


# BMJ Open Acute care for patients exposed to a chemical attack: protocol for an international multicentric observational study

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## ABSTRACT

**Introduction** The use of weapons of mass destruction against civilian populations is of serious concern to public health authorities. Chemical weapons are of particular concern. A few studies have investigated medical responses in prehospital settings in the immediate aftermath of a chemical attack, and they were limited by the paucity of clinical data. This study aims to describe the acute management of patients exposed to a chemical attack from the incident site until their transfer to a medical facility.

**Methods and analysis** This international multicentric observational study addresses the period from 1970 to 2036. An online electronic case report form was created to collect data; it will be hosted on the Biomedical Telematics Laboratory Platform of the Quebec Respiratory Health Research Network. Participating medical centres and their clinicians are being asked to provide contextual and clinical information, including the use of protective equipment and decontamination capabilities for the medical evacuation of the patient from the incident site of the chemical attack to the moment of admission at the medical facility. In brief, variables are categorised as follows: (1) chemical exposure (threat); (2) prehospital and hospital/medical facility capabilities (staffing, first aid, protection, decontamination, disaster plans and medical guidelines); (3) clinical interventions before hospital admission, including the use of protection and decontamination and (4) outcomes (survivability vs mortality rates). Judgement criteria focus on decontamination drills applied to any of the patient's conditions.

**Ethics and dissemination** The Sainte-Justine Research Centre Ethics Committee approved this multicentric study and is acting as the main evaluating centre. Study results will be disseminated through various means, including conferences, indexed publications in medical databases and social media.

**Trial registration number** NCT05026645.

## INTRODUCTION

Over the past two decades, a staggering chain of epidemics and intermittent CBRNE

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The pioneering methods used in the measurement of medical responses in the contaminated area after a chemical attack—a topic that, to date to our knowledge, has not been studied thoroughly. The zone of interest consists of the interventions taking place in prehospital settings, beginning at the incident site and ending at the patient's transfer to a clean zone.
- ⇒ The interventions assessed in this study are based on three key integrated competences, namely, (1) protection (for the staff and the patients), (2) decontamination (immediate and specialised (medical decontamination)) and (3) medical interventions.
- ⇒ The inclusion of both civilian and military healthcare resources in the study.
- ⇒ Issues raised by authorities around the world restricting access to data may adversely affect this study.

incidents has captured the world's attention.<sup>1</sup> If anything, events like the Syrian chemical warfare, Russia's alleged use of Novichok in her spy games with the West, and the COVID-19 pandemic have neutralised the 'alarming level of ignorance' among civilians and the broader scientific community regarding the existence and capabilities of non-nuclear weapons of mass destruction (WMD).<sup>2</sup> In an era of cognitive and hybrid warfare,<sup>3–8</sup> the subtle and subversive use of WMD—and especially of chemical and biological agents—against military targets and civilian populations is likely to become the rule rather than the exception.

The use of WMD is of serious concern to civilian and military health authorities around the world.<sup>9–13</sup> A large number of chemical agents, each with its own characteristics,

including symptom onset (from seconds to hours) and contamination modalities (inhalation; ingestion; skin penetration) can be used in terrorist attacks, war, etc.<sup>12–30</sup> Such threats require health organisations to be ever more prepared to manage patients exposed to WMD.<sup>31–38</sup>

The literature on the way prehospital clinical management of casualties is conducted during CBRNE events reveals several deficiencies concerning elements such as clinical protocols, work environments, and protection and decontamination capabilities. These range from the lack of accurate medical information and the inclusion of outdated information to the absence of medical gold standards for medical evacuations in prehospital settings (eg, using oxygen safely, efficient airway management).<sup>12 16 19–30 39–48</sup> On the one hand, it has been noted that scientific publications did not address medical guidelines employed in actual acute settings conditions (ie, in real-life conditions). In the literature, mentions of clinical means in acute settings appeared to be limited to medical countermeasures capabilities (eg, HI-6/atropine and diazepam self-injectors for nerve agent exposures), which are only held by military and security forces and not by hospitals or pharmacies.<sup>12 16 19–30 39–48</sup> On the other hand, a review of the literature revealed that most studies involved clinical interventions taking place after the patient had already been admitted to the hospital or medical facility.<sup>12 16 19–30 39–48</sup>

