	$	$	$	$
2,192	Self-care at home	695 (31.7)	30.20	0.0	0.00	30.20	20,998	937.4
	Went to the doctor	227 (10.3)	30.20	43.7	0.00	73.90	16,750	
	Went to the hospital	1,270 (57.9)	30.20	0.0	1,588.40	2,016,990		
	Total						**2,054,738**	

Discussion

This study compared data of adults with acute poisoning for whom the BPC was called and who were advised to go to the hospital, with data of hospital admissions from a selection of hospitals of different region and size. The aim was to examine patient characteristics, involved agents and costs in both groups. We also focused on possible differences between individual hospitals, and assessed the compliance of the patients with the BPC advice.

Characteristics

Calls to the BPC were made by medical doctors in 25.0%. In case of the ED-admissions, only 5.4% to 17.4% of patients were referred by a medical doctor. Despite the fact that a referral by a medical doctor results in a lower individual financial contribution for the patient, the number of referrals by a medical doctor seems to be low [30]. A possible reason may be that patients are not aware of these differences in contribution. Moreover this cost is not charged immediately by the hospital and only has to be paid later. Other possible contributing factors to the high proportion of non-referred patients are the proximity of a hospital and habits influencing health-related behaviour. The question arises whether increasing the financial contribution for non-referral patients would have an impact on the number of referrals by a medical doctor [31-33]. Another question is what effect it would have on the behaviour of the victims, if the lower cost of €5.7 would be extended to people who first called the BPC before going to the hospital. It should be noted that one should be very careful in imposing financial barriers as these may affect healthcare accessibility especially for the socially deprived people.

In 25.9% of BPC calls, victims had no symptoms at the moment of the call, and in 13.8% of calls, skin problems or splashes in the eyes were mentioned. Due to the difficulty to have 24/7 access to dermatologists or ophthalmologists in private practices, people with skin and eye problems are often advised to go to the ED, regardless of symptom severity. However, these patients present only a small proportion of ED admissions (0.8%) (range 0.0%-0.9%). Among other factors, it cannot be excluded that for this type of patients a code was used that falls outside our inclusion criteria.

Intentionality

In BPC, 42.1% of calls were categorized as accidental which is much higher than in the hospitals (range between 0.5% and 6.1%). Clearly the BPC is more often called for accidental errors with medicinal agents, and for accidents with non-medicinal agents such as corrosive substances (e.g. drain cleaners, swimming pool products) and soaps/detergents (e.g. liquid laundry detergent capsules). The difference in proportion for intentional self-harm between the BPC and the hospitals (53.6% and 21.5%-28.2%, respectively) and substances of abuse (2.4% and 51.2%-72.1%, respectively) is remarkable. The difference may at least partially be explained by the lack of an unequivocal categorization guideline in the BPC and the hospitals, resulting in categorization inconsistencies.

Type of hospitalization

In the hospitals, 47.8%-64.1% of patients received ED-ambulatory care, 16.2%-26.6% ED-24-hours care, 4.6%-31.6% was hospitalized and 3.3%-4.6% was admitted to the ICU. The rates of Hosp1 and Hosp2 were in the same range of magnitude whereas for Hosp3.1 and Hosp3.2 a different percentage in distribution was observed. The much lower hospitalization rate of patients in Hosp3.2 may be explained by the referral of this patient group to the site of Hosp3.1. When taking both sites together, the mean admission rate is in the same order of magnitude: 54.1% ambulatory patients, 20.2% ED-24-hours patients, 21.2% hospitalizations and 4.5% ICU patients.

In a study from the Netherlands in six hospitals, hospital admission rates are different from the Belgian figures and ranged between 26.6% to 78.3% [34]. A possible explanation for these differences may be that there was no short stay unit (ED-24-hours unit) for patients with intoxication in the six hospitals.

Mortality rate

The mortality rate in the studied hospitals was 0.2%, which is in accordance with the literature [10,11,17,34,35-38].

Agents

The low presence of ethanol (184/2,115 cases, 8.4%) among BPC callers is remarkable compared to that in ED visitors (range between 268/409 cases (65.5%) – 195/259 cases (75.3%)). This may be explained by the fact that calltakers cannot physically evaluate the callers which may result in an underestimation of the involvement of ethanol. Another possible explanation is that ethanol alone is probably not often a reason to call the BPC as most people are familiar with the effects of ethanol.

Benzodiazepines are an important reason for referral to the hospital among callers to the BPC (22.7%) and are also frequently involved in patients admitted to the hospital (range between 13.6%-26.7%) as has also been reported in the literature [11-14,20]. This may be due to the frequent use of benzodiazepines. In Belgium, it is estimated that 1 in 10 people take benzodiazepines in a normal dose for a long period of time and that half of them are unintentionally dependent. [39].

Cases involving antidepressants were represented in 14.1% of BPC calls and range between 6.4%-9.7% for ED admissions. This observation is in line with the increasing number of Daily Defined Doses (DDDs) of antidepressants in Belgium. About 1.19 million persons out of a population of 11.3 million was reimbursed in 2014 by the National Health and Disability Insurance (NHDI, Rijksdienst voor Ziekte- en InValiditeitsverzekering) for at least one package of an antidepressant [40,41].

Cost and compliance

The difference in mean cost between the hospitals can mainly be explained by differences in length of stay (1.1, 3.5, 4.3 and 1.0, respectively) being one of the most important drivers of cost. The low cost in Hosp3.2 may be explained by the high percentage of ED-amb patients (64.1%) as more severe cases are sent to Hosp3.1.

As the cost to call the BPC is only a fraction of the cost for admission to the ED, it is worth considering whether people should be encouraged to first call the BPC in case of an acute poisoning (except for life-threating events) to reduce inappropriate use of medical services. Calls are indeed immediately handled by experts in toxicology after which the victim is referred to the appropriate level of care with a minimum delay. The mean time of a call to the BPC is less than three minutes. The results of our study underline that the BPC advice cannot be taken as the basis for cost calculation. The patient compliance with the BPC advice has to be taken into account when estimating the cost. In our study,

31.7% of patients preferred self-care at home and 10.3% consultation by a medical doctor. Watts et al. mention a non-compliance rate for hospital referrals of 23.9% [42].

The reason for not following the BPC advice needs further investigation. In literature, factors are mentioned that patients need physical action, emotional reaction, disruption of normal activities, and additional anxiety when going to a hospital [42], next to the fact that there could be influence of family members, minimization of the perceived threat, and psychosocial reasons for non-compliance [43]. Krot et al. studied the factors impacting on patient compliance with medical advice. [44]. She concluded that trust in the integrity and honesty of doctors, the benevolence and emotional support of doctors, and satisfaction are factors that promote compliance.

The BPC should be concerned about non-compliance in at-risk patients with potentially serious poisoning and has to consider strategies for improving compliance and closer follow-up of potentially serious poisoning cases to ensure that appropriate advice is followed [43].

Limitations and generalisability

A first limitation is that we do not know whether the patients included in the BPC dataset followed the BPC advice nor to which hospital they might have gone.

A second limitation is that there may be bias in the extrapolation of the survey results [23] to the BPC dataset as the survey was conducted at a different time and on other patients than those in the BPC dataset.

A third limitation is that we compared 2,192 patients advised to go to the hospital with hospital data, although we estimated that only 1,271/2,192 patients (58%) followed the BPC advice, which may induce bias in our results.

A fourth limitation is that we excluded the BPC callers with an ED-watchful-waiting strategy, i.e. the patients who were advised to go to the hospital only if their situation worsened or when symptoms appeared[23].

A strength of the study is the multicenter study design, with data of hospitals of different size, region and care burden. To our knowledge, this is the first study comparing hospital data with data from a poison centre.

Conclusion

Large differences between characteristics, involved agents and costs were found between the BPC and the included hospitals, although we found also a certain overlap. A better understanding is needed of the factors responsible for these differences in order to optimize the appropriate use of these medical services in poisoning cases. It may be clear that a two-sided follow up of patients is needed: a follow-up of patients with acute poisoning who called the BPC and were referred to the hospital, and (2) a follow-up of patients with acute poisoning admitted to the hospital with or without having called the BPC.

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Supplementary files

S5.1 Table. Total cost, mean cost and median cost of patients admitted with poisoning to Belgian hospitals, expressed in EURO's 2017.

Chapter 7

General discussion

Abbreviations

BPC: Belgian Poison Centre
ED: Emergency Department
GP: General Practitioner
GUH: Ghent University Hospital
OECD: Organisation for European Economic Co-operation
ED-amb: Emergency Department-ambulatory care
ED-24h: Emergency Department-24-hours-observation unit
Hosp: Hospitalization unit
GP: General practitioner
Hosp-watchful-wait: watchful waiting, referral in case of deterioration
Hosp-referral: referral to a hospital
Hosp-urgent-referral: urgent referral to a hospital
WHO: World Health Organisation
ICD-10: International Classification of Diseases, version 10
DALY: Disability-Adjusted Life Years
GDPR: General Data Protection Regulations
MZG: Minimal hospital data (Minimale Ziekenhuis Gegevens)
RQ: Research Question
UREG: Official Emergency Registration System at Emergency Departments (Urgentie REGistratiesysteem)

In this chapter, we first give an overview of the empirical findings in the five articles.

We then give some reflections on these findings: (1) the impact of (non)-compliance of the patients with the advice of the Belgian Poison Centre (BPC), (2) the question if the BPC and the hospital offer a complementary service in case of acute poisonings, (3) ethanol and the thin line between social drinking and problematic use, (4) large differences in the length of stay of poisoned patients between hospitals, (5) management of the patient flow in acute poisoning, and (6) the need for protocols.

Then, we focus on the strengths and limitations , and on the implications for practice and healthcare policy. Finally, we discuss a number of recommendations and suggestions for further research.

Overview of the empirical findings in article 1 to 5

By means of five separate articles, the present dissertation focused on acute poisonings for which people called the BPC or went to a hospital. Article 1 and 2 focused on emergency department (ED) admissions, article 3 and 4 on Belgian Poison Center (BPC) consultations, and article 5 compared the characteristics and costs of ED admissions versus BPC consultations in case of acute poisonings. As the inclusion criteria of the articles were different, Table 1 gives an overview of the target population and study perspective in the five articles.

Table 1. | Overview of the target population and study perspective in articles 1 to 5 of this dissertation

	Article 1	Article 2	Article 3	Article 4	Article 5
Acute poisoning	Y	Y	Y	Y	Y
Hospital cases	Y	Y	NA	NA	Y
BPC cases	NA	NA	Y	Y	Y
Adults	Y	Y	Y	Y	Y
Children	N	N	Y	Y	N
Health insurance	Y	Y	Y	Y	Y
Inclusion of uninsured patients	Y	N	Y	Y	Y
Unintentional	Y	Y	Y	Y	Y

	Article 1	Article 2	Article 3	Article 4	Article 5
Use of substances of abuse	Y	Y	N	Y	Y
Intentional	Y	Y	N	Y	Y
Advice care on site (home)	NA	NA	Y	N	N
Advice consult medical doctor	NA	NA	Y	N	N
Advice Hosp-watchful-wait	NA	NA	Y	Y	N
Advice Hosp-referral	NA	NA	Y	Y	Y
Advice Hosp-urgent-referral	NA	NA	Y	Y	Y
Time period	2017	2017	23 Feb-18 March 2016	1 Jan 2018-30 Jun 2018 Survey: 1 March-15 May 2019	BPC: Jan 2018- 30 Jun 2018 Hosp 1, 2: 2017 Hosp 3: 1 Jul 2016- 30 Jun 2017
Survey	N	N	Y	Y	N
Number	1,214	1,175	404	5,476 Survey: 561	BPC: 2,192 Hosp: 2,296

Emergency department admissions

Article 1 | Characteristics and costs in adults with acute poisoning admitted to the emergency department of a university hospital in Belgium

The aim of Article 1 was to answer RQ1: What are the characteristics of patients admitted with acute poisoning to the emergency department (ED) of Ghent University Hospital (GUH)? What are the factors associated with the hospitalization type? What are the general costs charged to the government and the patient?

1,214 cases were included on the basis of the following criteria:

- Victims admitted to the ED of the hospital: (1) ambulatory patients (ED-amb) discharged home after treatment, (2) patients requiring observation admitted to the ED-24-hours-observation-unit (ED-24h), and (3) patients admitted to the hospital ward (Hosp).
- Reason for admission: acute poisoning
- Age group: adults (14 years or older)
- Data: 2017.

Data of 2017 (1st January to 31st December) were collected prospectively and analyzed retrospectively using patients' medical records and hospital invoices. Factors associated with type of hospitalization were identified using appropriate statistics.

A total of 1,214 ED admissions were included, accounting for 3.6% of all ED admissions. Men (62.2%) and the age group 21-40 years (43.0%) accounted for the largest proportion. Substances most commonly involved were ethanol (52.9%), benzodiazepines (9.7%), cocaine (4.9%), cannabis (4.6%), antidepressants (4.6%) and psychostimulants (4.6%) (the percentages were calculated on the total number of agents involved, not on the total number of cases). A total of 4,561 treatment acts were recorded, most commonly monitoring of vital signs (63.6%) and medication and/or intravenous drip administration (62.9%). Patients were discharged home after having received care in the emergency department (ED-amb) in 54.5% of admissions, were admitted to the emergency-department-24-hours-observation unit (ED-24h) or were hospitalized (Hosp) in 24.6% and 20.9% of admissions, respectively. Factors found to be associated with hospitalization type were age, hour of admission, victim location, degree of severity, use of antidotes, involvement of antidepressants, antipsychotics, psychostimulants, benzodiazepines and ethanol. Total direct cost charged by the hospital to the government and the patient was €1,512,346 with an average of €1,287 per admission.

In article 1 we confirmed that poisonings entail a considerable percentage of patients admitted to an ED and financial burden. In particular, ethanol poisonings account for the largest proportion of all ED admissions. Comparison of our figures with other data was hampered by the heterogeneity in inclusion criteria. Availability of a uniform template would facilitate comparison and allow better monitoring policies for prevention and cost reduction.

Article 2 | Adults with acute poisoning admitted to a university hospital in Belgium in 2017: cost analysis benchmarked with national data

The aim of Article 2 was to answer RQ2: What are the more detailed costs and cost components charged to the government and the patient in case of acute poisoning for all types of hospitalization? What are the factors associated with the cost? Are the costs charged by Ghent University Hospital (GUH) in line with the costs as available in national data?

1,175 cases were included on the basis of the following criteria:

- Victims admitted to the emergency department (ED) of the hospital with a Belgian obligatory health and disability insurance: (1) ambulatory patients (ED-amb) discharged home after treatment, (2) patients requiring observation admitted to the ED-24-hours-observation-unit (ED-24h), (3) patients admitted to the hospital ward (Hosp) or (4) transferred to the intensive care unit (ICU) for further monitoring.
- Reason for admission: acute poisoning
- Age group: adults (14 years or older)
- Data: 2017

Patient records and invoices of all poisoning-related episodes of patients 14 years or older admitted to the ED of GUH in 2017 were analyzed. A generalized linear model with gamma loglink was applied to assess the variables associated with the cost. Our GUH data 2017 were compared with national data 2016 for all Belgian hospitals on the one hand, and for the subgroup of GUH 2016 data on the other hand. Data provided by the Technical Unit of the Federal Public Service Health were used, containing All Patient Refined Diagnosis Related Groups 812 (poisoning by medicinal agents) and 816 (toxic effects by non-medicinal substances).

The total direct cost for the treatment of 1,175 poisoned patients amounted to $1,830,870. Median direct cost per patient was $512 per episode, with $199 for ambulatory patients, $1,575 for patients admitted to the ED-observation-unit, $3,398 for hospitalized patients and $4,859 for patients treated in the intensive care unit. Factors associated with the cost were gender, degree of severity, type of hospitalization, intentionality, and involvement of ethanol, paracetamol, antidepressants or amphetamines. Median hospitalization cost per admission in GUH for medicinal agents was 70.5% higher than the cost reported in national hospitalization data. Median cost per admission in case of non-medicinal agents was 54.5% higher than the national median 2016.

