

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

Anne-Marie Descamps<sup>a,b,c</sup>, Dominique Vandijck<sup>b,c</sup>, Walter Buylaert<sup>d</sup>, Martine Mostin<sup>a</sup>, Peter De Paepe<sup>d</sup>

*a* Antigifcentrum/Centre Antipoisons, Bruynstraat 1, B – 1120 Brussels, Belgium, [anne-marie.descamps@poisoncentre.be](mailto:anne-marie.descamps@poisoncentre.be), ORCID 0000-0003-0448-4420; [martine.mostin@poisoncentre.be](mailto:martine.mostin@poisoncentre.be);

*b* Department of Public Health of Ghent University, Corneel Heymanslaan 10, 4K3, B – 9000 Ghent, Belgium, [dominique.vandijck@ugent.be](mailto:dominique.vandijck@ugent.be), ORCID [0000-0003-4464-8522](https://orcid.org/0000-0003-4464-8522);

*c* [Department of Medicine and Health Sciences of Hasselt University, Agoralaan, D, B – 3590 Diepenbeek, Belgium.](https://www.uhasselt.be)  
[dominique.vandijck@uhasselt.be](mailto:dominique.vandijck@uhasselt.be), ORCID [0000-0003-4464-8522](https://orcid.org/0000-0003-4464-8522);

*d* Department of Emergency Medicine of Ghent University Hospital, Corneel Heymanslaan 10, B – 9000 Ghent, Belgium,  
[peter.depaepe@uzgent.be](mailto:peter.depaepe@uzgent.be), ORCID [0000-0001-6596-4095](https://orcid.org/0000-0001-6596-4095); [walter.buylaert@uzgent.be](mailto:walter.buylaert@uzgent.be).

Contact:

Anne-Marie Descamps, [annemarie.descamps@ugent.be](mailto:annemarie.descamps@ugent.be) or [anne-marie.descamps@poisoncentre.be](mailto:anne-marie.descamps@poisoncentre.be), Antigifcentrum/Centre Antipoisons, Bruynstraat 1, B-1120 Brussels, Belgium, +32 2 264 96 36

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## ABSTRACT

**Objective:** The aim of this study was (1) to assess the characteristics of patients with acute poisoning who called the Belgian Poison Centre (BPC) and were advised to go to the hospital, (2) to identify factors associated with the type of hospital referral and (3) to estimate direct payer's cost.

**Methods:** Medical and financial data 2018 of BPC and financial data 2017 of Ghent University Hospital (GUH) were used. Toxic agents involved were categorised according to the World Health Organization ICD-10 classification. Three types of referrals were distinguished: referral in case of deterioration of the patient's condition (Hosp-watchful-wait), referral to the hospital (Hosp-referral) or urgent referral to the hospital (Hosp-urgent-referral). Factors associated with type of recommendation for hospitalisation were identified using multivariate logistic regression.

**Results:** 5,476 referrals were included (20.1% of all calls): 72.4% accidental poisoning, 25.3% intentional self-harm, 1.2% substance abuse, and 1.1% unclear intentionality. Adults accounted for 56.9%. There were 43.2% Hosp-watchful-wait cases, 48.9% Hosp-referrals and 7.9% Hosp-urgent-referrals. In Hosp-watchful-wait cases, soaps and detergents were most frequently involved (20.5%), followed by topical agents primarily affecting skin, mucous membrane or ophthalmological, otorhinolaryngological and dental drugs (8.1%), and noxious substances ingested as food (7.5%). In Hosp-referral cases, benzodiazepines (12.7%), antidepressants (7.9%) and antipsychotics (6.7%) were most frequently involved. In Hosp-urgent referral cases, the most frequent categories were benzodiazepines (15.1%), antidepressants (7.6%), and acetaminophen (7.3%). Factors associated with hospitalisation type were number of symptoms, intentionality, type of agent(s) involved and the advice to use antidotes (all  $p < 0.05$ ). Total estimated cost was €7,184,731.04 or €1,312.04/patient.

**Conclusion:** A considerable percentage of patients are advised by the BPC to go to the hospital and our estimate indicates considerable cost. Our data provide some insight into the characteristics of these patients. Further studies on the motivation and accuracy of referrals are warranted.

Keywords: poisoning; prehospital care; cost efficiency; hospitalisations; emergency care systems.

## “What this paper adds” box

### *Section 1: What is already known on this subject*

- Analysis of characteristics of patients referred to the hospital and agents involved for acute poisoning by poison control centres without distinction between the type of hospital referral.
- Missing link between hospitalisation and estimated cost.

### *Section 2: What this study adds*

- Analysis of agents involved in calls for acute poisoning to the poison control centre, categorised according to three types of hospital referral: referral in case of deterioration of the patient's condition, referral to the hospital, or urgent referral to the hospital.
- Analysis of factors estimated to be associated with the type of the poison control centre advice with regard to type of hospital referral.
- Analysis of the estimated cost for the government and the patient.

## Abbreviations

BPC: Belgian Poison Centre; FPS Health: ED: Emergency Department; Federal Public Service Health; GUH: Ghent University Hospital; Hosp-watchful-wait: 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; NSAID: non-steroidal anti-inflammatory drugs; WHO: World Health Organization.