A recent systematic review<sup>49</sup> assessing past medical responses in prehospital settings after chemical attacks<sup>50–53</sup> constitutes one study,<sup>49</sup> confirming the existence of these gaps and standardisation issues in clinical care, as well as in protection<sup>12–15 17–30 39–41 49 54–56</sup> and decontamination capabilities<sup>12–15 17–30 39–41 49 54–56</sup> for both patients and staff. These deficiencies are directly related to the medical extraction of casualties exposed to chemical attacks from the incident site to the point of transfer to a medical facility (ie, acute settings), which the systematic review also revealed to be an area that has hardly been studied.<sup>49</sup>

Given the scarcity of information regarding validated medical response data in acute settings,<sup>49</sup> it is necessary to conduct studies on medical responses during a CBRNE event, starting with chemical exposures.

## Aim

The aim of this multicentric observational study is to describe the acute medical management of patients wounded in a chemical event during their medical extraction to medical facilities.

## Objectives

The first objective of the study is to retrospectively describe the three following interrelated competences during a medical extraction: (1) the use of protection capabilities for staff and patients, (2) the use of decontamination capabilities for staff and patients (levels: immediate and specialised) and (3) medical treatments provided.

The second objective is to collect any existing protocols and guidelines established by the concerned authorities

that would form part of their disaster plan in the event of a chemical attack causing mass casualties, and to retrospectively compare them with what happened in real-life conditions.

## Research questions

The research questions are: (1) What integrated protection capability was used in medical interventions? (2) What integrated decontamination capability was used in medical interventions? (3) What medical treatments did clinicians provide in acute settings (airway, breathing and circulation management; pharmaceutical and non-pharmaceutical products; medical technologies)? and (4) If algorithms such as protocols and guidelines were developed, how were they applied in emergency settings?

## METHODS AND ANALYSIS

### Study design

This is an ongoing multicentric observational study in which the assessment of the medical response to chemical attacks is conducted retrospectively over two distinct periods. The first is for events that occurred in the past five (5) decades (1970–2020). The second is for future chemical attacks that may occur within the next 15 years (2021–2036). Of note, the data collection will be performed retrospectively and after a participating medical centre receives approval by an ethics review board (ERB) (see the Ethics and dissemination, ethics approval, amendment and governance section).

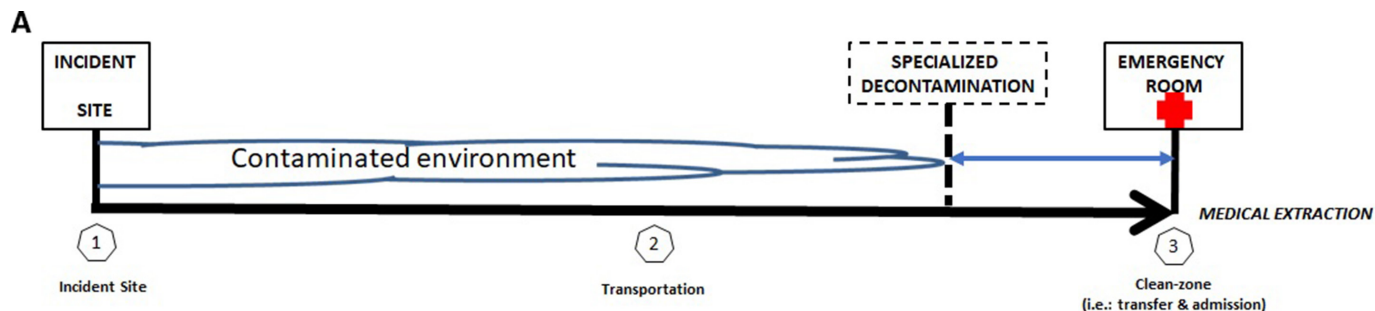
### Eligible chemical events

The eligibility of a chemical attack requires that it: (1) be confirmed either by the governmental authority of the attacked country or/and by at least one medical authority related to the attacked country, such as the International Committee of the Red Cross (ICRC), Doctors Without Borders, the United Nations Refugee Agency (UNHCR); (2) be confirmed by an institution relying on security intelligence sources such as the WHO, the Canadian Security Intelligence Service, etc and (3) occurred between January 1970 and December 2036.