In article 2 we confirmed that the type of hospitalization has a high impact on the cost, primarily due to the length of hospital stay, with accommodation accounting for a large proportion of the costs. It is important to benchmark individual hospital data with (inter)national data to evaluate its own cost management in the context of continuous improvement. At this moment, this proves difficult. In order to reach this goal it will be necessary (1) to do a meta-analysis of existing studies specifying the definition of cost and their method of cost calculation, and (2) to conduct a prospective study using a template in which all possible costs which can be charged are included.

Poison center consultations

As the aim of this dissertation was to compare emergency department (ED) admissions with poison center consultations, article 3 and 4 focused on the calls to the Belgian Poison Centre (BPC).

Article 3 | Belgian Poison Center impact on healthcare expenses of unintentional poisonings: a cost-benefit analysis

The aim of Article 3 was to answer RQ3: to evaluate the impact of the BPC on national healthcare expenses for calls from the public for unintentional poisonings and to estimate the cost-benefit of the BPC.

404 cases were included on the basis of the following criteria:

- Calls from the public
- Reason for calling: unintentional acute poisoning
- Age group: children (13 years or younger) and adults (14 years or older)
- Financial data: 2017
- Survey: 23 February – 18 March 2016

The probability of either calling the BPC, consulting a general practitioner (GP) or an emergency department (ED) was examined in a telephone survey (Feb-March 2016). Callers were asked what they would have done in case of unavailability of the BPC. The proportion and cost for ED-ambulatory care (ED-amb), ED-24-hours-observation (ED-24h) or hospitalization (Hosp) was calculated from individual invoices. All key parameters were validated by a telephone survey of 404 patients who called the BPC in case of unintentional poisoning, and by the cost analysis of the individual invoices of 796 patients with unintentional poisoning or use of substances of abuse admitted to Ghent University Hospital (GUH) in 2017. A cost-benefit analysis was performed.

Unintentional cases (n=485) from 1,045 calls to the BPC were included. After having called the BPC, 92.1% did not seek further medical help, 4.2% consulted a GP and 3.7% went to an ED. In the absence of the BPC, 13.8% would not have sought any further help, 49.3% would have consulted a GP and 36.9% would have gone to the hospital. The average BPC cost per call was €24.94. The average cost for consulting a GP was €36.11 of which €30.28 was reimbursed by the government and €5.83 was paid by the patient. The average cost for the government for hospital services was based on the analysis of the invoices of 796 patients with acute poisoning admitted to GUH: €199 for ED-ambulatory consultation, €1,1121 for ED-24-hours-observation, and €5,792 for hospitalization. The cost-benefit ratio of the availability of the BPC versus its absence was estimated at 5.70.

In article 3 we confirmed that financial savings can be made if people first call the BPC for unintentional poisonings. The aim of the telephone triage by the physicians of the BPC is to guide patients to the appropriate care, and this in a qualitative and cost-efficient way. In the absence of the BPC, it seems that victims of unintentional poisoning would inappropriately use other, more expensive medical services, such as physician's consultations and hospital use. This represents an estimated cost-benefit-ratio of 5.70. In terms of avoided costs for the Belgian government this represents an estimated saving of €9,568,339 in 2017 for unintentional poisonings. Therefore, patients have to be sensitized by policy makers to first call the Poison Centre in case of unintentional poisoning.

To be able to compare emergency department (ED) admissions with poison center consultations, we had to analyze a selection of poison center cases, i.e. the poison center cases for which the advice was to go to the hospital.

Article 4 | Hospital referrals of patients with acute poisoning by the Belgian Poison Centre: analysis of characteristics, associated factors and costs

The aim of Article 4 was to answer RQ4: What are the characteristics and associated factors of patients with acute poisoning advised by the Belgian Poison Centre (BPC) to go (conditionally) to the hospital? Can we assess the compliance and potential health-economic impact of referral advice?

5,476 cases were included on the basis of the following criteria:

- Victims advised (1) to go to the hospital if symptoms appear or their condition worsens (Hosp-watchful-wait), (2) to go to the hospital (Hosp-referral), or (3) to go urgently to the hospital (Hosp-urgent-referral).
- Reason for calling: acute poisoning
- Age group: children (13 years or younger) and adults (14 years or older)
- Data analysis 1: January 2018- June 2018
- Data analysis 2, Survey: 1 March-15 May

A dataset of three types of referrals to the hospital of patients who called the BPC between 1 January and 30 June 2018 was analyzed: referrals in case of deterioration of the patient's condition (Hosp-watchful-wait), referrals (Hosp-referral) and urgent referrals (Hosp-urgent-referral). Factors associated with type of recommendation were registered. A survey was conducted on a second dataset of patients who called the BPC between 1 March and 15 May 2019 and were referred (conditionally) to the hospital. Intentional cases were excluded from the survey.

5,476 referrals were included: 72.4% for accidental poisoning, 25.3% for intentional self-harm, 1.2% for substance abuse, and 1.1% with unclear intentionality. There were 2,368 (43.2%) Hosp-watchful-wait cases, 2,677 (48.9%) Hosp-referrals and 431 (7.9%) Hosp-urgent-referrals. In Hosp-watchful-wait cases, soaps and detergents were represented most (20.5%), followed by agents primarily affecting skin, mucous membranes or ophthalmic, otorhinolaryngological and dental drugs (8.1%), and noxious substances ingested as food (7.5%). In Hosp-referrals, benzodiazepines (12.7%), antidepressants (7.9%), and antipsychotics (6.7%) predominated. In Hosp-urgent-referrals, these were benzodiazepines (15.1%), antidepressants (7.6%), and paracetamol (7.3%).

Factors associated with hospitalization type were number of symptoms, intentionality, type of agent(s) involved and advising antidotes. The follow-up survey showed that 7.8% of Hosp-watchful-wait patients went to the hospital versus 57.3% of Hosp-referrals and 59.6% of Hosp-urgent-referrals. The mean cost for Hosp-watchful-wait patients, Hosp-referrals and Hosp-urgent-referrals was estimated at €127, €767 and €796 respectively.

In article 4 we confirmed that this analysis is a first step in the assessment of the optimization of the BPC triage process to the hospital. It identifies the differences in the characteristics, associated factors and costs of three types of referrals to the hospital of victims for whom the Belgian Poison Centre (BPC) is called: conditional referrals, referrals and urgent referrals. Only a proportion of patients follows the advice of the

BPC to go (conditionally) to the hospital. The reason why patients did not go to the hospital deserves further exploration. A systematic follow-up of cases is recommended to examine whether the BPC referral advice can be improved. In addition to the "safety first" principle, a substantial insight into the financial impact of advice is also an important element in the triage process as non-compliance of patients with the advice of the poison centre has a substantial health-economic impact.

Comparison of emergency department admissions versus poison center consultations

Article 5 | Comparison of adults with acute poisoning advised by the Belgian Poison Centre to go to a hospital with adults admitted to the emergency department of a hospital with acute poisoning

Article 5 tried to find an answer on RQ5, which is: Can we find similarities and differences in characteristics, involved agents and costs between patients who called the Belgian Poison Centre (BPC) and were referred to a hospital, and patients who were admitted to the emergency department (ED) of a hospital?

BPC: 2,192 cases were included on the basis of the following criteria:

- Victims for whom was called to the BPC and were advised to go to a hospital (Hosp-referral) or to go urgently to a hospital (Hosp-urgent-referral)
- Reason for admission: acute poisoning
- Age group: adults (14 years or older)
- January 2018 - June 2018

Hosp1, Hosp 2 and Hosp3 (Hosp3.1 and Hosp 3.2):

- Victims admitted to the emergency department (ED) of the hospital: (1) ambulatory patients (ED-amb) discharged home after treatment, (2) patients requiring observation admitted to the ED-24-hours-observation-unit (ED-24h) and (3) patients admitted to the hospital ward (Hosp).
- Reason for admission: acute poisoning
- Age group: adults (14 years or older)
- Hosp1, Hosp 2: 2017
- Hosp 3.1, Hosp 3.2: July 2016 - June 2017

Electronic data forms, the financial report and a follow-up survey of the BPC were analyzed. Patients' medical records and hospital invoices of three hospitals (of which one with two sites) were examined. Pearson Chi-Square or Fisher's Exact Test was used.

2,192 BPC calls and 2,296 ED admissions were included. Fourty-two percent of BPC cases were accidental, 2.4% were use of substances of abuse and 53.6% intentional self-harm. In the hospitals, accidental cases ranged between 0.5%-6.1%, use of substance abuse between 52.1%-71.8%, and intentional cases between 21.5%-

28.2%. Twenty-six percent of victims reported not to have any symptoms at the time of the call to the BPC, 15.6% showed a change in consciousness, and 13.8% had dermatological, ophtalmological or nose-throat-ear complaints. In hospitalized patients a change in consciousness ranged between 10.6%-22.8%, and behavioural disorders between 16.8%-57.7%.

Agents most frequently involved in BPC calls were benzodiazepines (22.7%), antidepressants (14.1%), anti-psychotics (10.4%), and ethanol (8.4%). In the hospitals, ethanol was most frequently involved (range 65.5%-75.3%), followed by benzodiazepines (13.6%-25.5%). Cocaine, cannabis, antidepressants, antipsychotics, psychostimulants and paracetamol were also commonly encountered. The mean cost for a call to the BPC was $30 funded by the government. The mean cost charged by the hospital to the government and the patient ranged between $1,169-$3,491, and the median cost between $222-$1,090.

In article 5 we cannot confirm that patients advised by the BPC to go to the hospital have the same characteristics compared with those who went to the three hospitals analyzed. A better understanding is needed of the factors responsible for the similarities and differences between characteristics, involved agents and cost between the BPC and the hospitals to optimize the appropriate use of these medical services in poisoning cases. We also have to take into account that 40% of patients advised by the BPC to go to the hospital, were not compliant with that advice.

Reflections on the empirical findings in article 1 to 5

In this chapter, we give some comments on the results presented in the different articles: (1) the impact of (non)-compliance with the advice of the BPC on the type of referral, estimated cost, and risk of morbidity and mortality, (2) the question whether the BPC and the hospital offer a complementary service in case of acute poisonings, (3) the major role of ethanol in poisoning cases, (4) large differences in the length of stay between hospitals, (5) the management of the flow of patients with acute poisoning to the most appropriate level of care, and (6) the need for study protocols.

(Non)-compliance of the patients with the advice of the BPC: impact on the type of referral, estimated cost, and risk of morbidity and mortality

(Non)-compliance of the patients with the advice of the BPC influences the type of healthcare service level used and the cost, and may impact morbidity and mortality.

Impact on the type of referral

In this thesis, the (non)-compliance of the patients with the advice was estimated by conducting two surveys at the BPC, the first between 23 February and 18 March 2016, and the second between 1 March and 15 May 2019.

Type of referral, based on the survey conducted between 23 February and 18 March 2016

In article 3, we examined whether financial savings could be made if the public first called the BPC for unintentional poisonings (calls for adults and children). The cost-benefit ratio of the availability of the BPC versus its absence was estimated at 5.7.

We assumed that callers followed the advice given by the BPC. Table 2 presents the number of victims of unintentional poisoning advised by the BPC to stay at home, to consult a medical doctor, or to go to the hospital, versus the number of patients who stayed at home, consulted a medical doctor or went to the hospital. All calls came from the public.

Indeed, 388/404 (96.1%) patients confirmed to be compliant with the advice. When we look in more detail, more patients than advised by the BPC decided to stay at home (372/364, 102%), while less patients went to the medical doctor (17/22, 77%) or to the hospital (15/18, 83%).

Table 2. | Number of patients advised by the Belgian Poison Centre to stay at home, to consult a medical doctor, or to go to the hospital, versus the number of patients who stayed at home, consulted a medical doctor or went to the hospital. Survey conducted between 23 February-18 March 2016.

Referred to	Advice of the Belgian Poison Centre	Decision of the patient
	n(%)	n(%)
Self-care at home	364 (90.1)	372 (92.1)
Medical doctor	22 (5.4)	17 (4.2)
Hospital	18 (4.5)	15 (3.7)
Total	**404 (100.0)**	**404 (100.0)**

Type of referral, based on the survey conducted between 1 March and 15 May

Table 3 shows the results of the compliance of the patient with the advice of the BPC for referral to the hospital, extrapolated from the follow-up survey presented in *article 4*.

(1) Type of referral for 5,476 Hosp-watchful-wait, Hosp-referral or Hosp-urgent-referral patients, children and adults

In article 4, a total of 5,476/ 26,406 (20.7%) total calls for acute poisoning between 1 January and 30 June 2018 were advised to go (conditionally) to the hospital. Of those, 1,736/5,476 (31.7%) were compliant with the advice and went to the hospital. A total of 3,357 (61.3%) decided to stay at home, and 383 (7.0%) went to the doctor.

We know from the results of the survey that in case of Hosp-watchful-wait-cases only 7.8% went to the hospital (article 4, Table 4). This low degree of compliance in Hosp-watchful-wait-cases is not surprising, as the Hosp-watchful-wait category should be considered as 'stay at home, and go only to the hospital in the event of a worsening situation'. The non-compliance of the Hosp-watchful-wait patients is not necessarily a negative element, as we would like these patients to present if symptoms worsened or developed from the time of the initial call.

For that reason, it seemed to be appropriate to take into account only the categories Hosp-referral and Hosp-urgent-referral, which gives a more realistic picture. Moreover, this is the group included in article 5 (only adults).

(2) 2,192 Hosp-referral or Hosp-urgent-referral patients, adults

In article 5, 2,192/ 12,632 (17.4%) calls for acute poisoning in adults between 1 January and 30 June 2018 were advised to go (urgently) to the hospital. Of those, 1,271/2,192 (58.0%) were compliant with the advice and went to the hospital. A total of 695 (31.7%) decided to stay at home (care on the site), and 226 (10.3%) went to the doctor.

Table 3. | Proportion of patients who were compliant with the advice of the BPC extrapolated from the results of a follow-up survey conducted between 1 March and 15 May 2019.

Action after BPC call	Total	Hosp-watchful wait	Hosp-referral	Hosp-urgent-referral
	n(%)	n(%)	n(%)	n(%)
Group 1 [1]				
Self-care at home	3,357(61.3)	2,519(88.1)	663(32.2)	175(31.6)
Went to the doctor	383(7.0)	119(4.1)	214(10.4)	50(8.8)
Went to the hospital	1,736(31.7)	222(7.8)	1,182(57.4)	331(59.6)
	5,476(100)	**2,860(100)**	**2,060(100)**	**556(100)**
Group 2 [2]				
Self-care at home	695(31.7)	-	487(29.1)	207(40.0)
Went to the doctor	226(10.3)	-	168(10.0)	59(11.4)
Went to the hospital	1,271(58.0)	-	1,020(60.9)	251(48.6)
	2,192(100)		**1,675(100)**	**517(100)**

[1] Group 1: Calls for children and adults for which the advice of the BPC was Hosp-watchful-wait, Hosp-referral, or Hosp-urgent-referral
[2] Group 2: Calls for adults for which the advice of the BPC was Hosp-referral, or Hosp-urgent-referral

Impact on the estimated cost

Estimated cost, based on the survey conducted between 23 February and 18 March 2016

In article 3, the cost-benefit ratio was calculated already taking into account the patient's compliance with the advice.

Taking into account the original BPC advice, and not the compliance of the patients with the advice, the cost-benefit ratio is almost the same: 5.3 (330/62) because of the compliance of the patient with the advice, which was estimated to be 96.1%. However, as yet mentioned, the compliance of the patients with the BPC advice to go to the hospital was lower, namely 15/18 (83.3%).

Estimated cost, based on the survey conducted between 1 March and 15 May (20.1% intentional cases excluded)

There is a major cost impact due to the fact that people do not always follow the advice given.
Table 4 shows the assumed cost of care as corrected for the compliance of the patient with the advice of the BPC as analyzed in the follow-up survey conducted between 1 March and 15 May 2019. Two situations are presented: (1) Hosp-watchful-wait, Hosp-referral or Hosp-urgent-referral patients, children and adults, and (2) Hosp-referral or Hosp-urgent-referral patients, adults.