## **INTRODUCTION**

Intoxications are an important social problem with a considerable impact on clinical workload and expenses. It is expected that an expertise centre in toxicology such as a poison centre will guide the patient confronted with (suspected) poisoning to the most appropriate medical care in an efficient, qualitative and safe way. Speed, competence and applicability are key factors during this process.

In 2016, 25.04% of patients who called the Belgian poison centre (BPC) with a (suspected) poisoning, were given the advice to go the hospital[1]. In order to check whether patients effectively followed the advice, a survey was conducted in 2016 on 404 patients who had called the BPC in case of a non-intentional poisoning: 97.1% confirmed to have followed the advice (author's unpublished data, 2018).

In this context, a further distinction in degree of seriousness and urgency for patients recommended to go the hospital is a key factor. It is important to distinguish between (1) patients referred to the hospital only if symptoms or deterioration of the situation occurs, i.e. staying at home and watchful waiting for symptoms to occur (Hosp-watchful-wait), (2) patients referred to the hospital (Hosp-referral) and (3) patients urgently referred to the hospital (Hosp-urgent-referral). Literature data and our previous research indicate that hospitalisation has an important impact on the cost of poisonings[2-12]. The type of referral to the hospital by the poison centre is a burden to the patient (induction of anxiety, problems to reach the hospital, waiting times in the hospital, fear for costs,...), the emergency department (ED) (overcrowding, less time for seriously ill patients,... ) and the government (cost,...).

As far as we know, no study focused on the link between characteristics, associated factors and costs of patients with acute poisoning referred to the hospital by a poison centre. Therefore, the aim of this study was (1) to assess the characteristics of patients with acute poisoning who were advised by the BPC to go to the hospital (Hosp-watchful-wait, Hosp-referral or Hosp-urgent-referral), (2) to identify factors associated with the type of referral advised and (3) to calculate direct BPC cost and estimate hospital costs.

## **MATERIALS AND METHODS**

We used the "Strengthening the Reporting of Observational Studies in Epidemiology" STROBE Statement as a guideline for reporting[13].

### **Study design and setting**

This observational study was set up in November 2017 to analyse all poisoning-related information files of calls to the BPC between 1 January 2018 and 30 June 2018. The BPC is a public foundation, funded by the Federal Public Service Health (FPS Health) in the context of emergency medical assistance. Physicians and pharmacists give 24/7 toll-free telephone advice to lay persons and healthcare professionals in Belgium (11,358,357 inhabitants in 2018)[14] and the Grand Duchy of Luxembourg (602,005 inhabitants in 2018)[15] in cases of (suspected) toxic exposures. According to the risk assessment made, the advice given is either (1) to stay at home and/or advice on first aid, (2) to consult a general practitioner (3) or to go to the hospital. Patients who are advised to go to the hospital are first assessed in the emergency department (ED), followed by (1) discharge home, (2) observation in the 24-hours-observation unit of the ED, (3) hospitalisation or (4) admission to the intensive care.

### **Participants**

Patients (children and adults) were included if they were advised by the BPC (1) to go to the hospital if symptoms appeared or their condition worsened (Hosp-watchful-wait), (2) to go to the hospital (Hosp-referral) or (3) to go urgently to the hospital (Hosp-urgent-referral).

Phone calls from mobile intensive care unit teams were also included. In case of multiple victims, calls were only included if data were available at individual patient level. Requests for information were excluded.

## **Variables and data sources**

The electronic data forms filled in by the physician/pharmacist during or immediately after the call were used. This registration system contains information on caller and victim type, location of the caller and the victim, symptoms, circumstances, agent(s) involved, route of exposure, location advised for treatment and examinations proposed. Cases from the group 'referral to the hospital' were further categorised into Hosp-watchful-wait, Hosp-referral or Hosp-urgent-referral.

Cost was defined as the payer's cost. The call to the BPC is free of charges to the caller due the financial subvention of the BPC by the government. The cost/call was calculated by taking 70% of the governmental subsidies divided by the total number of calls in 2017[16].

As there was no follow-up available in the BPC of the included patients advised to go to the hospital, the cost/admission to the hospital was estimated from patients with acute poisoning admitted to the emergency department (ED) of Ghent university hospital (GUH) in 2017 (author's unpublished data, 2018). The cost for the hospital is partly paid by the government, through contributions from the mandatory health and disability insurance via one of the seven health insurance funds. The part not refunded is a personal fee paid by the individual patient (or his/her supplementary health insurance).

## **Bias**

It was not possible to follow up the individual patients after their call to the BPC. As a consequence, the BPC was not informed about the hospital of admission. It is therefore possible that the estimated hospitalisation cost of GUH, used in this study, is higher than in non-academic, regional hospitals.

## **Study size**

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

## **Quantitative variables**

Agents were based on patient report and noted in the electronic file. After the call, they were grouped according to the World Health Organisation (WHO) International Classification of Diseases ICD-10[17] T36-T50 (poisoning by drugs, medicaments and biological substances) or T51-T65 (toxic effects of substances chiefly nonmedicinal as to source). Patients who were in contact with an agent that could not be categorised in T36-T65 but who were referred to the hospital were given an own code '700'.

Symptoms were grouped according to the emergency registration system for hospital EDs, named UREG[18].