### Inclusion and exclusion criteria for participating Institutions/centres

Inclusion criteria are:

- The chemical attack caused at least one casualty who required the assistance of the participating healthcare system (eg, physicians, nurses, paramedics and other healthcare specialists of a medical facility) during a medical extraction from the incident site until admission to a medical facility (figure 1).
- Patients are eligible if they were exposed to the chemical attack.
- Medical information concerning the chemical exposures, even if partial, is accessible to healthcare professionals for the purposes of filling out the online electronic case report form (eCRF).



- B**
- Variables/Questions: measuring the patient's extraction from the incident site up-to the his/her transfer/admission into a medical facility!
- Motive leading to a chemical event
  - Chemical agent used and its mean of delivery
  - First aid
  - Medical system resources deployed
  - Disasters plans used
  - Inter-integrated competences
    - Clinical interventions (onsets of the distress versus the treatment provided)
    - Protection capabilities used (for the patient and clinician)
    - Decontamination capabilities used (immediate and specialized for the patient and clinician)
  - Outcomes for the patient

Nb.: once a clinician would become inflicted by the chemical agent, he/she is processed as a patient.

**Figure 1** Illustration summarising the medical extraction and the zone of interest. This illustration summarises the medical extraction and the study's zone of interest, which begins at the incident site and ends when the patient is transferred and admitted to the emergency room or its equivalent (eg, a walk-in clinic). Part A. Step 1: patient management begins, step 2: transportation to the medical facility and step 3: patient admission to the emergency room. This is also the point at which continuity of care will normally proceed in a clean zone after patient decontamination. Ideally, the specialised decontamination facility will be located such that the patient will have been decontaminated prior to reaching the hospital. For that reason, it is represented by dashed lines. Emergency services found in cities that have such specialised assets may also have a specialised medical decontamination line that has the highest level of expertise to deal with injured, unconscious and deteriorating patients while they are being processed for a transfer to a clean zone. Part B: illustrates the correspondence between the detection of the patient's clinical presentation and the medical response during the entire medical extraction. Part C: illustrates the frequency of patient monitoring.

- iv. Participants must be able to complete the online eCRF in English.
- v. The approval of an ERB is obtained by each medical centre participant.

Exclusion criteria: a negative response to any of the inclusion criteria results in an exclusion.

### Target population and recruitment

Populations being studied include all individuals linked to a chemical event/attack who were affected by a chemical agent and needed the intervention of their local healthcare system (including anyone who was exposed and turned to a medical organisation for help sometime after an attack). As a third party recruited for this study, participating medical facilities that treated at least one patient will be responsible to make the selection based on the inclusion criteria and to anonymously manage clinical information for processing into the study eCRF.

### Sample size calculation

As this is an observational study, there is no limitation on the number of patients that can be included per chemical

event. In [table 1](#), known chemical events that caused numerous casualties are shown. In other words, since a chemical attack/event may result in very few to hundreds of casualties, the sample size will vary accordingly.

Where a participating medical centre managed numerous patients, the clinician representing the centre will determine the number of cases to be reported according to two factors: (1) data accessibility and (2) the burden associated with the task of completing the eCRF for each patient meeting the study criteria. Participating centres or clinicians will be requested to provide data on as many patients as they can. Given the chaotic nature of mass casualty events, data may be lost or incomplete. Participating centres are nevertheless encouraged to provide the data available for each patient.