(1) 5,476 Hosp-watchful-wait, Hosp-referral or Hosp-urgent-referral patients, children and adults
The total cost is €2,384,804: a cost of €2,277,701 for hospitalized patients, a cost of €83,724 for the patients who decided to stay at home, and € 23,379 for patients who went to the doctor. Assuming that all patients would have gone to the hospital, the estimated cost would have been €7,184,183 (5,476 x €1,312.04) or 3.0 times higher.

(2) 2,192 Hosp-referral or Hosp-urgent-referral patients, adults
The total cost is €1,699,181: a cost of €1,668,045 for hospitalized patients, €17,314 for patients who decided to stay at home, and €13,822 for patients who went to the doctor.

Assuming that all patients would have gone to the hospital, the estimated cost would have been €2,875,992 (2,192 x €1,312.04) or 1.7 times higher.

Table 4. | Assumed cost of care as corrected for the compliance of the patient with the advice of the Belgian Poison Centre as analyzed in the survey conducted between 1 March and 15 May 2019.

Advice		Action after BPC call		Cost/type of care				Total cost	Mean cost
				BPC	Doctor	Hospital	Total		
	n (%)		n (%)	€	€	€	€	€	€
Group 1 [1]									
Hosp-watchful wait	2,860(52.2)	Self-care at home	2,519(88.1)	24.94	0	0	24.94	62,824	126.4
		Went to the doctor	119(4.1)	24.94	36.1	0	61.04	7,264	
		Went to the hospital	222(7.8)	24.94	0	1287.1	1,312.04	291,273	
Hosp-referral	2,060(37.6)	Self-care at home	663(32.2)	24.94	0	0	24.94	16,535	767.8
		Went to the doctor	214(10.4)	24.94	36.1	0	61.04	13,063	
		Went to the hospital	1,183(57.3)	24.94	0	1287.1	1,312.04	1,552,143	
Hosp-urgent-referral	556(10.2)	Self-care at home	175(31.6)	24.94	0	0	24.94	4,365	794.4
		Went to the doctor	50(8.8)	24.94	36.1	0	61.04	3,052	
		Went to the hospital	331(59.6)	24.94	0	1287.1	1,312.04	434,285	
Total	**5,476 (100)**		**5,476**					**2,384,804**	
Group 2 [2]									
Hosp-referral	1,675(76.4)	Self-care at home	487(29.1)	24.94	0	0	24.94	12,156	812.4
		Went to the doctor	168(10.0)	24.94	36.1	0	61.04	10,224	
		Went to the hospital	1,020(60.9)	24.94	0	1287.1	1,312.04	1,338,379	
Hosp-urgent-referral	517(23.6)	Self-care at home	207(40.0)	24.94	0	0	24.94	5,158	654.6
		Went to the doctor	59(11.4)	24.94	36.1	0	61.04	3,598	
		Went to the hospital	251(48.6)	24.94	0	1287.1	1,312.04	329,666	
Total	**2,192(100)**		**2,192**					**1,699,181**	

[1] Group 1: Calls for children and adults for which the advice of the BPC was Hosp-watchful-wait, Hosp-referral, or Hosp-urgent-referral
[2] Group 2: Calls for adults for which the advice of the BPC was Hosp-referral, or Hosp-urgent-referral

Impact on morbidity and mortality

The reason why people with acute poisoning are not compliant with the advice is unclear. Possible explanations are difficulties to reach a hospital, or the advice being perceived as disproportionate.

Krot [1] studied the factors impacting on patient compliance with medical advice. She concluded that control of doctor's competences is one of the strongest factors. Factors that promote compliance are trust in the integrity and honesty of doctors, the benevolence and emotional support of doctors, and satisfaction.

In the context of the BPC phone service, the factors mentioned by Krot are even more crucial, as the experts of the BPC have only a few minutes to build trust in order to convince patients to comply with their advice.

Non-compliance with medical advice may obviously be dangerous and may lead to morbidity and even mortality.

BPC and hospital: do they offer a complementary service in case of acute poisonings?

In this dissertation, five research questions were answered.

Our original motivation at the beginning of this study was to examine whether a cost-efficient workflow was possible between the BPC and the ED by raising awareness in people with a suspected poisoning to first call the BPC instead of going to the ED immediately. The ultimate question is to what extent both services offer a complementary service and serve a different population. In case of an overlap between the two services, an optimized referral strategy may result in an equally high-quality service at a lower cost.

The BPC offers an estimated 83.2% complementary service to the hospital in cases of acute poisoning.

Advice of the BPC in cases of acute poisoning for adults and children

In article 4, we presented in Figure 1 the number of victims for whom was called to the BPC between 1 January and 30 June 2018. From the 26,406 victims, 2,346 were animal victims. From the 24,060 adults and children for whom was called to the BPC, 2,075 victims were in the hospital already, and 21,985 were not in the hospital already.

The experts of the BPC gave the advice to 12,949 victims to be cared for on the site, to 3,560 victims

to consult a medical doctor, and to 5,476 to go to the hospital: 2,368 were Hosp-watchful-wait-patients, 2,677 were Hosp-referrals and 431 were Hosp-urgent-referrals.

Compliance with the advice of the BPC in cases of acute poisoning for adults and children

However, as presented yet in Table 3 of the General Discussion, not all patients were compliant with the BPC advice. More information can be found in supplementary File S7.1.

From these figures we can estimate that from the 21,985 human victims for whom was called to the BPC and who were not in the hospital already, 74.2% (16,306 = 12,949 + 3,357) were cared for on the site, 17.9% (3,943 = 3,560 + 383) went to the doctor and 7.9% (1,736) went to the hospital.

Taking into account all human 24,060 victims, also those who were in the hospital already, 67.8% (16,306) could be cared for on site, 16.4% (3,943) went to the GP, and 15.8% (7.2% + 8.6%) (3,811 = 1,736 + 2,075) were hospitalized or were in the hospital already.

If we multiply these half-year results of 2018 by two, an estimated total of 40,498 ((16,306 x 2) + (3,943 x 2) called the BPC in case of a suspected human poisoning and was not sent to the hospital. An estimated 3,472 (1,736 x 2) went to the hospital, and 4,150 (2,075 x 2) were in the hospital already.

Overlap between (1) patients who went to the hospital after a call to the BPC, or for whom was called from the hospital to the BPC, (2) and patients who are admitted to the hospital for acute poisoning.

Admissions to the ED after a call to the BPC, and calls from the hospital to the BPC for patients in the hospital already.

An estimated 15.8% of all human victims who contacted the BPC were either admitted to the ED, or were in the hospital already and called the BPC. On an annual basis, this represents 7,622 victims (adults and children).

Admissions to the ED in case of acute poisonings

In 2014 there were 1,519,621 ED admissions in Belgium spread over 139 hospital sites with an ED, or an average of 10,932 per ED, although not equally distributed [2]. More information can be found in supplementary File S7.2. In article 5, 1,234/ 34,000 (3.6%) adults with acute poisoning were admitted to the ED of Hosp1 in the period of one year. In Hosp2, it concerned 409/ 19,308 (2.1%) adults, and in Hosp3, 673/46,438 (1.4%).

Overlap between BPC and ED

It may be clear that the estimated 7,622 BPC victims represent only 0.5% of the 1,519,621 patients admitted to one of the 139 EDs in Belgium.

However, in the FPS national data 2016 presented in article 2, Table 3, 12,645 admissions to the hospital for victims categorized in APR-DRG 812 (poisoning by medicinal agents) and APR-DRG 816 (toxic effects by non-medicinal substances) were calculated. From these 12,645 poisoning cases, an estimated 7,622 (60.3%) were sent to the hospital by the BPC or were in the hospital already when calling the BPC.

Assuming that an average of 2% of all ED admissions were acute poisoning cases, this represents 30,392 on an annual basis. From these 30,392 poisoning cases, an estimated 7,622 (25.1%) were sent to the hospital by the BPC or were in the hospital already when calling the BPC.

It may be clear that there is a certain overlap between the two services, but it will be difficult to develop an optimized referral strategy resulting in an equally high-quality service at a lower cost without further research. It may be clear that a two-sided follow-up of patients is needed: a follow-up on patients with acute poisoning who called the BPC and were referred to the hospital, and (2) a follow-up on patients with acute poisoning admitted to the hospital with or without having called the BPC.

Ethanol: the thin line between social drinking and problematic use

Ethanol consumption in the Organisation for European Economic Co-operation (OECD)

Health at a Glance 2017 [3] presents comparisons of key indicators for health and health system performance across the 35 OECD countries.

Ethanol consumption in the OECD averaged 9 litres of pure ethanol per person per year, equivalent to 96 bottles of wine. This figure is driven by the sizeable share of heavy drinkers: 30% of men and 12% of women binge-drink at least once per month. In Belgium, ethanol consumption averaged 12.6 litres of pure ethanol per person per year. Excessive alcohol consumption is a considerable health burden, associated with an increased risk for a range of illnesses, including cancer, stroke, liver disease, as well as social problems, with an estimated 2.3 million deaths per year. Populations in Belgium, Austria and France consume considerably more litres per capita than the OECD average. In 13 OECD countries ethanol consumption has increased since 2000, most notably in Belgium, Iceland, Latvia and Poland.

The involvement of ethanol in ED admission cases

The involvement of ethanol is a major factor for admissions in hospitals for poisoning.

In article 1, we discussed the high involvement of ethanol in ED admission cases in literature. In article

5, ethanol was involved in 899/1,214 cases (74.1%), 268/409 cases (65.5%), 278/414 cases (67.1%), and 195/259 cases (75.3%) in Belgian hospitals 1, 2, 3.1 and 3.2, respectively.

In Supplementary File S7.3 of the General Discussion, we present a further analysis on the use of ethanol as a co-ingestant in GUH in 2017. The results were submitted as an abstract for the EAPCCT-congress 2020 in Talinn, Estonia.

Governments have to take the necessary preventive measures such as limiting availability by restricting points of sale, set strict age limits for purchase and consumption, increase the price via taxes, and forbidding advertising which are proven to be effective [4].

Large differences in the length of stay between hospitals

In articles 2 and 5, we mentioned large differences in hospital length of stay. In article 2, the mean length of stay in GUH (ED-ambulatory patients excluded) was 2.7 days versus 5.2 days in national data. In article 5, the mean length of stay (all types of admission, also ED-ambulatory patients) for the university Hosp1 was 1.1 versus 3.5 for the regional Hosp2, and 3.0 for the general Hosp3. As mentioned, the reason for shorter stays in the university hospital could be the presence of a team of experts in toxicology.

Another factor may be – especially in the case of regional and general hospitals - that it could be financially interesting to keep the patient longer in the hospital if the hospital has one or more beds available: additional costs could be charged, not only for accommodation, but also for technical and other services provided by the staff.

Management of the flow of patients with acute poisoning calling the BPC to the appropriate level of care

One of the questions is on which criteria the experts of the BPC advised people to go to the ED. The advices given by the doctors and pharmacists of the BPC are not based on protocols they have to follow. Answers are based on scientific literature, toxicological databases such as Micromedex, Toxbase, and Toxinz, books and exchange of experience among the BPC experts. This means that every doctor and pharmacist has a considerable amount of freedom, but also a major responsibility, with regard to the advice given to the patient. In case of less experienced doctors or pharmacists, it may be that a number of patients were sent to the hospital too quickly. From the point of view of the patient, it is possible that he or she took a big risk not following the BPC advice. This should be part of further research, combined with an extensive follow-up.

Need for study protocols

As yet mentioned in article 1, it is difficult to compare results on admissions for poisoning between different EDs .This is due to incompleteness of data on the one hand and the lack of uniformity in reporting on the other hand. A possible solution would be to recommend for epidemiological study purposes a uniform template aimed to report data on poisoning in a standardized way. This is in analogy with registration methods that appeared useful in other domains of emergency medicine like the Utstein template in patients with cardiopulmonary arrest [5] and the registration by the 'Deutsche Gemeinschaft für Unfallchirurgie' [6] of patients with severe trauma. Such registrations allow benchmarking of the care. With regard to poisoning cases admitted to the emergency department, a template would be very helpful, with a clear definition of the collected variables using a uniform definition of poisoning, involved agents, intentionality, charges versus cost together with information on country-specific health organizational structure which would be very valuable.

Strengths and limitations of the studies

Strengths

One of the major strengths of this thesis is the **multidisciplinarity** by the combination of elements from medicine and life sciences with concepts from both economics and management.

Another strength is the use of **different study designs**. In the articles on the hospital(s), we were able to link demographic and clinical data from different sources with financial data from the individual patients' invoices. This information was benchmarked with findings from international literature. In the articles on the BPC, we used information from the patient files and we could enrich this information by using the methodology of a decision tree, by conducting two surveys, and by comparing our results with international studies.

A third strength is that **large patient samples** were included in the empirical studies, allowing for robust findings and conclusions.

The World Health organization (WHO) International Classification of Diseases 10th Revision **(ICD-10)** was used as categorization tool which improved international comparability allowing the scientific community to compare and share data in a consistent and standard way. This may be a first step in the development of a template for uniform data reporting in order to facilitate international comparison.

To our knowledge we provided the first studies that **simultaneously** investigated **acute poisoning cases presenting to both a poison center and an emergency department** including ambulatory care, 24-hours observation, hospitalization, and admission to the intensive care unit.

Finally we examined the **compliance of the patient with the advice of the BPC**.

Limitations

Articles 1 and 2 were **monocentric studies** of GUH, a university hospital with one of the highest category of care weight mix in Belgium. Data may not be representative for all hospitals in Belgium and could not simply be extrapolated to other settings. Therefore, we analyzed data from 3 other hospitals of a different region, size and care burden in order to balance the data collected at GUH.

Nevertheless, these hospitals were located in Flanders, which still hampers generalizability of research findings and practical recommendations for Belgium as a country.

Because we had to rely on **data collected** during routine work in the hospitals and the BPC, it is likely that some information is missing in the databases and/or that a number of cases were not correctly categorized.

Given the restriction that hospital data were anonymized and restricted to the data recorded during the hospital stay, there was no possibility to collect **additional data** on the social situation of the patients, such as more detailed information about family situation, residence, race, language, education level, occupation, income, comorbidities. These factors obviously may have had an impact on the help seeking behaviour, type of hospitalization and the duration of the hospital stay.

Our study found **multiple associations with hospitalization type**, but obviously we should keep in mind that causal relationship cannot be derived from our data.

We did not include **pre- and post-hospital costs nor indirect costs** of poisoned patients. The financial burden for patients, government and society is even much larger when taking into account the loss of working days, disability-adjusted life years (DALYs), morbidity and mortality.

The **inclusion criteria are not the same in all articles**, which hampered generalization. In the analysis of the patients admitted for poisoning in the hospital studies, for example, children were not included. This hampered the comparison with the BPC data, as children account almost for half of calls to the BPC. On the other hand, by using different inclusion criteria, it was possible to analyze the data from different points of view.

Comparison of our figures with **international cost data** was hampered by the heterogeneity of the international literature with regard to inclusion criteria, social security systems, and the costs of staff in other countries. The bias caused by the use of different currencies was compensated in articles 2 and 5 by using international dollars.

We need to take into account possible bias when conducting surveys because of the social **pressure** participants may feel to give a socially accepted answer.

In Article 3 (calls from the public for unintentional calls to the BPC), we assumed that callers would really do what they declared in the survey. In the absence of the BPC, 13.8% would not have sought any further help, 49.3% would have consulted a GP and 36.9% would have gone to the hospital. In Article 5, (Hosp-referral and Hosp-urgent referral adults) 57.9% went to the hospital. The population involved in Article 3 is estimated to be in most cases of lower degree of severity than the population of article 5. It may be that the percentage of 36.9% may be an overestimation. Indeed, it is difficult to

extrapolate whether people, in real life confronted with poisoning in the absence of the BPC, would have taken the same decision as what they answered in the survey. It is very humane that people try to comply with the social norm and give an answer according to what they consider socially acceptable.