## **Statistical methods**

A descriptive study was performed on the variables. Categorical data were reported as a percentage frequency of occurrence. Chi-Square test and Fisher's Exact Test were used. Univariate analysis was used to assess predicting variables related to the advice of the BPC concerning the hospital admission type. A multivariate logistic regression model was applied for the variables achieving statistical association in the univariate analysis ( $p < 0.05$ ). The step by step procedure was used to retain the variables that significantly contributed to the model. The Akaike Information Criterion (AIC) was used to compare the quality of the models. All analyses were performed using SPSS 25.0 (IBM®).

## **Ethical considerations**

The analysis of the GUH data was approved by the Ethical Committee of GUH. The anonymous BPC data was analysed according the General Data Protection Regulation (GDPR) guidelines of the BPC, published on its website[19].

## RESULTS

### Demographics and characteristics of the patients

A total of 5,476 calls were included out of 27,724 calls between 1 January 2018 and 30 June 2018; 56.9% of the victims were adults. Forty-three percent were Hosp-watchful-wait cases, 48.9% Hosp-referral cases and 7.9% Hosp-urgent-referral cases. Fifty-two percent came from family members and 16.0% from the victim. Almost half of the calls (49.8%) were made between 8am and 6pm. In 20.2% of cases, the call was made by a medical professional. At the moment of the call, 86.4% of the victims were at home.

Table 1. Demographic data and characteristics of 5,476 patients with suspected poisoning for whom a call was made to the BPC leading to the advice to go to the hospital. Categorization was performed according to the type of hospital referral and figures are presented as percentages.

	Total n=5,476 %	Hosp-watchful-wait n=2,368 %	Hosp-referral n=2,677 %	Hosp-urgent-referral n=431 %	Chi-square
<b>Gender<sup>1</sup></b>					<0.001
Female	54.2	49.7	56.8	63.0	
Male	45.8	50.3	43.2	37.0	
<b>Age</b>					<0.001
Adult >=14y	56.9	39.0	69.3	78.2	
Child <14y	43.1	61.0	30.7	21.8	
<b>Hour of the day</b>					<0.001
8 am-6 pm	49.8	55.2	46.7	39.9	
6 pm- 12 pm	44.0	41.8	44.9	50.3	
12 pm- 8 am	6.2	3.0	8.5	9.7	
<b>Language</b>					<0.001
French	59.5	54.3	62.7	68.2	
Dutch	40.2	45.2	37.1	31.6	
Other	0.3	0.4	0.2	0.2	
<b>Caller</b>					<0.001
Family	52.3	67.6	41.0	38.1	
Victim	16.0	16.8	15.8	13.0	
General practitioner/physician	8.8	2.3	13.7	13.5	
Other medical caregiver	7.7	4.4	9.9	12.1	
Others	7.7	5.2	8.5	16.5	
Emergency medical dispatcher	3.7	0.6	6.2	5.3	
Profession other than medical	3.1	3.0	3.5	0.9	
Policeman/firefighter	0.8	0.2	1.4	0.7	
<b>Victim location</b>					<0.001
Home	86.4	89.2	84.8	81.4	
Institute <sup>2</sup>	7.2	6.9	7.2	8.1	
Working place	2.5	1.9	3.1	1.6	
Public place	0.9	0.5	1.0	2.6	
Physician's practice/ pharmacy	1.3	1.0	1.6	0.7	
Other	0.9	0.3	1.3	1.9	
Mobile intensive care unit	0.8	0.1	0.9	3.7	

<sup>1</sup>Total of 5,169 calls

<sup>2</sup>Senior care facility, psychiatric care home, school

### Characteristics of patients and advice given

Based on the assessment of information obtained by the physicians/pharmacists, 72.4% of calls were categorised as accidental, 25.3% as intentional self-harm, 1.2% as abuse of substances and in 1.1% intentionality was uncertain.

In Hosp-watchful-wait cases 93.9% were categorised as accidental and 92.7% were single agent exposures. In 69.0%, there were no symptoms at the time of the call. When symptoms were present, 39.6% were dermatological, ophthalmological or otorhinolaryngological complaints. In Hosp-referral cases, 58.5% of referrals were accidental and 38.5% intentional self-harm cases. The most common symptoms were dermatological, ophthalmological or otorhinolaryngological complaints (22.0%), a change in consciousness (18.6%) and nausea or vomiting (11.4%). Activated charcoal or antidote administration was advised in 1.9%.

In Hosp-urgent-referral cases, 54.1% were categorised as intentional self-harm, 24.4% involved exposure to two or more agents and 28.3% suffered from a change in consciousness. Calling the mobile intensive care unit was mentioned and advised in 65.7%. Referral for antidote administration was advised in 3.2%.

Table 2. Characteristics and advice given to 5,476 patients with suspected poisoning for whom a call was made to the BPC leading to the advice to go to the hospital. Categorization was performed according to the type of hospital referral and figures are presented as percentages.