### Data collection and measurements

#### Data collection, quality, validation

Participating medical centres/clinicians are to use each patient's medical chart to enter data into the study online eCRF. For data collection purposes, the eCRF is accessible

**Table 1** Summary of past chemical exposures that have, to date, resulted in victims<sup>12 14 49 52 59–70</sup>

Incident name	N	Chemical agent	Country	Year
Markov's case	1	Ricin (toxin)	United Kingdom	1979
Aum Shinrikyo's first attempt (Matsumoto)	>100	Sarin (nerve agent)	Japan	1994
Aum Shinrikyo's second attempt (Tokyo)	>1000	Sarin	Japan	1995
Iran-Iraq war	>1000	Mustard gas, cyclosarin, sarin, hydrogen cyanide, tabun*	Iraq	1980–1988
Syrian Regime	>100	Mustard gas, chlorine, sarin	Syria	2014
ISIL, attack in Syria	>100	Mustard gas, sarin, chlorine, phosphine	Syria	2015
ISIL, Iraq campaign	>100	Mustard gas, chlorine, phosphine	Iraq	2015
Kim Jong-nam	>1	VX (nerve agent)	Malaysia	2017
Salisbury attack	3	Novichok (nerve agent)	United Kingdom	2018
Amesbury	1	Novichok (nerve agent)	United Kingdom	2018

Note. During this study, the electronic case report form will help rectify some basic facts about the use of chemical weapons in cases where disparities are found in different literature sources (<https://cbrne-obs-ltb.cred.ca/>; a product of the Biomedical telematics Laboratory: <https://rsr-qc.ca/en/ltb/>). For instance, Schulz-Kirchrath<sup>14</sup> reported that Tabun was used during the Iran-Iraq war (\*) while the Centers for Disease Control and Prevention (CDC) speculated about its use.<sup>59</sup> Moreover, CDC also reported that VX was probably used during this same conflict.<sup>70</sup>

through a secure website hosted on the Biomedical Telematics Laboratory Platform of the Quebec Respiratory Health Research Network. The link is only sent to designated staff at participating centres that have obtained ERB approval. Six data gathering categories comprise the eCRF. These are: (1) overview of the chemical attack; (2) deployment of resources; (3) hospital emergency room area; (4) patient information (including rescuers, first responders and clinicians suffering from secondary exposure effects); (5) medical extraction and interventions and (6) outcomes (survivability vs mortality rates). The healthcare and medical facility information section is composed of the following: (1) the clinical presentation; (2) treatments and (3) patient monitoring frequency. The latter is measured throughout the chemical attack casualty's complete medical management starting at the incident site, and continuing during the medical evacuation and emergency room interventions (figure 1). Information will also be collected about the use of disaster plans (ie, how the medical authorities planned to respond to a chemical attack and what literature and references they relied on). Participating medical centre clinicians will be trained on a demonstration version of the eCRF before they begin entering data into the operational version (Demo: <https://cbrne-obs-demo-ltb.cred.ca/>; Operational: <https://cbrne-obs-ltb.cred.ca/>). Members of the study team will routinely validate the data entered in the eCRF. They will also answer questions and address any issues raised by participating medical centres and clinicians. However, a residual information bias cannot be excluded as an independent data quality assurance and validation on each participating site will not be performed. This limitation will be addressed in the final publication once the study has ended.

### Other eCRF specifications

The eCRF is an interactive web-based platform developed and implemented by the Laboratoire Télémédical (LTB) du Réseau en santé respiratoire du Québec du Fonds de recherche du Québec-Santé (Biomedical Telematics Laboratory: <https://rsr-qc.ca/en/ltb/>). The LTB has expertise in the development of such tools.<sup>57 58</sup> Each participant recruited remotely inputs data into the eCRF under a personal profile that is protected by an encrypted password. Before an eCRF can be submitted, a number of mandatory questions must be answered. In addition, certain eCRF fields have answer options that allow for reporting that data are missing or non-existent. This makes it possible to assign a numerical value when assessing information gaps. All protected health and event-related information is stored in a secure location of the LTB. Epiconcept was certified as a Health Data Host on 19 April 2019, and the certification applies to the eCRF.

### Criterion of primary judgement

The number of patients reported as wounded by a chemical weapon on whom a minimum of one decontamination procedure was performed before admission to the medical centre.