Home messages for practice and healthcare policy

In this chapter, we (1) first focus on the complex balance between registration of data versus data management. Without the availability of the data, used in this thesis, it would not have been possible to write this dissertation. However, from the viewpoint of the persons who have to collect the data, there is in some cases a certain registration fatigue. To avoid this, it is important to clearly define the aim for which data have to be collected. In our research, we had the advantage of having large numbers and detailed data available, both from the BPC as from the hospitals. This is not always the case in research. The digital revolution 3.0 focusing on the use of artificial intelligence can be a solution, under the condition that one also takes into account the privacy of the patient. We (2) then focus on the use of technology in poison centers, especially in the US, with the development of webPOISONCONTROL.org. Third (3), we focus on the General Data Protection Regulations (GDPR) and ethical committees and the barriers to access data in research. Then (4), we deal with the importance of understanding the mechanics of financing of the hospitals. Ultimately (5) we focus on the importance of creating partnerships.

Data collection: the complex balance between registration and data management

Registration fatigue: put measurement on a diet

> Pascal Selleslagh (Tweet Apr 10, 2019)
> ***"Ziekenhuizen hebben moeite met registratielast".***
>
> Dave Allegaert, (Tweet Feb 1, 2019)
> ***"Minder papier, meer zorg a.u.b. en nee, een chief deregulation officer zal het probleem niet oplossen. Ga de werkvloer op, praat met de collega's, leer het proces kennen en bekijk de toegevoegde waarde van elke registratie."***
>
> Dave Allegaert (Tweet Apr 11, 2019)
> ***"Put measurement on a diet! Laat ons minder meten, maar wat we meten gebruiken voor kwaliteitsverbetering en minder ter verantwoording."***

The administrative workload for doctors, nurses and others in hospitals should not be underestimated. Healthcare staff experiences this in many cases as a waste of time that could be better spent on the core of their job: delivering care. This is often referred to as registration fatigue: "the hands of the nurses and doctors belong to the bed and not to the laptop".

This difficult balance also affects the data collection in the BPC. We notice a certain tension between the acquisition of the data needed to provide an accurate response to the people with a poisoning problem, versus the acquisition of additional data in the context of research and management.

Hospitals have to spend a lot of money on data collection systems, in the first place for management purposes. Systems have often grown organically resulting in different data systems for patient management, accountancy, invoicing and obligatory data entry for government agencies. All these systems were once created to meet certain needs but they are often not compatible with each other. Also between different hospitals, data systems often differ which hampers electronic data interchange and collaboration.

The government, as one of the main hospital financiers, imposes structured data transmission on hospitals. Apart from a.o. the Minimal hospital data (MZG) data, the government introduced an obligatory registration for emergency departments, named UREG. For many hospitals, this obligation added to the administrative burden, because their system was not equipped to create the output in the format required by the government. Because of these problems, UREG registration is no longer obligatory.

Dave Allegaert (Tweet Jul 9, 2019)

"Laat ziekenhuizen meten om te verbeteren, niet ter verantwoording. Het schrappen van de spoedgevallenregistratie #Ureg is een goeie stap richting administratieve vereenvoudiging en geeft wat zuurstof!"

Find a balance between registration and data management

Dominique Vandijck

There has to be a pragmatic approach in registering and monitoring data so that there remains enough time for patient contact (...) The question is what you are going to do with all the data and information you get (...). Data becomes information from the moment it's useful and a lot of the data which we have in healthcare now isn't always useful." [7]

The frustration of healthcare professionals about data collection is obvious as it leaves less time left for patient care. A second frustration is that they do not always perceive the added value of the registration which is often experienced as collecting data for the purpose of collecting data. This feeling is further reinforced when the collected data are used ineffectively or if they remain untouched afterwards.

The digital revolution 3.0

De Specialist (Maa 26, 2019)

"Artificial intelligence aims to mimic human cognitive functions. It is bringing a paradigm shift to healthcare, powered by increasing availability of healthcare data and rapid progress of analytics techniques. » [8]
"Dienst radiologie AZ Maria Middelares gebruikt artificiële intelligentie (AI) om specifieke levensbedreigende aandoeningen sneller op te sporen in CT-scans, met name die van het hoofd of de nek.".

Zorgvisie.NL (Oct 04, 2019)

"Zorgbestuurder zonder digitale strategie graaft diepe kuil voor zichzelf".

Johan Decruyenaere (Tweet Nov 05, 2019)

"Artificiële intelligente en digitale geneeskunde als een hulpmiddel, niet als een toekomstige vervanger."

However, there is no way back. A new digital revolution is born: artificial Intelligence will change healthcare.

Our research was limited to 1 BPC and 3 hospitals. It is not unthinkable that this research could be carried out on a much larger scale with the development of artificial intelligence and machine learning, with algorithms that analyze and interpret a mass of data at a very fast speed. However, data entry will continue to be a people's job.

In what follows, we quote the key ideas from an article by Dominik Bertram about artificial intelligence and machine learning. It gives an idea of what the future will bring and which obstacles we still have to overcome [9].

"Imagine you're not feeling well and you trudge into a doctor's office. As usual, your blood pressure, temperature, weight, and blood tests are taken, and the results are entered into your record. But then, rather than ask you a bunch of questions you've already answered before, the doctor hits a button and calls up your entire healthcare history—all your past test results and your risks for hereditary and lifestyle-influenced diseases—along with findings from the latest, relevant scientific studies. After asking some computer-assisted questions about your symptoms, the doctor has the system churn through all this information to make recommendations for treatments, medicines, and lifestyle changes to make you better."

This level of personalized medicine is the promise behind the growing influence of machine learning and artificial intelligence (AI) in healthcare. The technology that is being developed by companies like Arterys (AI and radiology) and Freenome (AI and cancer detection) will change healthcare forever, and it will save lives by enabling more accurate diagnoses, more precise treatments, and improved collaboration among patients and healthcare providers.

"Governments, the healthcare and tech industries, and patients should all work together to create the life-saving, life-changing medical care that will improve every trip to the doctor's office."

The promise of machine learning in medicine: the wisdom contained in the decisions made by nearly all clinicians and the outcomes of billions of patients should inform the care of each patient [10].

The use of ICT in health information technology in poison centers

In the BPC, 99% of all requests for help in case of a suspected poisoning are handled by phone. This was the case 50 years ago, and is still the case. We cannot deny that the direct communication by phone has its merits in a stressful situation where it is crucial to gain as much information as necessary from the victim to give the most appropriate advice.

However, a number of issues do exist. The number of calls is increasing, it is not easy to find extra doctors/pharmacists to strengthen the team and the night shifts are physically difficult, especially for a team that is getting older. The identification of products (mushrooms, plants, medicines, drugs) is not always easy via telephone. It is also not easy to make a distinction between calls for information, and urgent or very urgent calls. There can also be a psychological barrier which restrains people from calling the

BPC, despite the fact that the calls are anonymous.

ICT can be one of the tools supporting the activities of the BPC. Opponents of the introduction of modern technology argue that not every household is equipped with the necessary ICT-tools and that older people cannot handle it. In what follows, we wish to contradict this with concrete figures by focusing on the use of ICT in Belgian households. We then focus on an interesting app webPOISONCONTROLorg, developed by 16 poison control centers in the US, supporting the activities of the US poison centres.

ICT use in Belgian households

Over the past decade, there has been a change in the way people access information. In 2017, 86% percent of households and 96% of households with children in Belgium had an internet connection. Only 9.8% of individuals (aged 16 to 74) never used the internet, a decrease of 1.4% compared to 2016. Seventy-two percent of Belgian individuals (aged 16 to 74) used the internet to communicate via social networks [11].

Belgian internet users most often use a mobile device to surf the internet. The smartphone comes first (82%), followed by laptop or notebook (67%), fixed computer (45%) and tablet (43%). The use of smart TV is also increasing: in 2018, 16% said they used their TV to surf the internet (11% in 2016) [12].

webPOISONCONTROL .org

> Litovitz
> ***"Webpoisoncontrol augments traditional poison control services by providing automated, accurate online access to case-specific triage and first aid guidance for poison ingestions. It is safe, quick, and easy to use. [13]"***

webPOISONCONTROLorg [14] provides solutions to a number of issues mentioned above. This online tool uses algorithms to make the right recommendation to the user faced with a poison emergency through a series of simple questions to determine the toxicity.

The app helps people decide what to do when substances are swallowed, splashed in the eye or on the skin, inhaled, or injected. After providing the name of the substance, estimated amount, age and weight, the user is given a case-specific recommendation. The recommendation could be that it's safe to stay home because the risk of toxicity is minimal, that Emergency Room evaluation is required, or that further guidance from Poison Control (a phone call to 1-800-222-1222) is needed. In case it's safe to stay home, the user is also given information on specific symptoms that are likely to occur and not of concern, and symptoms that should trigger a call to Poison Control or a visit to the hospital.

webPOISONCONTROL is used as an initial triage tool if the exposed person meets the following criteria: age 6 months to 79 years; a single acute exposure (not for chronic exposures or repeated use); unintentional

(no self-harm intended); only one product involved (although it can have multiple ingredients), not pregnant, and no serious underlying medical problems.

Definitive guidance by webPOISONCONTROL is only provided for cases that can be managed at home, without intervention by a healthcare provider. That leaves the more difficult cases - the complex, intentional, nuanced or serious cases - to be handled by the experts of the poison centre.

The website mentions that webPOISONCONTROL has had unexpected benefits for the 16 poison centers participating in the project. The implementation of standardized triage algorithms – 1,540 of them at present – has been the first step towards harmonizing poison exposure triage thresholds between and within poison centers. Not only have these algorithms led to standardization, they've also improved operating efficiency as specialists in poison information no longer have to repeatedly take the time (every time there's a case) to research the potentially toxic dose to determine the safe triage threshold. In addition, training new staff is facilitated by access to more specific triage guidance.

At this time, the volume of webPOISONCONTROL cases has not measurably affected telephone call volume at traditional poison centers. Many webPOISONCONTROL users are individuals who would not have called.

Of course, it may be clear that the development of such a tool should be a European exercise. The price of webPOISONCONTROL was approximately $153 million in 2015, with an annual cost of $2 million/year annual budget covering maintenance and enhancements, of which $1.2 million/year for software development and maintenance and $800,000/year for quality assurance, product entry, algorithm development, toxicologists and databases.

General data protection regulation (GDPR) and ethical committees: barriers to accessing data in research

For the hospital data used in articles 1, 2 and 5, the study protocol was approved by the Ethical Committee of the respective hospitals. For the BPC data used in articles 3, 4 and 5, anonymized BPC data were used according to the GDPR guidelines of the BPC. For the surveys in article 3 and 4, informed consent was asked during the initial call. One of the challenges is to find a balance between the protection of the privacy of patients and the use of data for research and management. There is a need for compromise, a "good enough" standard that benefits the patient, healthcare professionals, researchers, and institutions so that barriers to accessing data do not hinder the development of medical innovations [9].

The GDPR, which has been in force since 25 May 2018 in the European Union, creates a uniform European legislative framework and gives citizens/data subjects more control over how personal data is processed. The GDPR requires transparency and responsibility from organizations towards citizens/data subjects about how and why they process personal data. In Belgium, the law on the protection of natural persons with regard to the processing of personal data was published in the Belgian "Staatsblad" on 5 September 2018 [15].

Understanding the mechanics of financing of the hospitals

> *"Although the hospitals sector continues to show a healthy financial structure in terms of solvability, debt ratio and liquidity level, an increasing number of hospitals has a solvability ratio of less than* **20%***. The current result is problematic, with a turnover of only* **0.2%** *and with a deficit for* **40%** *of the hospitals. The* **MAHA***-study of Belfius* **2018** *gives information about the situation of the Belgian hospitals in* **2017** *[16]."*

The financial pressure on hospitals is high, with a turnover of 0.2% and a deficit for 40% of the hospitals in 2017. The quote of the MAHA-study of Belfius 2018 perfectly summarizes the difficult financial state of the Belgian hospitals. Hospital financing in Belgium is complex and constantly in evolution. Article 2 of this dissertation deals with this in more detail.

In article 5, we see a range of the mean cost per episode between €1,287 in the university Hosp1 and €2,884 in the general Hosp3. As yet mentioned, this difference is for the most part due to the length of hospital stay. Healthcare providers themselves should understand the financing mechanism of the hospitals. In this context, insight into the coding system of medical interventions by the healthcare professionals, which is directly linked to the financing, is crucial. Healthcare providers, coders and financial services must work together to optimize the hospital's income.

Creating partnerships: guiding people to information channels and specific assistance

Providing information and referring people to the right level of care in acute poisoning is the primary mission of the BPC. Apart from referring people to the medical doctor or the hospital, it can be very useful to suggest additional help services to the victim, especially if it concerns an addiction problem and/or psychological suffering. In what follows, we focus on three services that can help patients who called the BPC with an acute poisoning problem, but for whom our experts feel that the acute problem is an expression of a deeper problem for which the patient needs help. This is the case, for example, with the use of drugs, suicidal self-harm or psychosocial problems. Of course, this help is complementary and does not replace a doctor's consultation.

Druglijn 078 15 10 20

The Drug Line in Flanders (Infor-Drogues in French-speaking part of the country) is an example of this. Volunteers of the Drug Line offer information, initial advice or addresses for help and prevention. The Annual Report 2017 of the Drug Line [17] shows that the top five products for which calls were made to the Drug Line were cannabis (36%), alcohol (28%), cocaine (22%), medication (11%) and speed (7%). The Drug Line was also contacted via e-mail for cannabis (29%), alcohol (34%), cocaine (11%), medication (8%) and speed (5%). They were contacted via the chat function in 36% of the cases for cannabis (36%), alcohol (23%), cocaine (13%), medication (9%) and speed (amphetamines, 5%).

Zelfmoordlijn 1813

The Suicide Line 1813 [17] is an anonymous helpline for anyone who thinks of suicide or is worried about someone. The emergency line can be reached via telephone, chat and e-mail and is answered by expertly trained volunteers. In 2016 1,057 people died of suicide in Flanders and in 2017 there were an estimated 10,288 suicide attempts [19].

Tele-onthaal 106 onlinehulp

Tele-Reception [20] is anonymously available at telephone number 106 (24/7) or via chat. Tele-Reception works with volunteers. In 2018, Tele-Reception received 107,442 phone calls (294 a day) and 14,357 chats (39 a day). The top ten themes are relations, health, loneliness, suicide, socio-economic themes, addiction, coping with loss, religion, and sexuality. Seven percent of phones and chats in males were about addiction.

Implications and future research perspectives

Need for a template to enable uniform data reporting and facilitate (international) comparison

Comparison of our figures with national and international data was often hampered by the heterogeneity in data reporting. It is important to compare individual data with (inter)national data to evaluate one's own management but at present this proves difficult.

With regard to the characteristics of poisoning cases, a template would be very helpful, with, among other things, a clear definition of the collected variables using a uniform definition of poisoning, a uniform categorization system of involved agents, a clear definition of intentionality, guidelines on how to deal with missing data and with readmissions, and strict inclusion criteria for e.g. age groups.

Inspiration can be found e.g. in the Utstein-style guidelines for cardiac arrest, and in the Deutsche Gemeinschaft für Unfallchirurgie for patients with severe trauma.

With regard to the cost of poisoning cases, guidelines are needed for, among other things, the definition of cost (charges versus cost), the method of cost calculation, the use of international dollars (Purchasing Power Parity), the year of the study, together with information on country-specific health organizational structure.

Variables strongly associated with the BPC referral to hospital: triage tool in daily practice?

As mentioned in Table 4 of Article 4, in the multivariate analysis, we presented a number of variables significantly associated with the referral type: number of symptoms present at the time of the call, intentionality, type of agents involved and advice for administration of antidotes. In the univariate analysis, age, gender, time of the call, location of the victim, number of symptoms present, intentionality, type of transport, number of agents, number of symptoms, examinations and need for antidotes, and type of agents were significantly associated with the referral type ($p<0.05$). The variables used in the univariate and multivariate analysis are variables based on the electronic data reports filled in by the BPC medical doctor/pharmacist during or immediately after the call.