	Total n=5,476 %	Hosp- watchful- wait n=2,368 %	Hosp- referral n=2,677 %	Hosp- urgent- referral n=431 %	Chi-square
<b>Intentionality</b>					<0.001
Accidental (unintentional)	72.4	93.9	58.5	40.1	
Intentional self-harm	25.3	5.1	38.5	54.1	
Substances of abuse	1.2	0.5	1.7	2.3	
Unclear intentionality	1.1	0.5	1.3	3.5	
<b>Number of agents involved</b>					<0.001
1	85.4	92.7	80.5	75.6	
2	9.5	5.5	12.1	15.8	
>=3	5.1	1.8	7.4	8.6	
<b>Type of agents involved</b>					<0.001
T51-T65	48.2	60.8	59.1	64.0	
T36-T50	45.5	34.8	33.8	27.4	
T36-T50 & T51-T65	6.3	4.4	7.2	8.6	
<b>Patient transport<sup>1</sup></b>					<0.001
Ambulance	63.3	66.7	66.8	25.7	
Mobile Intensive Care Unit (MICU)	32.6	29.6	31.5	65.7	
By own means	4.1	3.7	1.7	8.6	
<b>Route of exposure</b>					<0.001
Oral/oromucosal	79.1	77.2	79.4	88.2	
Cutaneous/eye	9.8	10.1	10.4	4.9	
Inhalation	6.3	6.5	6.4	4.6	
>1 route	2.5	4.0	1.5	0.7	
Other/unknown <sup>2</sup>	2.2	2.2	2.4	1.6	
<b>Presenting symptoms<sup>3</sup></b>					
Dermatological, ophthalmological, otorhinolaryngological complaints	25.6	39.6	22.0	13.1	0.02
Changes in consciousness	16.5	6.5	18.6	28.3	0.393
Nausea and/or vomiting	11.1	11.8	11.4	7.4	<0.001
Respiratory problems	8.3	12.5	6.7	7.4	0.105
General malaise	5.7	2.3	6.6	9.0	<0.001
Behavioural and emotional disorders	5.2	4.7	5.6	4.4	0.053
Other	4.7	4.4	4.1	9.0	0.287
Tremor, coordination disorders	3.9	1.7	4.3	6.8	<0.001
Abdominal pain	3.6	2.6	4.3	2.2	0.011
Dizziness, vertigo	2.7	2.2	3.0	1.9	<0.001
Headache	2.3	1.9	2.7	1.1	<0.001
Pain in the limbs, neck, back shoulder and pelvic belt	1.9	3.2	1.5	0.5	0.003
Signs of neurological failure	1.3	0.9	1.4	1.6	<0.001
Palpitations	1.2	0.3	1.4	1.6	<0.001
Diarrhoea	0.8	0.9	0.9	0.0	0.956
Wound, bite, sting	0.7	1.3	0.5	0.5	0.001
Fever and convulsion	0.7	0.6	0.8	0.5	0.104
Retrosternal and thoracic pain	0.5	0.3	0.7	0.0	<0.001
External signs of bleeding or bleeding	0.5	0.1	0.6	0.3	0.003
Life-threatening situation	0.2	0.0	0.2	0.8	<0.001
Urinary problems	0.2	0.0	0.2	0.3	<0.001
All types of non-specific, generalized symptoms	2.3	2.1	2.3	3.3	
<b>Number of symptoms present</b>					<0.001
No symptoms	53.5	69.0	42.6	35.7	
1 symptom	35.3	25.8	41.7	48.3	
2 symptoms	8.8	4.6	12.0	12.1	
>= 3 symptoms	2.4	0.5	3.8	3.9	
<b>Laboratory testing advised</b>					<0.001

No	94.0	98.9	91.1	84.2	
Yes	6.0	1.1	8.9	15.8	
<b>Medical imaging advised</b>					<0.001
No	96.7	99.6	94.2	96.8	
Yes	3.3	0.4	5.8	3.2	
<b>Monitoring vital signs advised</b>					<0.001
No	92.9	98.2	89.5	84.2	
Yes	7.1	1.8	10.5	15.8	
<b>Advice for antidotes<sup>4</sup></b>					<0.001
No	98.7	99.7	98.1	96.8	
Yes	1.3	0.3	1.9	3.2	

<sup>1</sup> In 4,778 calls, information was missing

<sup>2</sup> Otic, rectal, subcutaneous

<sup>3</sup> Total of 3,322 symptoms mentioned by the caller. In 53.5% no symptoms were mentioned.

<sup>4</sup> 47.1% N-acetylcysteine, 14.3 % activated charcoal, 11.4% oxygen, 7.1% flumazenil, 4.3% glucagon, 2.9% atropine, 2.9% calcium gluconaat, 2.8% ethanol, 1.4% deferoxamine, 1.4% digoxin antibodies, 1.4% hydroxocobalamin, 1.4% naloxone

## Agents involved

Table 3 summarizes data on the 6,778 agents involved in the 5,476 calls. Soaps and detergents (10.5%), benzodiazepines (9.4%), corrosive substances (6.6%), agents primarily affecting skin, mucous membranes and ophtalmological, otorhinolaryngological and dental drugs (6.0%), antidepressants (5.5%) and antipsychotics (4.8%) were among the most frequently involved agents. They were followed by pesticides (3.7%), ethanol (3.4%) and acetaminophen (3.4%).