As mentioned in the limitation section, in addition to these objective data, also less tangible factors influence the triage advice factors, such as: mental status of the victim (is the patient anxious or under heavy stress), family situation (is the patient alone or not), comorbidity (heart problems, other diseases), mobility, ... This is the implicit part of the triage process.

We have to consider to add some of these factors to the electronic patient form.

Webpoisoncontrol.Org

In the United States, WebPOISONCONTROLorg is used as an initial triage tool for poisoning cases that can be managed at home. This online tool uses algorithms to help patients aged between 6 months and 79 year, not pregnant, without serious underlying problems, with a single acute unintentional exposure, and with the involvement of only one product. More complex cases are redirected to the call number of the poison centre. It is worth exploring whether such a tool could also be developed at European level. It could be helpful to give poison centres more time to focus on the most serious intoxications.

Appropriate use of healthcare services in cases of acute poisonings

In article 5, we tried to gain insight into the characteristics for referral to the ED by the BPC, compared with hospitalization data of poisoned patients. Large differences between characteristics, involved agents and costs were found between the BPC and the included hospitals, although we found also a certain overlap. From these results, we cannot confirm whether patients advised by the BPC to go to the hospital have the same characteristics compared with those who went to the three hospitals analyzed. Hence, to find an answer on the question whether the BPC and the hospital offer a complementary service in case of acute poisonings, further research is needed.

First, a systematic follow-up of Hosp-referral and Hosp-urgent-referral cases is recommended to examine the reason why people did not follow the BPC advice to go to the hospital. The non-compliance could be due to on the one hand the behavior of the patients, and on the other hand the referral procedure of the highly

qualified BPC experts, with almost no standardization in the manner of working.

In addition to the "safety first" principle, a substantial insight into the financial impact of advice is also an important element in the triage process as non-compliance of patients with the BPC advice has a substantial health-economic impact.

Secondly, a systematic follow-up on patients with acute poisoning admitted to the hospital without having called the BPC is needed to find out whether among these hospitalized patients there were some who better should have contacted the BPC initially.

Qualitative research

After obtaining informed consent from the BPC callers, we conducted two close-ended surveys. In future research, it could be useful to use also qualitative research methods such as open-ended surveys or in-depth-interviews to better understand the complex relationships between the characteristics of socio-economic groups, behavioural determinants, and the use of care services.

In order to conduct this type of research, working together with researchers from other disciplines, such as social sciences is an interesting option for future research.

Ethanol and other agents

The data collected in the hospitals and the BPC give us a wealth of information for further analysis. We observed a high proportion of ethanol poisoning in the hospitals which is of major concern. Our data may provide an incentive for the government to take the necessary preventive measures such as limiting availability by restricting points of sale, setting strict age limits for purchase and consumption, increasing the price via taxes and prohibiting advertising which are proven to be effective.

Children

In the United States, the aim of a recently published study was to identify unintentional pediatric poisoning exposures presenting to a large US children's hospital that could have been managed onsite (i.e., at home) if consultation with a poison centre had occurred prior to the ED visit. The conclusion was that nearly half of ED visits for pediatric patients with unintentional poisoning exposures could have been avoided by contacting a poison centre [20]. It would be interesting to do the same exercise as in the US in a European context.

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Supplementary files

S6.1 Abstract. EAPCCT Congress, Talinn, Estonia, 19-22 May 2020, cancelled because of Covid-19.

Chapter 8

Nederlandstalige samenvatting & Curriculum vitae

Nederlandstalige samenvatting

1. Een eerste doelstelling van deze dissertatie bestond erin om te onderzoeken wat de karakteristieken waren van intoxicaties waarvoor slachtoffers naar het hospitaal gingen. We stelden ons tevens de vraag welke variabelen een rol speelden bij het type hospitalisatie: ambulant verblijf op de spoedgevallendienst, 24-uur observatie op de spoedgevallendienst, of hospitalisatie.

Hierbij wilden we ons niet alleen focussen op accidentele intoxicaties, maar ook op intoxicaties door misbruik en intentionele intoxicaties.

Het Universitair Ziekenhuis van Gent werd als testcase uitgekozen. Er werd een analyse uitgevoerd op de 1,214 patiënten die in 2017 omwille van een intoxicatie naar het ziekenhuis gingen. Gezien er slechts zeven kinderen voorkwamen, werd de focus gelegd op volwassenen van 14 jaar en ouder. Hieruit bleek dat 54.4% ambulant kon worden behandeld, 24.6% in observatie werd gehouden in de spoedgevallendienst en 20.9% werd gehospitaliseerd. Mannen hadden het overwicht met 62.2% en ethanol was goed voor 52.9% van de agentia (74.1% van de cases), benzodiazepines voor 9.7% (13.6% van de cases), cocaïne voor 4.9% (6.8% van de cases) en cannabis, antidepressiva en psychostimulantia voor 4.6% (6.4% van de cases). De agentia werden gecategoriseerd volgens ICD-10, met een groep T36-T50, (vergiftiging door drugs, geneesmiddelen en biologische substanties) en een groep T51-T65 (toxische effecten van substanties waarvan de bron voornamelijk niet-medicinaal is). Variabelen die konden worden geassocieerd met het type opname (ambulante behandeling in de spoedgevallendienst, observatie in de spoedgevallendienst voor max. 24 uur, hospitalisatie) waren: leeftijd, het tijdstip van opname, waar het slachtoffer zich bevond, de graad van ernst, de nood aan antidota en de betrokkenheid van antidepressiva, antipsychotica, psychostimulantia, benzodiazepines of ethanol.

2. Een tweede doelstelling was om van dezelfde groep patiënten uit het Universitair Ziekenhuis van Gent de kost voor de overheid en de patiënt te berekenen en te onderzoeken uit welke onderdelen de kost bestond, inclusief hun onderlinge verhouding.

Omwille van het feit dat de berekening voor niet verzekerde patiënten compleet afwijkt van de in België verzekerde patiënten, werd ervoor gekozen de 39 niet in België verzekerde patiënten uit te sluiten en de analyse te doen op de 1,175 in België verzekerde patiënten.

Kosten geassocieerd met type van opname waren:

geslacht, ernstgraad, soort hospitalisatie, intentionaliteit, en de betrokkenheid van ethanol, paracetamol, antidepressiva of psychostimulantia.

De totale kost bedroeg 1,5 miljoen euro met een gemiddelde kost van 1,287 euro per episode per patiënt.

Voor ambulante patiënten werd een kost berekend van €197, voor patiënten die voor een maximum van 24 uur in de spoedgevallendienst werden geobserveerd €1,343, voor gehospitaliseerde patiënten €3,386 en voor patiënten die moesten worden opgenomen in de intensieve zorgen €7,426 euro. Het remgeld voor patiënten bedroeg 4.3%. De overheid stond in voor de resterende 95.7%.

Gezien het feit dat het hierbij om de kostenberekening van slechts 1 ziekenhuis ging, wensten we deze gegevens af te toetsen aan nationale data. Hiervoor gebruikten we de financiële gegevens van de Technische Cel van de overheid. Deze Cel verbindt de medische informatie, beschikbaar bij de FOD Volksgezondheid, met de kostprijsgegevens, beschikbaar bij het RIZIV. Specifiek voor intoxicaties waren de All Patient Refined Diagnosis Related Groups (APR-DRG) APR-DRG 812 en APR-DRG 816 van belang voor ons onderzoek. Deze onderverdeling van APR-DRG loopt immers parallel met ICD-10, T36-T50 voor geneesmiddelen (vergelijkbaar met APR-DRG 812) en ICD-10, T51-T65 voor niet-geneesmiddelen (vergelijkbaar met APR-DRG 816) die we in ons onderzoek gebruikten.

De Technische Cel gaf de kostprijs weer van enerzijds intoxicaties met geneesmiddelen (APR-DRG 812) en anderzijds intoxicaties met niet-geneesmiddelen (APR-DRG 816) en dit voor nationale gemiddelden in 2016, maar ook voor het gemiddelde van ons bestudeerde ziekenhuis in 2016.

Hoewel de gemiddelde kost voor intoxicaties met geneesmiddelen (APR-DRG 812) 23.2% lager lag bij UZGent 2017 dan het nationaal gemiddelde (€2,710 versus €3,338), lag de gemiddelde kost per dag 62.9% hoger (€1,021 versus €642), en dit omwille van het groter aanbod hooggespecialiseerde zorg. Omwille van die hogere graad van pathologiemix wordt door de overheid immers een hoger bedrag per dag toegekend. Het aantal dagen verblijf in het ziekenhuis in UZGent lag daarentegen 96% lager dan het nationaal gemiddelde (2.7 dagen versus 5.2 dagen), waardoor de totale prijs lager lag dan het nationaal gemiddelde.

Voor intoxicaties met niet-geneesmiddelen (APR-DRG 816) was de totale gemiddelde kost voor UZGent ten opzichte van het nationaal gemiddelde op enkele euro's na hetzelfde (€2,549 versus €2,545), hoewel de gemiddelde kost per dag voor UZGent 66% hoger lag (1,040 versus €688). Dit verschil werd ook hier verklaard door een verschil in aantal dagen hospitalisatie van 51% (2.5 dagen versus 3.7 dagen).

De gegevens van de Technische Cel voor UZGent 2016 lagen voor intoxicaties met geneesmiddelen in dezelfde lijn als onze resultaten voor UZGent 2017. Voor intoxicaties met niet-geneesmiddelen lag de totale kost in 2016 daarentegen 72.4% lager ten opzichte van 2017 (€1,845 versus €2,549) en het aantal dagen 69% lager (1.7 versus 2.5).

3. Een derde doelstelling bestond erin te onderzoeken wat het zou betekenen indien er geen Antigifcentrum zou bestaan. Waar zouden mensen hulp zoeken en welke invloed zou dit hebben op de kost?

Het Antigifcentrum van België bestaat al meer dan 50 jaar en groeide in die tijd uit tot een organisatie die 60,000 oproepen per jaar verwerkt, zowel van het publiek als van medische professionelen.

Via een enquête bij het publiek werd er gepeild naar wat mensen in het geval van accidentele intoxicaties zouden doen. De enquête werd afgenomen bij een publiek van niet-professionele zorgverleners (in casu het publiek) die in feb-maart 2006 belden naar het Antigifcentrum. Uit de 404 antwoorden bleek dat 13.8% niets zou gedaan hebben, 49.3% contact zou opgenomen hebben met een arts en dat 3.7% naar het ziekenhuis zou gegaan zijn. Wat de gehospitaliseerde patiënten betreft, konden we afleiden dat 46% ambulant kon behandeld worden in de spoedgevallendienst, 20.8% in observatie in de spoedgevallendienst moest blijven en 36.9% zou gehospitaliseerd zijn. Dit zou een geschatte kostenbatenratio van 5.7 met zich meebrengen.

4. Een vierde doelstelling bestond erin de karakteristieken te beschrijven van de slachtoffers van intoxicatie aan wie door het Antigifcentrum het advies gegeven werd om (1) naar het hospitaal te gaan indien er symptomen optraden of indien de toestand van de patiënt verergerde, (2) sowieso naar het hospitaal te gaan of (3) dringend naar het hospitaal te gaan, en dit zowel voor kinderen als voor volwassenen. Verder werd via een enquête gepolst of patiënten het advies van het Antigifcentrum daadwerkelijk volgden.

Met de verdere evolutie van de dataverzameling in het Antigifcentrum, werd sedert 2018 de mogelijkheid gecreëerd om een onderscheid te maken tussen patiënten die conditioneel werden gehospitaliseerd (Hosp-watchful-wait), patiënten die effectief het advies kregen om naar het hospitaal te gaan (Hosp-referrals) en patiënten die geadviseerd werden om dringend naar het hospitaal te gaan (Hosp-urgent-referrals). De conditioneel gehospitaliseerde patiënten maakten 43.2% uit, de gehospitaliseerde patiënten 48.9% en de dringend gehospitaliseerde patiënten 7.9%.

Hierbij ging het om 72.4% accidentele intoxicaties, 25.3% intentionele, 1.2% misbruik van substanties (use of substances of abuse) en 1.1% onduidelijke intentionaliteit. Volwassenen maakten 56.9% van het totaal uit.

Voor conditioneel gehospitaliseerde patiënten ging het om 22.8% zepen en detergenten, 9.0% huidproblemen en 8.3% voedsel. Voor gehospitaliseerde patiënten ging het om 16.9% benzodiazepines, 10.6% antidepressiva en 8.9% antipsychotica. Bij dringend gehospitaliseerde patiënten waren er 20.6% benzodiazepines, 10.4%

antidepressiva en 10.0% paracetamol betrokken.

Elementen geassocieerd met opname waren het aantal symptomen, de intentionaliteit, het type agens en het gebruik van antidota.

Er werden 561 patiënten ondervraagd: 293 (52.2%) Hosp-watchful-wait patiënten, 211 (37.6%) Hosp-referrals en 57 (10.2%) Hosp-urgent-referrals.

Van de Hosp-watchful-wait patiënten ging 7.8% naar het hospitaal, 4.1% naar de arts en 88.1% werd ter plaatse behandeld. Voor Hosp-referral patiënten en Hosp-urgent-referral patiënten, ging er respectievelijk 57.3% en 59.6% naar het ziekenhuis, 10.4% en 8.8% raadpleegde een arts, en 32.2% en 31.6% werd ter plaatse behandeld. Opmerkelijk is dat een deel van de patiënten het advies om naar het ziekenhuis te gaan niet opvolgde.

De kost werd geschat op €126, €768 en €795 voor respectievelijk Hosp-watchful-wait patiënten, Hosp-referral patiënten, en Hosp-urgent-referral patiënten.

5. Een vijfde doelstelling bestond erin om te analyseren of de karakteristieken, betrokken agentia en kost van de patiënten aan wie het Antigifcentrum het advies gaf om naar het hospitaal te gaan te vergelijken waren met deze van de gehospitaliseerde patiënten in een universitair ziekenhuis, een regionaal ziekenhuis en de twee campi met een spoedgevallendienst van een algemeen ziekenhuis.

Er werden 2,192 patiënten die naar het Antigifcentrum belden, in de studie opgenomen (Hosp-referrals en Hosp-urgent-referrals). In het universitair ziekenhuis ging het om 1,214 hospitalisaties, in het regionaal ziekenhuis om 409 hospitalisaties, versus 414 in campus 1 van en 259 in campus 2 van het algemeen ziekenhuis.

In het Antigifcentrum werden 42.1% gevallen als accidenteel gecategoriseerd en 53.6% als intentioneel. In de ziekenhuizen waren er tussen 0.5% en 6.1% accidentele gevallen en tussen 21.5% en 28.2% intentionele gevallen.

Zesentwintig procent van de slachtoffers meldde geen symptomen te hebben op het moment van de oproep aan het Antigifcentrum, 15.6% vertoonde bewustzijnsverande-ringen en 13.8% had dermatologische, oftalmolo-gische of neus-keel-oor klachten. In de groep patiënten die zich aanmeldde op de spoedgevallendiensten vertoonden tussen 10.6% en 22.8% bewustzijns-veranderingen en tussen 16.8% en 57.7% gedrags- en emotionele stoornissen. Minder dan één procent had dermatologische, oftalmologische of neus-keel-oor klachten.

Middelen die het meest betrokken waren bij het Antigifcentrum waren benzodiazepines (22.7%), antidepressiva (14.1%), antipsychotica (10.4%) en ethanol (8.4%). In de ziekenhuizen was ethanol het meest betrokken (65.5%-75.3%), gevolgd door benzodiazepines (13.6%-26.7%). Cocaïne, cannabis,

antidepressiva, antipsychotica, psychostimulantia en paracetamol behoorden ook tot de meest voorkomende middelen.

De gemiddelde kost voor een telefonisch contact met het Antigifcentrum bedroeg €25, volledig gefinancierd door de overheid. De gemiddelde kost die door het ziekenhuis aan de overheid en de patiënt in rekening werd gebracht, bedroeg €1,287 in het universitair ziekenhuis, €2,083 in het regionaal ziekenhuis, € 2,884 in campus 1 van het algemeen ziekenhuis en €966 in campus 2 van het algemeen ziekenhuis. De mediane kost bedroeg respectievelijk €423, €424, €901 en €186.

Er werden aanzienlijke verschillen gevonden tussen de kenmerken, de betrokken middelen en de kosten tussen het BPC en de ziekenhuizen, maar ook tussen de afzonderlijke ziekenhuizen onderling. Verder onderzoek is nodig om een beter inzicht te krijgen in de factoren die verantwoordelijk zijn voor deze verschillen, teneinde het juiste gebruik van deze medische diensten in vergiftigingsgevallen te optimaliseren.

CURRICULUM VITAE

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Master of Science in Health Care Management and Policy
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Master of Arts in Classical Music, option Piano
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Statistical analysis SPSS, 11/09/2017- 20/09/2017, Antwerp
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Master of Science in Health Care Management and Policy (Ghent University). Year 2019.

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Master of Science in Health Care Management and Policy (Ghent University). Year 2019.

Naessens Astrid. **Analyse van de oproepen van de hospitalen naar het Antigifcentrum bij intoxicatie in 2018.**
Master of Science in Health Care Management and Policy (Ghent University). Year 2019-2020.

Kestens Eva. **Hoe communiceren antigifcentra? Overzicht van het gebruik van sociale media wereldwijd en analyse van het gebruik en de functie van sociale media bij een selectie van antigifcentra.**
Master of Science in Health Care Management and Policy (Ghent University). Year 2019-2020.

PUBLICATIONS

Publications in international, peer-reviewed journals

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Descamps A., Moens J., Van Baelen J., Mostin M., van Ham F., Vandijck D. Availability of antidotes in Belgian hospitals: is there still room for improvement? *International Forum on Quality and Safety in Healthcare* (2019). Poster presentation.

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Chapter 9

Supplementary files

Supplementary files

Supplementary files, article 2

S2.1 Text. Belgian system of the hospitalization cost charged by the hospital to the government and the patient, 2017.

Financing of the healthcare cost

A substantial part of the healthcare cost is covered by the government, financed via contributions to the social security system by professionally active citizens and by revenues from general taxes. Belgian citizens have a mandatory insurance against disease and invalidity and must subscribe to one of seven health insurance funds.

The health insurance funds are a.o. responsible for the payment of a substantial part of hospitalization costs, charged by the hospital to the government and the patient. The residual fraction of the cost has to be paid via a fee from the patient or in some cases by a supplementary private but non-obligatory insurance. The personal fee charged to the patient is determined by an agreement negotiated in a committee of the National Health and Disability Insurance Service (RIZIV) with representation of employers, employees, health insurance funds and representatives of care providers. The Minister of Public Health determines the cost and reimbursement rates for a list of medical acts on the basis of a proposal from the committee.

Financing of the hospital

In Belgium, there are four sources of funding for the hospitals: the federal government, the health insurance funds, the contribution by the patient, and the regional states. There are also different types of funding, e.g. funding of the infrastructure and the operational costs.

Financing of the infrastructure of the hospital

The financing of the hospital infrastructure is mainly covered by subventions from the federal government, and the regional states.

Financing of the operational costs of the hospital

The operational costs of the hospital are covered for approximately 36.5% within a closed federal budget, called 'Budget of Financial Resources' (Budget Financiële Middelen, BFM). Fees contribute for 40.9% (part of the physicians fees is withheld by the hospital for the use of the hospital's infrastructure), revenues from rebates on pharmaceutical products for 17.2%, and lump sums and supplements (e.g. for the use of single rooms, cost charged to the patient and/or his private insurance) for 5.4%.

Hospitalization cost charged by the hospital to the government and the patient

The hospitalization cost is paid partly via an advance payment from the BFM-budget and partly via the invoice. This cost is composed of four parts: (1) costs for accommodation and nursing (not applicable for ED-amb patients), (2) pharmaceuticals, (3) physicians' fees, and (4) other items (for extra utilities, e.g. bottle of water).

The cost for accommodation and nursing comprises a fixed and a variable part and includes the cost for nursing staff, administration, maintenance, laundry, legal obligations with regard to the quality and safety of care, investment in medical equipment, the operational cost of the hospital pharmacy, and lump sums per day for clinical biology and pharmaceuticals. The fixed part is covered by the government via an advance payment from the BFM-budget. The variable part depends on the number of hospitalization days and is charged by the hospital via the invoice to two parties: a major contribution is charged to the government and paid via one of the health insurance funds, a smaller part being charged to and paid by the individual patient (personal fee).

For pharmaceuticals and physician's fees, a flat rate amount per admission to the hospital plus an amount that varies from patient to patient is charged to the government via the invoice and paid by one of the health insurance funds. The individual patient pays also a personal contribution via the invoice for pharmaceuticals and physician's fees and some small other costs for extra utilities to the hospital. The physicians' fees contain the lump sums per admission for clinical biology, medical imaging and medical 24 hour cover, together with the fees of the individual physicians involved in the patient care.

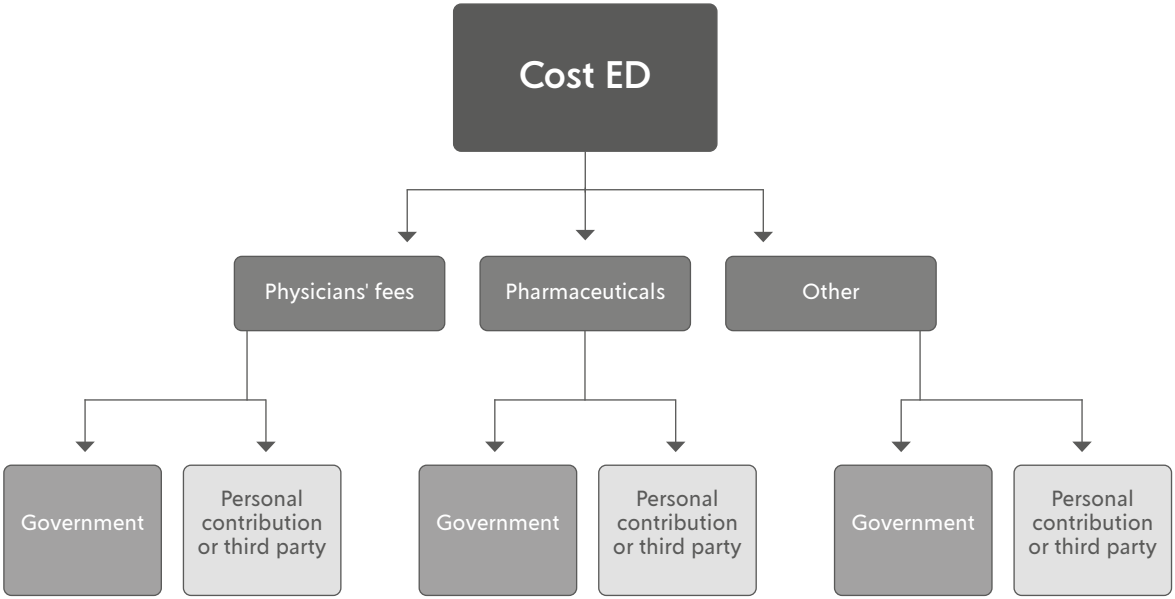
The fees in the Belgian system are fee for service based and are independent of physician status (consultant vs. specialist-in-training). There is a national standard list of agreed tariffs, which are largely reimbursed by the social security system. Whether it is allowed to charge these costs depends on the physician discipline, not on the physician status. For specialty trainees, the same tariffs are charged, knowing they are obliged to work under supervision of a consultant of that certain discipline. Senior specialty trainees (ST3+) work under consultant supervision on a 24/7 basis, with consultant presence on the working floor twelve hours per day and on-call cover for the remaining twelve hours.

Creation of national standards

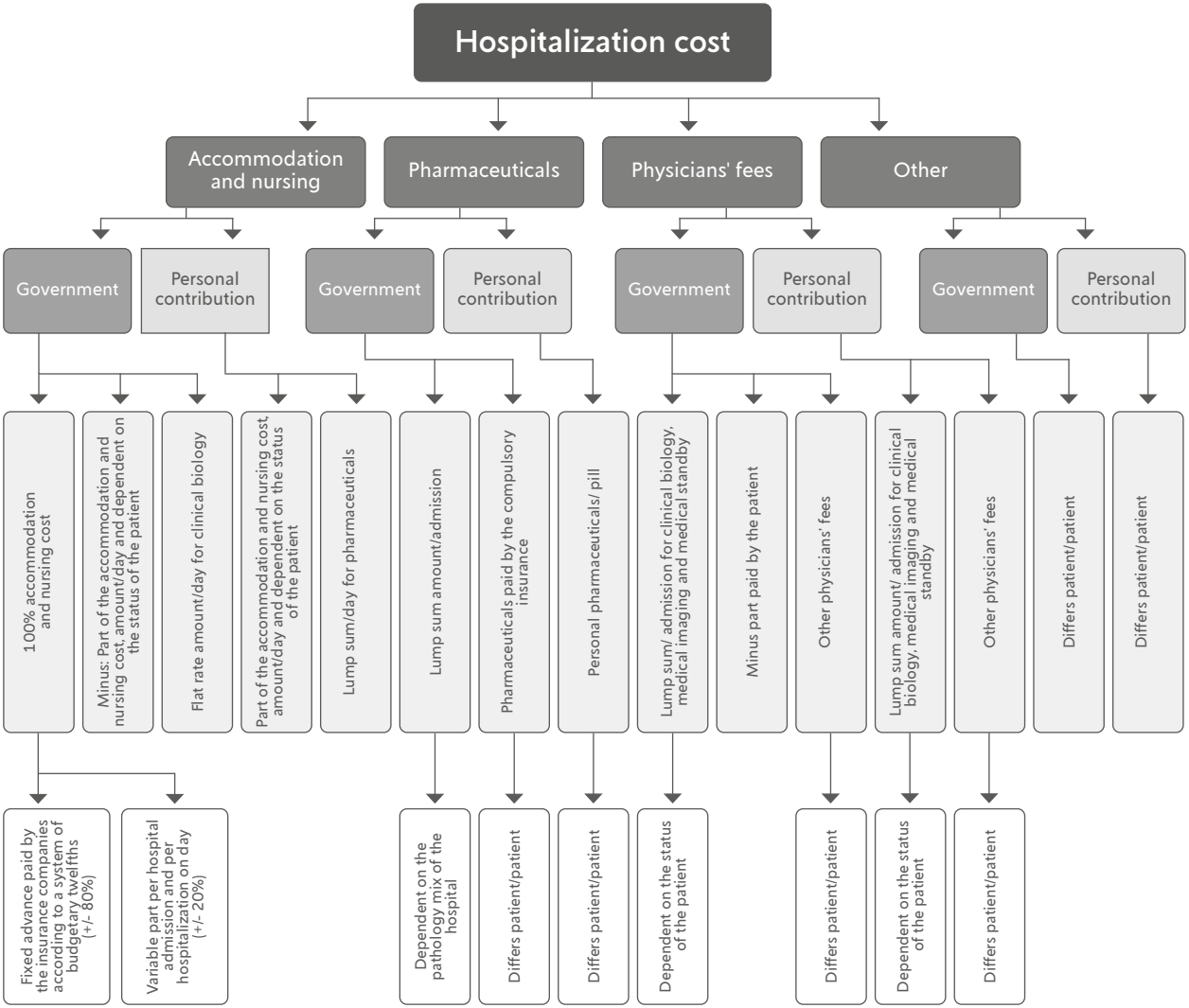
Belgian hospitals are obliged to provide Minimum Hospital Data (Minimale Ziekenhuisgegevens, MZG) to the Federal Public Service (FPS) Health. The health insurance funds dispose of the billing data for hospital admissions.

The Technical Unit of FPS Health is responsible for making a link between the hospital data and the financial data, provided by the health insurance funds. The Technical Unit provides a.o. feedback on the number of hospital admissions and the mean and median cost of different 'All Patient Refined Diagnostic Related Groups' (APR-DRGs). This information enables the government to benchmark the cost charged by Belgian hospitals for APR-DRG's of the same category and to create national standards.

S2.2 Figure. | Structure of the payer's cost for patients admitted in the Emergency Department of the hospital with acute poisoning in Belgium, 2017.



S2.3 Figure. | Structure of the payer's cost for hospitalized patients admitted with acute poisoning in Belgium, 2017.



S2.4 Table. | Total, mean and median cost in EUROs of patients admitted for poisoning to Ghent University Hospital, 2017.

Cost[1]	TOTAL	ED-amb[2]	ED-24h[3]	Hosp[4]	ICU[5]
	1,175 patients	637 patients	290 patients	209 patients	39 patients
	€ (%)	€ (%)	€ (%)	€ (%)	€ (%)
Total cost[6]	**1,512,346.4 (100.0)**	**125,325.6 (100.0)**	**389,539.2 (100.0)**	**707,771.8 (100.0)**	**289,709.8 (100.0)**
ED	198,677.2 (13.1)	125,325.6 (100.0)	38,383.5 (9.9)	26,540.6 (3.7)	8,427.4 (2.9)
Physicians' fees	195,746.1 (98.5)	122,765.7 (98.0)	38,127.6 (99.3)	26,489.4 (99.8)	8,363.3 (99.2)
Pharmaceuticals	1,906.6 (1.0)	1,881.0 (1.5)	15.8 (0.0)	6.7 (0.0)	3.1 (0.0)
Other	1,024.5 (0.5)	678.9 (0.5)	240.1 (0.6)	44.5 (0.2)	61.1 (0.7)
Hospitalization	1,313,669.1 (86.9)	0.0 (0.0)	351,155.7 (90.1)	681,231.2 (96.3)	281,282.2 (97.1)
Physicians' fees	280,759.9 (21.4)	0.0 (0.0)	107,794.6 (30.7)	117,597.4 (17.3)	55,367.9 (19.7)
Pharmaceuticals	85,493.7 (6.5)	0.0 (0.0)	39,702.5 (11.3)	33,701.8 (4.9)	12,089.4 (4.3)
Accommodation	937,439.7 (71.4)	0.0 (0.0)	202,362.5 (57.6)	526,639.7 (77.3)	208,437.5 (74.1)
Other	9,975.8 (0.8)	0.0 (0.0)	1,296.1 (0.4)	3,292.3 (0.5)	5,387.4 (1.9)
	€ (%)	€ (%)	€ (%)	€ (%)	€ (%)
Total cost[7]	**1,512,346.4 (100)**	**125,325.6 (100)**	**389,539.2 (100)**	**707,771.8 (100)**	**289,709.8 (100)**
Patient	65,719.4 (4.3)	12,094.5 (9.7)	19,217.1 (4.9)	23,677.3 (3.3)	10,730.5 (3.7)
Insurance	1,446,627.0 (95.7)	113,231.1 (90.3)	370,322.1 (95.1)	684,094.5 (96.7)	278,979.3 (96.3)
	€ (SD)	€ (SD)	€ (SD)	€ (SD)	€ (SD)
Mean cost[8]	**1,287.1 (2.653)**	**196.9(147)**	**1,343.2 (292)**	**3,386.5 (3,102)**	**7,428.5 (8,994)**
ED	169.1 (129)	196.9 (147)	132.4 (77)	127.0 (92)	216.1 (155)
Hospitalization	1,118.0 (2,655)	0.0 (0)	1,210.8 (280)	3,259.5 (3,095)	7,212.4 (8,973)
	€ (SD)	€ (SD)	€ (SD)	€ (SD)	€ (SD)
Mean cost[9]	**1,287.1 (2.653)**	**196.9(147)**	**1,343.2 (292)**	**3,386.5 (3,102)**	**7,428.5 (8,994)**
Patient	55.9 (119)	19.0 (22)	66.2 (122)	113.3 (155)	276.2 (308)
Insurance	1,231.2 (2,585)	177.9 (137)	1,277.0 (211)	3,273.2 (3,052)	7,152.3 8,795)
	€ (Q1-Q3)	€ (Q1-Q3)	€ (Q1-Q3)	€ (Q1-Q3)	€ (Q1-Q3)
Median cost[10]	**422.6 (154.5-1,471.7)**	**164.5 (93.4-253.1)**	**1,300.8 (1,237.1-1,396.5)**	**2,807.0 (2,136.7-3,627.4)**	**4,013.6 (2,421.2-5,925.8)**
ED	140 (81.6-215.7)	164.5 (93.4-253.1)	117.8 (71.9-172.8)	112.0 (58.4-173.4)	185.8 (130.8-268.4)
Hospitalization	0.1 (0.1-0.1)	0.0 (0-0)	1,170.0(1,108.9-1,261.0)	1,731.2 (1,022.6-3,474.8)	3,844.3 (2,304.4-5,778.3)
	€ (Q1-Q3)	€ (Q1-Q3)	€ (Q1-Q3)	€ (Q1-Q3)	€ (Q1-Q3)
Median cost[11]	**422.6 (154.5-1471.7)**	**164.5 (93.4-253.1)**	**1,300.8 (1,237.1-1,396.5)**	**2,807.0 (2,136.7-3,627.4)**	**4,013.6 (2,421.2-5,925.8)**
Patient	24.6 (7.6-75.1)	11.6 (4.6-28.2)	57.3 (14.4-91.6)	95.5 (32.9-141.5)	153.8 (76.6-357.4)
Insurance	390.3 (133.1-1,397.4)	149.1 (80.1-231.1)	1,244.3 (1,181.6-1,329.5)	2,751.9 (2,082.8-3,494.7)	3,739.5 (2,270.4-5,257.7)