In Hosp-watchful-wait cases, soaps and detergents were most frequently involved (20.5%), followed by agents primarily affecting the skin, mucous membrane or ophtalmological, otorhinolaryngological and dental drugs (8.1%) and by noxious substances eaten as food (7.5%). In Hosp-referral cases, benzodiazepines (12.7%), antidepressants (7.9%) and antipsychotics (6.7%) were the 3 most frequently involved categories. In Hosp-urgent-referral cases, the most frequent categories were benzodiazepines (15.1%), antidepressants (7.6%) and acetaminophen (7.3%).

Table 3. Agents involved in calls for acute poisoning to the BPC during which patients were advised to go to the hospital and categorised according to the type of hospital referral. Percentages are presented.

ICD-10	ICD-10 agents <sup>1</sup>	Total 6,778 agents	Hosp- watchful- wait 2,628 agents	Hosp- referral 3,561 agents	Hosp- urgent- referral 589 agents	Chi- square
		%	%	%	%	
<b>T42</b>	<b>Anti-epileptic, sedative-hypnotic, antiparkinsonism drugs</b>	<b>11.6</b>	<b>5.4</b>	<b>15.0</b>	<b>18.8</b>	<b>&lt;0.001</b>
T42.4	Benzodiazepines	9.4	3.5	12.7	15.1	<0.001
	Anti-epileptics	1.5	1.3	1.4	2.4	0.053
<b>T43</b>	<b>Psychotropic drugs, NEC</b>	<b>11.6</b>	<b>4.3</b>	<b>16.3</b>	<b>16.0</b>	<b>&lt;0.001</b>
	Antidepressants	5.5	1.8	7.9	7.6	<0.001
	Antipsychotics	4.8	1.8	6.7	6.8	<0.001
	Psychostimulants	1.1	0.6	1.4	1.2	0.003
<b>T55</b>	<b>Soaps and detergents</b>	<b>10.5</b>	<b>20.5</b>	<b>4.6</b>	<b>1.7</b>	<b>&lt;0.001</b>
<b>T65</b>	<b>Other and unspecified substances</b>	<b>7.6</b>	<b>9.6</b>	<b>6.6</b>	<b>4.9</b>	<b>0.001</b>
T65.2	Tobacco and nicotine	0.9	1.0	0.8	0.8	0.977
T65.6	Paints and dyes, not elsewhere classified	0.1	0.3	0.1	0.2	0.12
<b>T39</b>	<b>Nonopioid analgesics, antipyretics, antirheumatics</b>	<b>6.9</b>	<b>2.9</b>	<b>9.0</b>	<b>11.7</b>	<b>&lt;0.001</b>
T39.1	Paracetamol	3.4	0.8	4.6	7.3	<0.001
T39.3	Other nonsteroidal anti-inflammatory drugs [NSAID]	2.9	1.6	3.8	3.6	<0.001
<b>T54</b>	<b>Corrosive substances</b>	<b>6.6</b>	<b>7.2</b>	<b>6.4</b>	<b>4.8</b>	<b>0.271</b>
T54.3	Corrosive alkalis and alkali-like substances	3.7	4.1	3.5	2.9	0.816