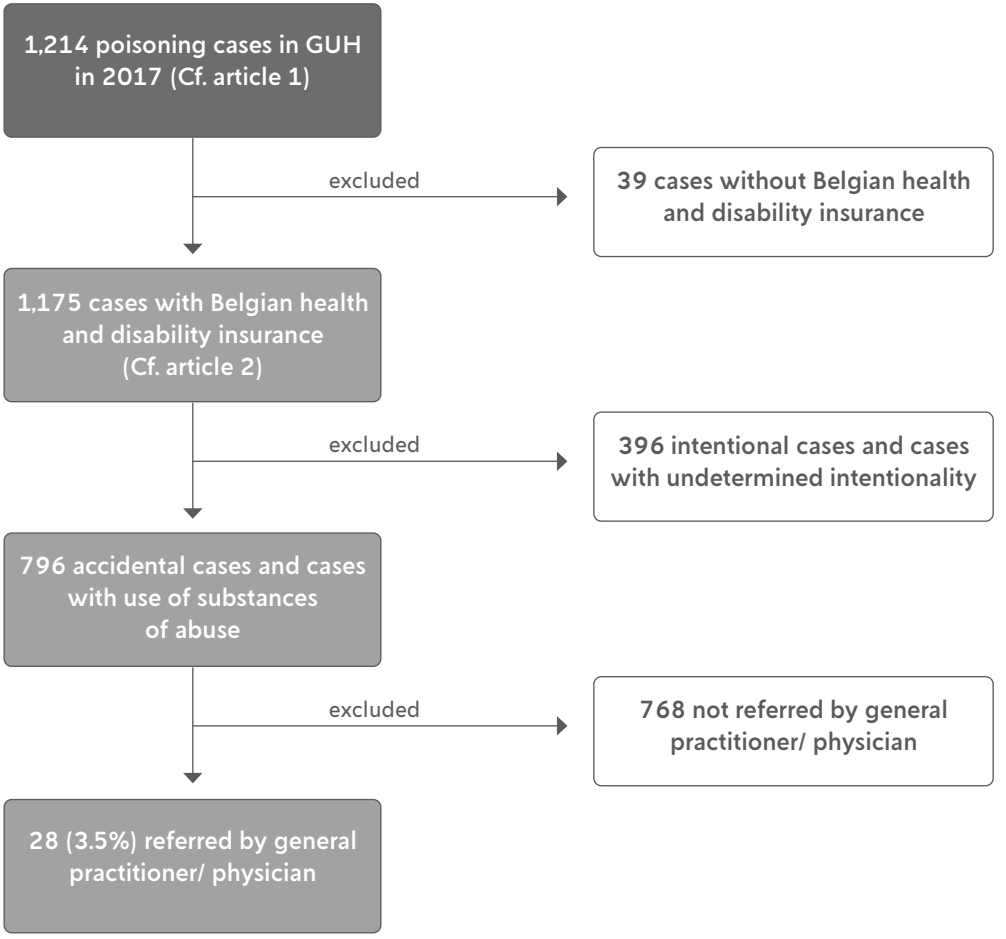
S2.5 Table. | Comparison of the Ghent University Hospital data 2017 with Ghent University Hospital data 2016 and national data 2016 of the Technical Unit of FPS Health, in EUROs, Belgium, 2017.

	GUH 2017	FPS, data GUH 2016	FPS, national data 2016
Medicinal agents	ICD-10, T36-T50[1]	APR-DRG 812[2]	APR-DRG 812[2]
Number of cases	**153**	**97**	**10,946**
Mean age	**34**	**35**	**44**
Median age (IQR)	**32 (23-42)**	**33 (21-45)**	**44 (26-58)**
Mean hospitalization days	**2.7**	**3.0**	**5.2**
Median hospitalization days (IQR)	**1.0 (1.0-3.0)**	**1.0 (1.0-3.0)**	**1 (1.0-5.0)**
Total mean cost/case (€)	**2,709.92**	**2,833.82**	**3,337.64**
Physicians' fees (€)	661.7	772.1	823.5
Pharmaceuticals (€)	173.3	46.4	69.8
Accommodation (€)	1,874.9	2,015.3	2,444.3
Mean cost/day (€)	**1,021.1**	**944.6**	**641.9**
Physicians' fees (€)	249.3	257.4	158.4
Pharmaceuticals (€)	65.3	15.5	13.4
Accommodation (€)	706.4	671.8	470.1
Median cost (€) (IQR)	**1982.61 (1,310-3,073)**	**1,257.37 (985-2,848)**	**1,162.4 (782-3,245)**
Physicians' fees (€)	NA	NA	NA
Pharmaceuticals (€) (IQR)	137.7 (134-151)	7.6 (3-32)	7.1 (1-33)
Accommodation (€) (IQR)	715.6 (696-2,089)	696.4 (660-1,980)	676.5 (452-2,234)
Non-medicinal agents	ICD-10, T51-T653	APR-DRG 8164	APR-DRG 8164
Number of cases	**301**	**19**	**1,699**
Mean age	**47**	**43**	**39**
Median age (IQR)	**47 (38-57)**	**39 (28-54)**	**40 (17-57)**
Mean hospitalization days	**2.5**	**1.7**	**3.7**
Median hospitalization days (IQR)	**1.0 (1.0-3.0)**	**1.0 (1.0-3.0)**	**1 (1.0-2.0)**
Total mean cost/case (€)	**2,549.2**	**1,844.9**	**2,545.0**
Physicians' fees (€)	650.7	533.4	701.6
Pharmaceuticals (€)	156.5	22.9	57.5
Accommodation (€)	1,742.0	1,288.7	1,785.9
Mean cost/day (€)	**1,040.5**	**1,085.2**	**687.8**
Physicians' fees (€)	265.6	313.8	189.6
Pharmaceuticals (€)	63.9	13.5	15.5
Accommodation (€)	711.0	758.1	482.7
Median cost (€) (IQR)	1,533.6 (1,272-2,783)	1206.1 (944.7-2,983.6)	992.7 (779-1,766)
Physicians' fees (€)	NA	NA	NA
Pharmaceuticals (€) (IQR)	136.9 (134-144)	10.6 (3-28)	5.1 (0-24)
Accommodation (€) (IQR)	715.7 (696-2,089)	696.43 (660-1,980)	565.6 (539-1,131)

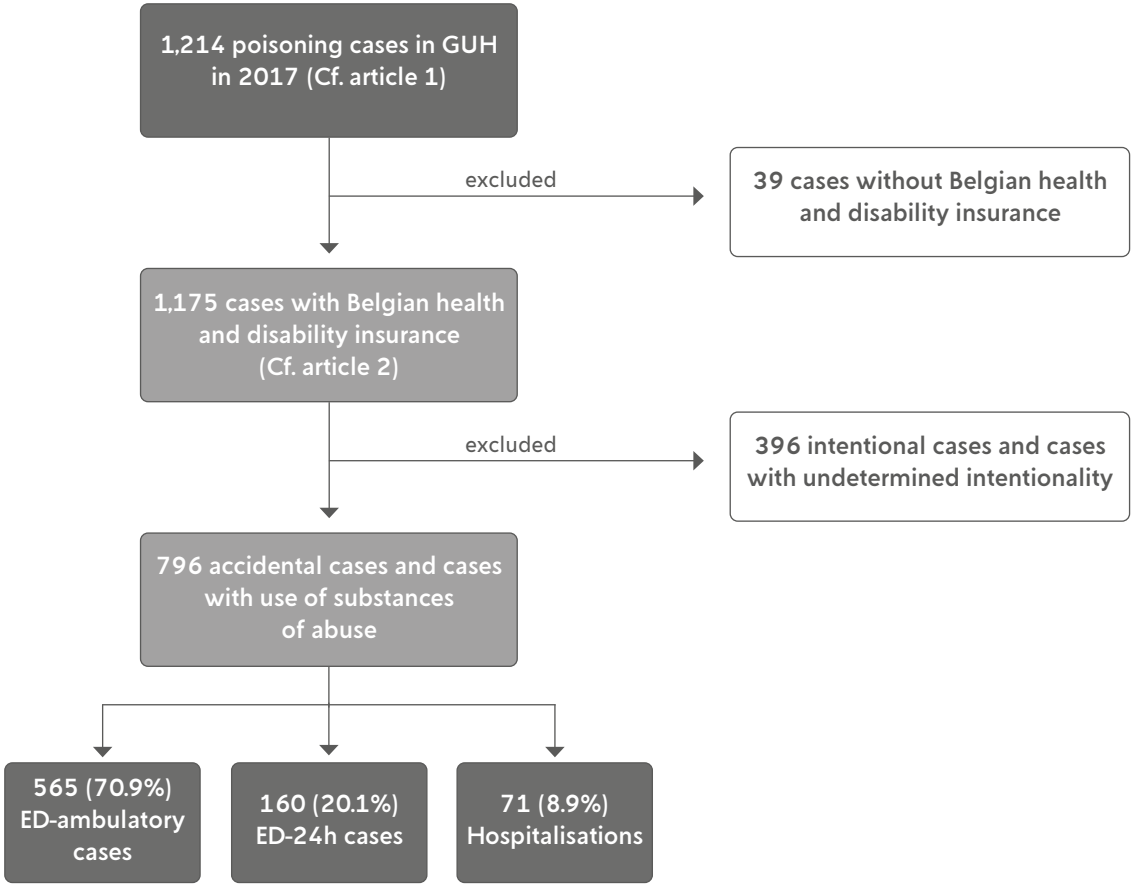
[1] International Classification of Diseases ICD-10, T36-T50, poisoning by drugs, medicaments and biological substances
[2] All Patient Refined Diagnosis Related Group (APR-DRG) 812, poisoning by medicinal agents
[3] International Classification of Diseases ICD-10, T51-T65, toxic effects of substances chiefly nonmedicinal as to source
4 All Patient Refined Diagnosis Related Group 816, toxic effects by non-medicinal substances

Supplementary files, article 3

S3.1 Figure. | Flowchart of the proportion of poisoning cases referred by a general practitioner or physician among the poisoning cases that occurred in Ghent University Hospital in 2017.

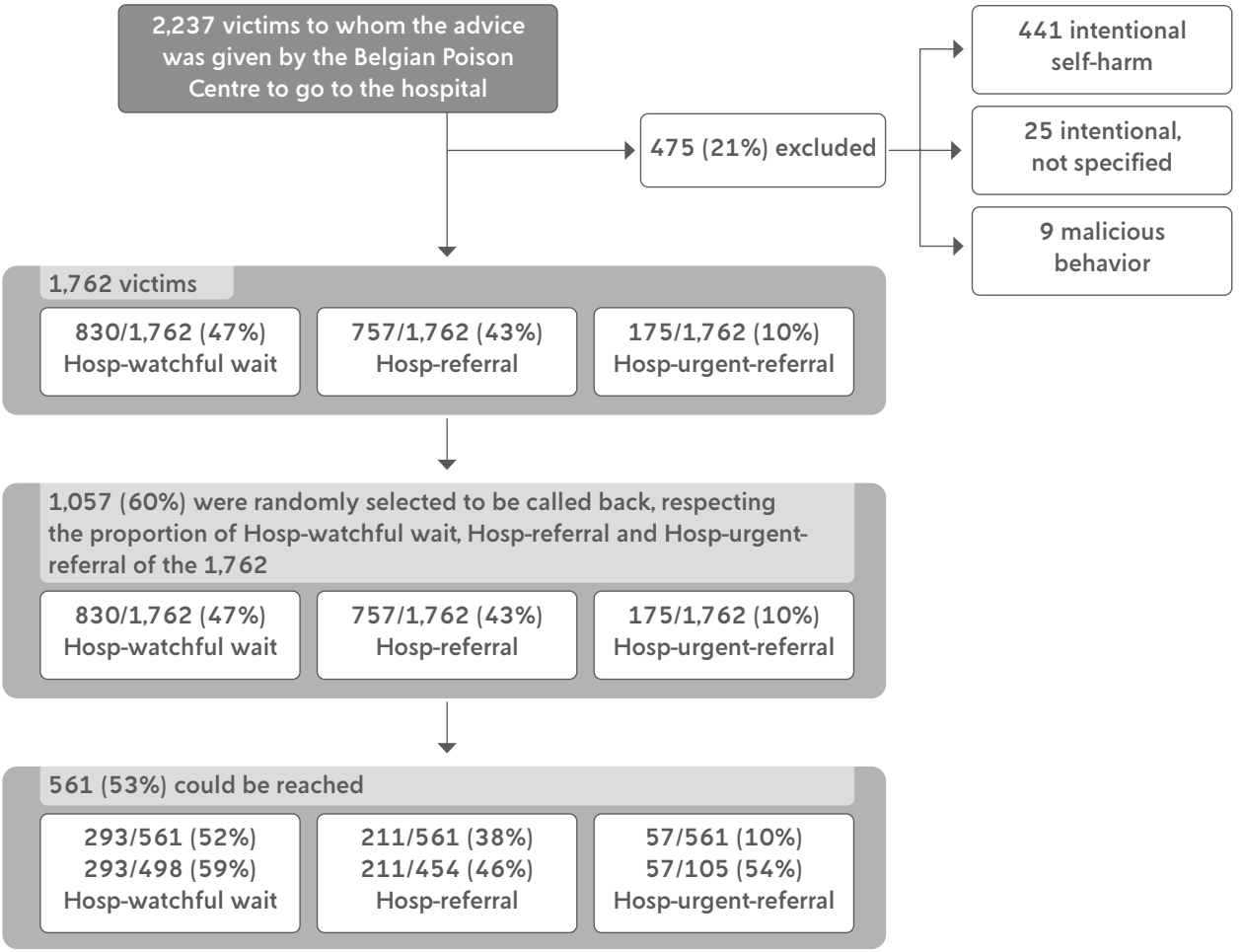


S3.2 Figure. | Flowchart of the proportion of ED-ambulatory cases, ED-24h cases and Hospitalizations among the poisoning cases that occurred in Ghent University Hospital in 2017.



Supplementary files, article 4

S4.1 Figure. | Flowchart of the selection of the Hosp-watchful-wait victims, Hosp-referral victims and Hosp-urgent-referral victims that could be reached during the telephone survey period between 1 March-15 May 2019 in the Belgian Poison Centre.