T54.2	Corrosive acids and acid-like substances	1.8	2.1	1.8	1.0	0.471
<b>T49</b>	<b>Agents primarily affecting skin, mucous membrane and ophthalmological, otorhinolaryngological and dental drugs</b>	<b>6.0</b>	<b>8.1</b>	<b>4.7</b>	<b>4.4</b>	<b>0.003</b>
<b>T51</b>	<b>Alcohol</b>	<b>4.3</b>	<b>2.9</b>	<b>4.8</b>	<b>7.1</b>	<b>&lt;0.001</b>
T51.0	Ethanol	3.4	1.4	4.3	6.3	<0.001
<b>T62</b>	<b>Noxious substances eaten as food</b>	<b>4.2</b>	<b>7.5</b>	<b>2.3</b>	<b>1.5</b>	<b>&lt;0.001</b>
T62.2	Ingested berries	2.6	4.7	1.3	1.0	<0.001
T62.0	Ingested mushrooms	0.4	0.8	0.2	0.0	0.001
<b>T60</b>	<b>Pesticides</b>	<b>3.7</b>	<b>5.3</b>	<b>2.6</b>	<b>2.9</b>	<b>0.04</b>
<b>T40</b>	<b>Narcotics and psychodysleptics (hallucinogens)</b>	<b>3.6</b>	<b>1.5</b>	<b>4.8</b>	<b>5.9</b>	<b>&lt;0.001</b>
T40.2	Other opioids	2.5	1.2	3.2	4.2	<0.001
T40.5	Cocaine	0.3	0.1	0.4	0.3	0.015
T40.7	Cannabis (derivatives)	0.3	0.2	0.4	0.2	0.233
T40.8	Lysergic acid diethylamide [LSD]	0.04	0.0	0.1	0.0	0.416
T40.1	Heroin	0.01	0.0	0.03	0.0	1
<b>T46</b>	<b>Agents primarily affecting the cardiovascular system</b>	<b>3.6</b>	<b>2.5</b>	<b>4.3</b>	<b>4.6</b>	<b>&lt;0.001</b>
	Beta-blockers	1.4	0.9	1.8	1.7	0.001
<b>T52</b>	<b>Organic solvents</b>	<b>2.8</b>	<b>4.3</b>	<b>1.9</b>	<b>1.2</b>	<b>&lt;0.001</b>
<b>T50</b>	<b>Diuretics and unspecified drugs, medicaments and biological substances</b>	<b>2.7</b>	<b>3.3</b>	<b>2.2</b>	<b>2.7</b>	<b>0.238</b>
<b>T47</b>	<b>Agents primarily affecting the gastrointestinal system</b>	<b>2.4</b>	<b>2.7</b>	<b>2.2</b>	<b>2.0</b>	<b>0.091</b>
<b>T45</b>	<b>Primarily systemic and haematological agents, NEC</b>	<b>2.0</b>	<b>1.2</b>	<b>2.4</b>	<b>2.7</b>	<b>&lt;0.001</b>
<b>T48</b>	<b>Drugs acting on smooth and skeletal muscles and respiratory system</b>	<b>2.0</b>	<b>2.5</b>	<b>1.9</b>	<b>0.8</b>	<b>0.113</b>
<b>700<sup>2</sup></b>	<b>Other</b>	<b>1.9</b>	<b>3.5</b>	<b>1.0</b>	<b>0.5</b>	<b>&lt;0.001</b>
<b>T36</b>	<b>Systemic antibiotics</b>	<b>1.5</b>	<b>0.8</b>	<b>2.0</b>	<b>1.4</b>	<b>&lt;0.001</b>
<b>T38</b>	<b>Hormones and their synthetic substitutes and antagonists, NEC</b>	<b>1.3</b>	<b>1.0</b>	<b>1.5</b>	<b>0.7</b>	<b>0.068</b>
<b>T63</b>	<b>Contact with venomous animals</b>	<b>0.7</b>	<b>0.9</b>	<b>0.6</b>	<b>0.5</b>	<b>0.646</b>
<b>T59</b>	<b>Other gases, fumes and vapours</b>	<b>0.6</b>	<b>0.7</b>	<b>0.4</b>	<b>1.2</b>	<b>0.055</b>
<b>T44</b>	<b>Drugs primarily affecting the autonomic nervous system</b>	<b>0.5</b>	<b>0.3</b>	<b>0.6</b>	<b>0.5</b>	<b>0.102</b>
<b>T58</b>	<b>Carbon monoxide</b>	<b>0.5</b>	<b>0.2</b>	<b>0.7</b>	<b>0.3</b>	<b>0.005</b>
<b>T37</b>	<b>Other systemic anti-infectives and antiparasitics</b>	<b>0.3</b>	<b>0.2</b>	<b>0.3</b>	<b>0.3</b>	<b>0.196</b>
<b>T53</b>	<b>Halogen derivative of aliphatic and aromatic hydrocarbons</b>	<b>0.2</b>	<b>0.2</b>	<b>0.3</b>	<b>0.0</b>	<b>0.213</b>
<b>T61</b>	<b>Noxious substances eaten as seafood</b>	<b>0.2</b>	<b>0.2</b>	<b>0.2</b>	<b>0.3</b>	<b>0.599</b>
<b>T41</b>	<b>Anaesthetics and therapeutic gases</b>	<b>0.1</b>	<b>0.1</b>	<b>0.1</b>	<b>0.3</b>	<b>0.196</b>
<b>T56</b>	<b>Metals</b>	<b>0.1</b>	<b>0.2</b>	<b>0.0</b>	<b>0.0</b>	<b>0.359</b>
<b>T57</b>	<b>Other inorganic substances</b>	<b>0.01</b>	<b>0.0</b>	<b>0.03</b>	<b>0.0</b>	<b>1</b>

<sup>1</sup> The main ICD-10-categories are given in bold and represent all involved agents in each category. The subcategories - not in bold - represent the most frequently involved agents out of the main categories.

<sup>2</sup> Under the code named 700 (not an ICD-10-code) we collected items like eye contour products, isolation materials, medical devices, water not suitable for human consumption, toys and foreign objects, inks, polymer compounds, weapons, lighting products and adhesives.

### Factors associated with type of referral for hospitalisation

Table 4 shows the results of the univariate (unadjusted OR) and multivariate (adjusted OR) analysis performed to identify the factors associated with the advice by type of referral for hospitalisation. The Hosp-watchful-wait advice was used as 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, use of antidotes and type of agents were significantly associated with referral type of hospitalisation (all  $p < 0.05$ ). In the multivariate analysis, number of symptoms present at the time of the call to the BPC, intentionality, type of agents involved and administration of antidotes advised ( $p < 0.05$ ) were significantly associated with referral type of hospitalisation.

The estimated odds of being admitted to Hosp-referral or Hosp-urgent-referral versus Hosp-watchful-wait was significantly higher with the increasing number of symptoms. Substances of abuse, unclear intentionality and intentional self-harm were also associated with higher estimated odds of being categorised to Hosp-referral or Hosp-urgent-referral. The estimated odds for Hosp-urgent-referral versus Hosp-watchful-wait was more than 20 times higher in case of intentional self-harm compared to accidental cases. The estimated odds for Hosp-referral or Hosp-urgent-referral versus Hosp-watchful-wait was more than two times higher for the categories T36-T50 compared to the categories T51-T65.

Table 4: Univariate (unadjusted OR) and multivariate (adjusted OR) analysis of factors possibly associated with the type of BPC advice with regard to type of hospital referral as compared with Hosp-watchful-wait used as the reference. The odds ratio and confidence interval are presented.

	Hosp-referral <sup>1</sup>		Hosp-urgent-referral <sup>1</sup>	
	UNIVARIATE OR <sup>2</sup> (CI <sup>3</sup> )	MULTIVARIATE OR <sup>2</sup> (CI <sup>3</sup> )	UNIVARIATE OR <sup>2</sup> (CI <sup>3</sup> )	MULTIVARIATE OR <sup>2</sup> (CI <sup>3</sup> )
<b>Number of symptoms present</b>				
>= 3 symptoms	11.14 (6.22-19.95)**	13.82 (7.59-25.18)**	13.88 (6.62-29.12)**	18.28 (8.45-39.56)**
2 symptoms	4.19 (3.33-5.26)**	5.35 (4.18-6.86)**	5.02 (3.47-7.26)**	6.80 (4.59-10.08)**
1 symptom	2.62 (2.32-2.97)**	3.23 (2.80-3.73)**	3.62 (2.88-4.55)**	4.56 (3.56-5.85)**
No symptoms	Ref	Ref	Ref	Ref
<b>Intentionality</b>				
Intentional self-harm	12.08 (9.90-14.74)**	9.81 (7.90-12.17)**	24.76 (18.92-32.38)**	20.54 (15.17-27.81)**
Undetermined intentionality	4.14 (2.14-8.00)**	3.92 (1.97-7.82)**	16.07 (7.41-34.87)**	15.37 (6.84-34.57)**
Substances of abuse	5.81 (2.99-11.26)**	2.74 (1.37-5.49)*	11.69 (4.90-27.90)**	5.16 (2.09-12.71)**
Accidental (unintentional)	Ref	Ref	Ref	Ref
<b>Type of agents</b>				
T36-T50 & T51-T65	2.71 (2.12-3.47)**	1.06 (0.78-1.43)	4.01 (2.64-6.07)**	0.97 (0.60-1.58)
T36-T50 <sup>4</sup>	3.28 (2.91-3.69)**	2.35 (2.04-2.70)**	4.38 (3.47-5.53)**	2.32 (1.76-3.06)**
T51-T65 <sup>5</sup>	Ref	Ref	Ref	Ref
<b>Antidotes advised</b>				
Yes	7.49 (3.21-17.51)**	6.98 (2.88-16.92)**	13.22 (5.05-34.59)**	13.00 (4.69-36.01)**
No	Ref	Ref	Ref	Ref

<sup>1</sup> Reference category = Hosp-watchful-wait

<sup>2</sup> OR: Odds ratio

<sup>3</sup> CI: Confidence interval

<sup>4</sup> T36-T50: poisoning by drugs, medicaments and biological substances

<sup>5</sup> T51-T65: toxic effects of substances chiefly nonmedicinal as to source

Significance level: \*  $p < 0.05$ ; \*\*  $p < 0.001$

## Cost

Since we do not dispose of data on the fate of BPC patients, we used the cost/admission to GUH from patients with acute poisoning. The mean payer's cost for poisoned patients in GUH 2017 (whole episode) was €1,287.1 (95% CI 1,030.0-1,329.7), of which 95.7% paid by the government via the insurance and 4.3% by the patient.. The mean payer's cost for the government in case of a call to the BPC was €24.9 (author's unpublished data, 2018). Extrapolating this cost to the 5,476 included cases in this study and assuming that each patient advised to go to the hospital actually did so, the estimated cost is €7,184,731.0 ((5,476 cases x € 1,287.1)+(5,476 cases x €24.9)) or €1,312.0 per patient. The estimated cost for the government is €6,878,458.4 (5,476 cases x 1,231.2)+(5,476 cases x €24.9) or a mean cost of €1,256.1 per patient and the cost for the patient is €306,272.7 (5,476 cases x 55.9) or a mean cost of €55.9. If we assume that only Hosp-referral and Hosp-urgent-referral patients actually went to the hospital (not the Hosp-watchful-wait patients) the total cost is €4,136,878.2 ((3,108 cases x 1,287.1)+(3,108 cases x €24.9)+(2,368 cases x €24.9)) or €755.5 per case for both government and patient (personal fee).

## DISCUSSION

Our study aimed to analyse data between January and June 2018 of patients calling the BPC in case of (suspected) poisoning and advised to go to the hospital. Factors associated with the type of recommendation for hospitalisation were identified, and payer's cost was estimated on the

basis of GUH data.

Analysing the intentionality of children and adults referred to the hospital (only Hosp-referral and Hosp-urgent-referral), 56.0% was categorised as accidental and 40.6% as intentional self-harm. The high percentage of accidental cases can be explained by the inclusion of children: accidental cases decreased to 42.1% and intentional self-harm cases increased to 53.6% among adults.

A link can be found between the involved agents in adults and the higher percentage for intentional self-harm cases. In adults, agents categorised in T36-T50 (medicinal agents) were most commonly used: benzodiazepines (13.4%), antidepressants (8.0%), antipsychotics (6.2%), acetaminophen (3.8%) and NSAIDs (3.0%).