S4.2 Table. | Compliance of the caller with the advice given by the BPC. Results of a telephone follow-up survey conducted between 1 March and 15 May 2019. Results, classified by children and adults

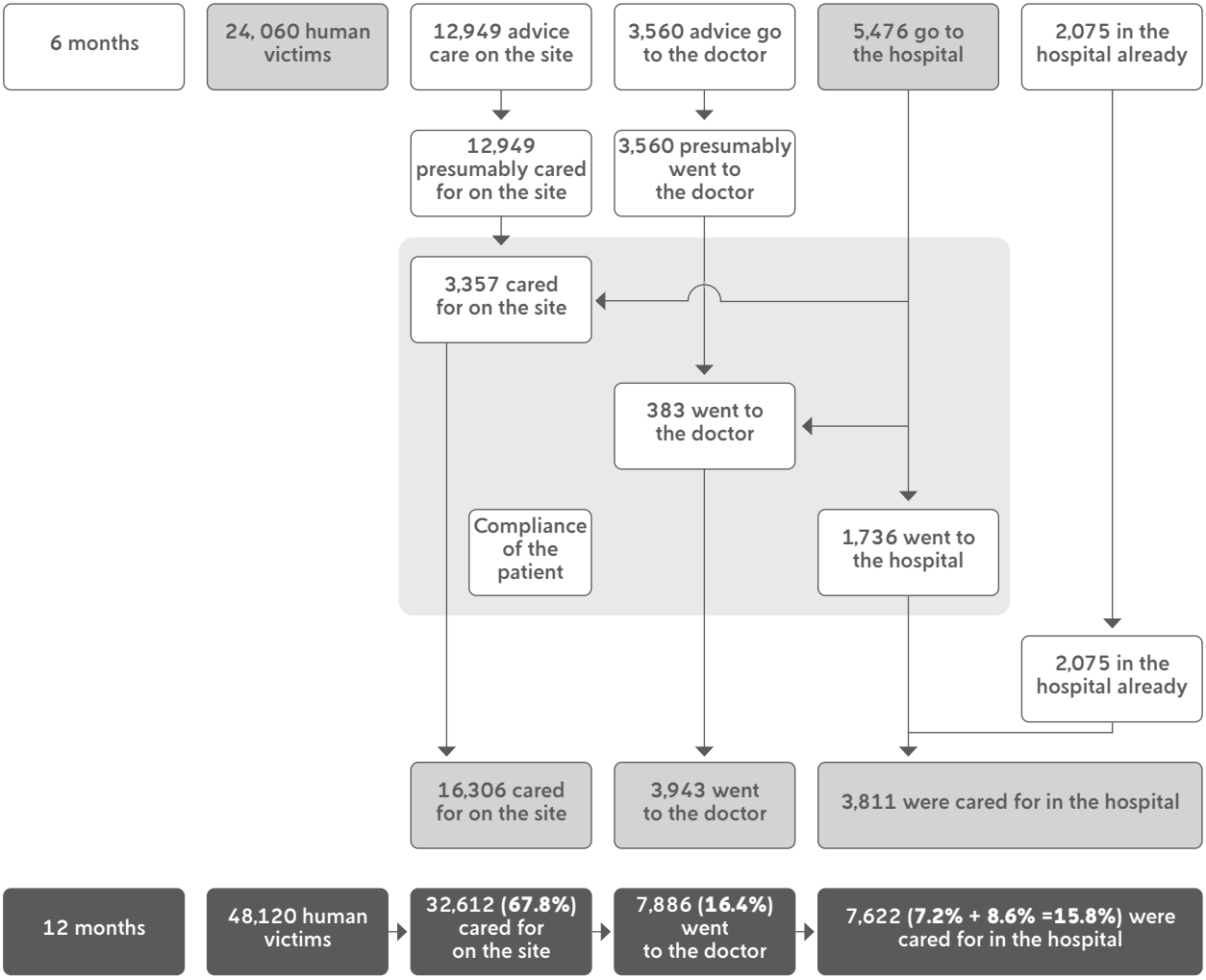
		Total	Hosp-watchful-wait	Hospital-referral	Hospital-urgent-referral
		n(%)	n(%)	n(%)	n(%)
Adults	**Total**	**249 (100.0)**	**101 (100.0)**	**113 (100.0)**	**35 (100.0)**
	Care on the site	128 (51.4)	82 (81.2)	32 (28.3)	14 (40.0)
	Went to a medical doctor	28 (11.2)	10 (9.9)	14 (12.4)	4 (11.4)
	Went to the hospital	93 (37.3)	9 (8.9)	67 (59.3)	17 (48.6)
	ED-amb[1]	52 (20.9)	6 (5.9)	40 (35.4)	6 (17.1)
	ED-24h[2]	18 (7.2)	2 (2.0)	13 (11.5)	3 (8.6)
	Hosp[3]	23 (9.2)	1 (1.0)	14 (12.4)	8 (22.9)
	ICU[4]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Children	**Total**	**312 (100.0)**	**192 (100.0)**	**98 (100.0)**	**22 (100.0)**
	Care on the site	216 (69.2)	176 (91.7)	36 (36.7)	4 (18.2)
	Went to a medical doctor	11 (3.5)	2 (1.0)	8 (8.2)	1 (4.5)
	Went to the hospital	85 (27.2)	14 (7.3)	54 (55.1)	17 (77.3)
	ED-amb[1]	57 (18.3)	12 (6.3)	36 (36.7)	9 (40.9)
	ED-24h[2]	10 (3.2)	0 (0.0)	7 (7.1)	3 (13.6)
	Hosp[3]	17 (5.4)	2 (1.0)	10 (10.2)	5 (22.7)
	ICU[4]	1 (0.3)	0 (0.0)	1 (1.0)	0 (0.0)

Supplementary files, article 5

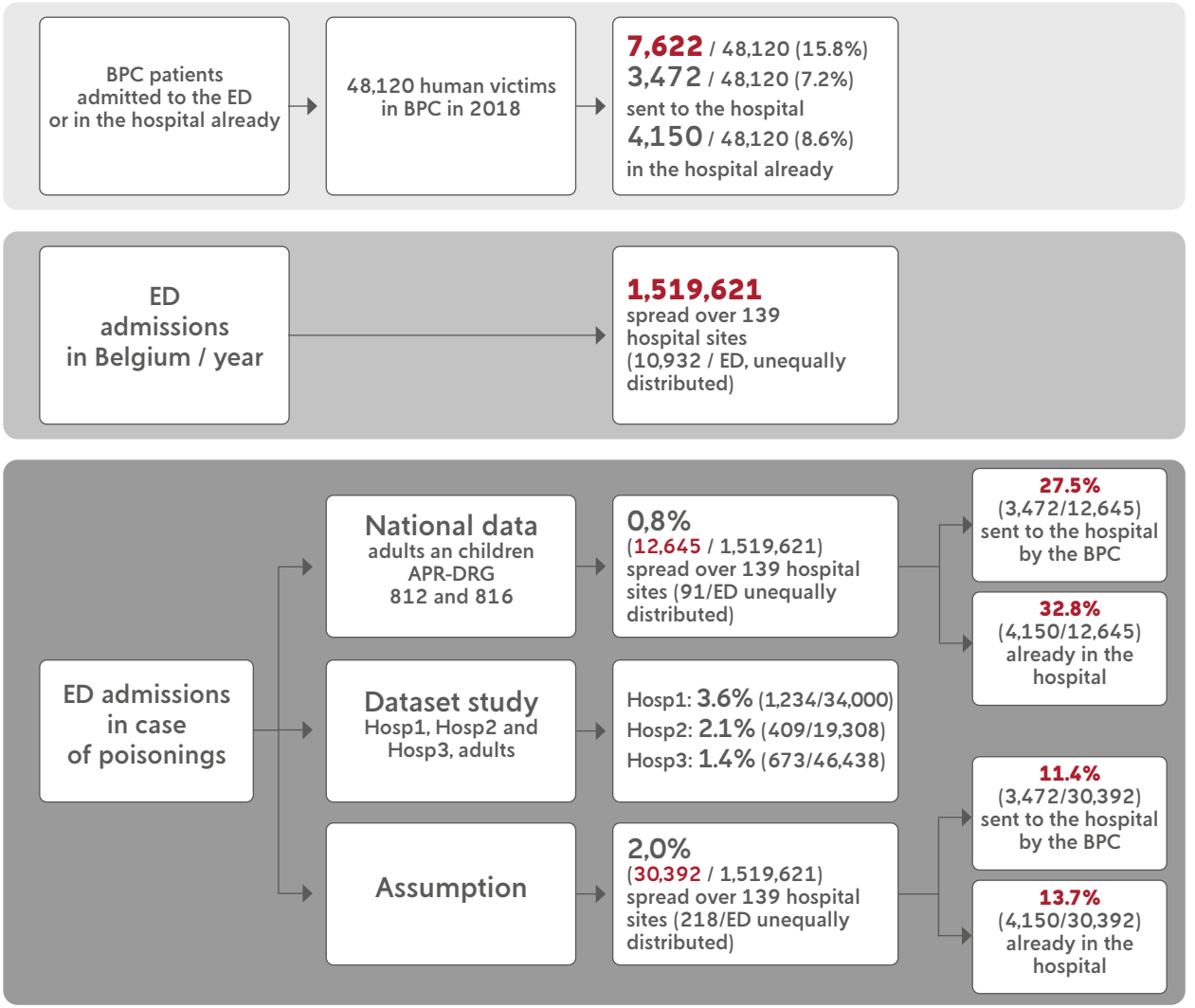
S5.1 Table. | Total cost, mean cost and median cost of patients admitted with poisoning to Belgian hospitals, expressed in EURO's 2017.

	Hosp1 [1]	Hosp2 [2]	Hosp3.1 [3]	Hosp3.2 [4]	Hosp3 [5]
Cost	n=1,175	n=404	n=407	n=246	n=653
	EUR (%)	EUR (%)	EUR (%)	EUR (%)	EUR (%)
Total cost	**1,512,346(100.0)**	**841,581(100.0)**	**1,173,719(100.0)**	**237,587(100.0)**	**1,411,306(100.0)**
ED	**198,677(13.1)**	**62,172(7.4)**	**48,912(4.2)**	**32,395(13.6)**	**81,307(5.8)**
Physicians' Fees	195,746(98.5)	57,506(92.5)	48,408(99.0)	31,791(98.1)	80,200(98.6)
Pharmaceuticals	1,907(1.0)	4,626(7.4)	463(0.9)	579(1.8)	1,042(1.3)
Other	1,025(0.5)	40(0.1)	41(0.1)	25(0.1)	65(0.1)
Hospitalization	**1,313,669(86.9)**	**779,409(92.6)**	**1,124,807(95.8)**	**205,192(86.4)**	**1,329,999(94.2)**
Physicans' Fees	280,760(21.4)	119,523(15.3)	188,048(16.7)	51,264(25.0)	239,312(18.0)
Pharmaceuticals	85,494(6.5)	19,560(2.5)	28,880(2.6)	14,977(7.3)	43,856(3.3)
Accommodation	937,440(71.4)	638,985(82.0)	905,729(80.5)	138,761(67.6)	1,044,490(78.5)
Other	9,976(0.8)	1,341(0.2)	2,151(0.2)	191(0.1)	2,342(0.2)
	EUR (%)	EUR (%)	EUR (%)	EUR (%)	EUR (%)
Total cost	**1,512,346(100.0)**	**841,581(100.0)**	**1,173,719(100.0)**	**237,587.00**	**1,411,306(100.0)**
Patient	65,720(4.3)	43,817(5.2)	44,544(3.8)	11,730(4.9)	56,275(4.0)
Insurance	1,446,627(95.7)	797,764(94.8)	1,129,175(96.2)	225,857(95.1)	1,355,031(96.0)
	EUR (SD)	EUR (SD)	EUR (SD)	EUR (SD)	EUR (SD)
Mean cost/episode	**1,287(2,653)**	**2,083(4,887)**	**2,884(4,991)**	**966(2,667)**	**2,161(4,364)**
ED	169(129)	108(132)	120(91)	132(107)	125(97.2)
Hospitalization	1,118(2,655)	1,975(4,894)	2,764(4,988)	834(2,662)	2,037(4,362)
	EUR (SD)	EUR (SD)	EUR (SD)	EUR (SD)	EUR (SD)
Mean cost/episode	**1,287(2,653)**	**2,083(4,887)**	**2,884(4,991)**	**966(2,667)**	**2,161(4,364)**
Patient	56(119)	141(277)	109(257)	48(106)	86(215)
Insurance	1,231(2,585)	1,942(4,635)	2,774(4,814)	918(2,569)	2,075(4,212)
	EUR (IQR)	EUR (IQR)	EUR (IQR)	EUR (IQR)	EUR (IQR)
Median cost/episode	**423(154-1,472)**	**424(126-959)**	**900.6(112-3,304)**	**186(104-965)**	**353(109-1,594)**
ED	140 (82-216)	121 (80-168)	101(65-141)	101(67-153)	101(67-146)
Hospitalization	0 (0-1,286)	0 (0-824)	829(0-3,147)	0(0-847)	0(0-1,475)
	EUR (IQR)	EUR (IQR)	EUR (IQR)	EUR (IQR)	EUR (IQR)
Median cost/episode	**423(154-1,472)**	**424(126-959)**	**901(112-3,304)**	**186(104-965)**	**353(109-1,594)**
Patient	25(8-75)	30(14-87)	31(15-97)	21(11-56)	27(13-81)
Insurance	390(133-1,397)	371(105-5,424)	850(93-3,220)	165(89-903)	325(90-1,548)

S7.1 Figure. | Compliance with the advice of the BPC in cases of acute poisoning for adults and children.



S7.2 Figure. | Overlap between (1) BPC patients who went to the hospital after a call to the BPC, or for whom was called from the hospital to the BPC, and (2) patients who are admitted to the hospital for acute poisoning.



Supplementary file, General Discussion

S7.3 Abstract, EAPCCT congress, Tallinn, Estonia, 19-22 May 2020

Anne-Marie K Descamps, Dominique M Vandijck, Walter A Buylaert , Peter De Paepe

Adults admitted to the emergency department of a university hospital in Belgium for acute poisoning with ethanol as a co-ingestant: characteristics and direct medical costs.

Objective: The aim of this study is to assess the characteristics and direct medical costs of poisonings with ethanol as a co-ingestant in adults (aged >=14 years) admitted to the emergency department (ED) of the Ghent University Hospital.

Methods: Data between 1 January and 31 December 2017 were analyzed using medical records and hospital invoices. Cost was defined as the cost charged by the hospital to the government and the patient. Readmissions were considered as separate admissions.

Results: A cohort of 170/1,214 (14.0%) ED admissions were included, of which 15 readmissions. Men accounted for 64.7% of admissions. Patients aged 21-40 years (65.3%) were the largest group, followed by patients aged 41-60 years (24.7%), 14-20 years (8.8%) and >60 years (1.2%).Fifty percent of the patients were admitted on Friday, Saturday or Sunday (17.1%, 17.1% and 16.5%, respectively). Co-ingested agents most frequently involved were benzodiazepines (35.5%), cannabis (25.4%), cocaine (22.5%), psychostimulants (14.8%), antidepressants (11.2%) and antipsychotics (6.5%). Changes in consciousness were observed in 22.4%, behavioural and emotional disorders in 13.5%, and nausea and vomiting in 9.4% of admissions. A laboratory analysis was carried out in 73.5%. Eighty-four percent received psychiatric care, which is much higher than the 59.6% of patients admitted to the hospital for acute poisoning with involvement of any types of agents. Patients were discharged home after having received care in the emergency department in 48.2% of the admissions. Admissions to the emergency-department-24-hours-observation unit accounted for 31.2%, and hospitalizations or admissions to the intensive care unit for 4.7% and 5.9% of the admissions, respectively. The mean and median length of hospital stay was 1.19 (SD 3.96) and 1.0 day (IQR 0.0-1.0), respectively. In admissions of acute poisoning with involvement of all types of agents, the mean and median length of hospital stay was 1.12 (SD 3.12) and 0.0 (IQR 0.0-1.0), respectively. The mean and median cost per admission was $1,398 (SD $3,101) and $1,251 (IQR $209-1,544), of which 96,4% was paid by the government and 3,6% by the patient. The mean and median cost for patients with any type of agents was $1,287 (SD $2,653), and $423 (IQR $154-€1,472), respectively.

Conclusion: Poisoning cases with ethanol as a co-ingestant are a limited but important group needing often psychological care. The mean cost is in the same range of acute poisoning cases involving any types of agents (7.9% higher), but the median cost is almost three times higher.

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