In children, agents categorised in T51-T65 (non-medicinal agents) were frequently involved: soaps and detergents (21.4%), agents primarily affecting skin, mucous membrane and ophthalmological, otorhinolaryngological and dental drugs (10.9%) and noxious substances eaten as food (7.1%, of which 4.5% ingested berries). NSAIDs and acetaminophen accounted for 2.8% and 2.7% respectively.

The low score of ethanol (4.8%) among adult callers is remarkable compared to the ethanol scores in hospitals. In unpublished data of poisonings in GUH [19], ethanol was used in 81.1% of the admissions as a single agent and in 18.9% as concomitant substance. The low score in our study is not surprising, as the BPC calltakers can not physically evaluate the callers which may deny their ethanol consumption. Another reason could be that patients do not mention spontaneously their use of ethanol, because ethanol alone is probably not often a reason to call the BPC, as the population is familiar with the effect of ethanol.

In the multivariate analysis, number of symptoms, intentionality, type of agents involved and administration of antidotes advised were factors significantly associated with the referral type. A higher number of symptoms present during the call was associated with a higher estimated odds for Hosp-referral or Hosp-urgent-referral, which is logical as the presence of multiple symptoms is an indication of severity. In cases of unclear intentionality, the higher odds for Hosp-referral and Hosp-urgent-referral compared with accidental cases may be explained by the fact that the call-taker did not want to take any risk if he/she could not determine definitely the intentionality of the patient or if there was a concern for psychosocial help. If agents T36-T50 (medicinal agents) were involved, the odds for Hosp-referral and Hosp-urgent-referral were more than two times higher compared with agents T51-T65 (non-medicinal agents). This can be explained by the high percentage of, amongst others, soaps and detergents (with a low toxicity risk) in the category Hosp-watchful-wait (20.5%) versus only 4.6% and 1.7% in Hosp-referral and Hosp-urgent-referral cases respectively. The need for antidotes was also a factor more frequently leading to Hosp-referral and Hosp-urgent-referral given that antidotes are an indication of the severity of poisoning and have to be administered in the hospital obviously.

Articles about factors that may be associated with the referral of patients from a pre-hospital situation to the hospital are rare. Woon Yon Kwon[20] developed a triage method to prevent unnecessary ED visits of out-of-hospital poisoned patients. He designed a triage protocol for out-of-hospital-toxicity-positive patients to determine a low- and high-risk group. His protocol consisted of five factors, ranked according to the height of the odds ratio: (1) minimally toxic substances, (2) unintentional exposures (3) without symptoms or signs (4) without pre-existing medical problems, current medication, pregnancy, or breast-feeding and (5) safe environment & observation possible. The three most important factors mentioned by Woon Yong Kwon correspond to those we found to be associated with type of referral: agents involved, intentionality and symptoms.

The mean payer's cost per admission for poisoned patients in GUH 2017 (whole episode) was €1,287.1. It was important to make a distinction between patients advised to go to the hospital under certain conditions (43.2%) and those referred (48.9%) or urgently referred to the hospital (7.9%). Analysing the characteristics of Hosp-watchful-wait patients (93.9% accidental, 92.7% single agent exposures, in 69.0% no symptoms at the time of the call), we assume that only a small part of the Hosp-watchful-wait patients went effectively to the hospital after the BPC call. As the average estimated cost for a patient who goes to the hospital with a poisoning problem is €1,287.1, versus €24.9 for a call to the

BPC, every patient who did not go to the hospital, reassured by the advice of the BPC, meant an important saving for the government and the patient and also helped to avoid overcrowding of the ED.

### **Strengths, limitations and generalisability**

In this study, we used ICD-10 as categorisation tool. BPC experts note the name(s) of the agent(s) involved in the electronic file, which is then linked to ICD-10 codes. This ensures that the original agent(s) behind the ICD-10 code(s) can always be consulted in the original file. This can be a response to the limitation, described by different authors, namely the frequent use of non-specific ICD-10 codes and the significantly underestimated incidence of drug overdose for any specific drug[20,21]. We think that the use of a clear and international standard allows the scientific community to compare and share data in a consistent and standard way and may be a first step in the development of a template for uniform data reporting in order to facilitate international comparison between organisations. Furthermore, the WHO took the initiative to respond to the limitations of ICD-10 by introducing a webplatform facilitating the preparation of ICD-11[22] .

A second limitation of our study is that we could not evaluate the validity of the referrals in function of the quality of care as it was not possible to do a follow-up.

Insight into characteristics for type of referral by the BPC can give information on the decision process. These data can be used in further studies using hospitalisation data to assess the quality of these referrals. This is important as payer's cost estimates showed that patients who are hospitalised because of poisoning entail a considerable financial burden.



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**Ethics approval statement**

The analysis of the Ghent University Hospital retrospective anonymous data was approved by the Ethical Committee of GUH (approval number B670201732651), Ghent, Belgium. The retrospective anonymous data of the Belgian Poison Center was analysed according the General Data Protection Regulation (GDPR) guidelines of the BPC, published on its website: Antigifcentrum. GDPR. Available from: <https://www.antigifcentrum.be/gdpr>; [cited 2019 Jan 23].

**Clinical Trial Registration**

Not applicable.

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**Competing Interests**

None declared.

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