### Criteria of secondary judgement

Four secondary judgement, criteria are defined as follows:

- ▶ The percentage of patients wearing protective equipment on whom a minimum of one decontamination procedure was performed and who did not experience any distress event requiring at least one medical treatment during medical extraction from the incident site to their admission at the hospital emergency



room or its equivalent (ie, endpoint of the medical extraction/evacuation).

- ▶ The percentage of patients wearing protective equipment on whom a minimum of one decontamination procedure was not performed and who experienced at least one distress event requiring at least one medical treatment during medical extraction from the incident site to their admission at the hospital emergency room or its equivalent (ie, endpoint of the medical extraction/evacuation).
- ▶ The percentage of decontaminated patients who did not experience any distress requiring a treatment and who wore protective equipment during a medical extraction until their admission at the hospital emergency room or its equivalent (ie, endpoint of the medical extraction/evacuation).
- ▶ The percentage of decontaminated patients who experienced a minimum of one distress event for which they received at least one treatment, and who did not wear any protective equipment during a medical extraction until their admission at the hospital emergency room or its equivalent (ie, endpoint of the medical extraction/evacuation).

#### Patient and public involvement

There has been no patient or public involvement in the design, recruitment, conduct, interpretation and dissemination of this study's results.

#### Biostatistical analysis

Continuous variables will be reported as mean±SD or median with IQR, including proportion, frequency and mode, according to the variable distributions. The normality assumption/distribution will be verified with the Shapiro-Wilk tests. Nominal variables will be reported as frequencies. Analyses will be conducted with the latest version of IBM SPSS Statistics Software or its equivalent in due time (SPSS; <https://www.ibm.com/analytics/spss-statistics-software>; Last accessed: 24 August 2022).

#### Impact of this study

It is anticipated that the results of this study will have the following impacts. It will:

- ▶ Highlight the strengths of participating healthcare facilities in the medical management of chemically exposed patients.
- ▶ Reveal gaps in the capability of participating healthcare facilities in the medical management of chemically exposed patients, thereby contributing to the optimisation of clinical standards and resource management during CBRNE incidents.
- ▶ Demonstrate the need for future studies, including politicised cases where access to classified information will be required.
- ▶ Pave the way for the implementation of a research programme in Chemical, Biological, Radiological, Nuclear, Explosive (CBRNE) defence through which medical algorithms and technologies for use by

medical clinicians will be developed to address identified gaps.

#### ETHICS AND DISSEMINATION

##### Ethics approval, amendment and governance

In order to conduct research involving human subjects, the approval of the Sainte-Justine Research Centre Ethics Committee was required. In March 2021, the committee approved the final amendment to the study plan (registration number 2020–2561). This amendment extended the study period to include future chemical attacks that will be analysed retrospectively. The solicitation of international medical centres and organisations as participants has begun since 2020 with the study's initial approval obtained. A similar solicitation effort will be undertaken for future chemical attacks. The addition of medical centres or clinicians as future participants will require the approval of their ERB and a signed document formalising an interinstitutional agreement.

In circumstances where ethical review board approval would be difficult to obtain, such as a civil war, etc, options have been developed. The first will come into play once the country becomes stable with a legitimate government after a period of political instability (eg, civil war). In that case, medical centres will be solicited. The second, currently underway, is to solicit international organisations deployed in an unstable country to provide medical care to the civilian population. Examples of these organisations are the ICRC, Doctors Without Borders, the UNHCR, the North Atlantic Treaty Organization. The participation of these organisations will require the approval of their respective ERB or a third-party organisation experienced in scientific study projects capable of providing such approval. Finally, the third option will be to conduct an interview directly with the patient via telemedicine (eg, Microsoft Teams). In such cases, a patient's signed consent will need to be kept on record at Sainte-Justine University Hospital Research Centre's medical archive department. When a medical centre or an international organisation does not have an ERB, ethics approval will need to be obtained from a third-party organisation, as suggested for option 2 (ie, a third-party organisation experienced in scientific study projects capable of providing such approval). However, in case of other obstacles, the matter will be referred to legal authorities in order to determine a suitable course of action. Finally, Sainte-Justine's ERB overseeing the study will regularly be kept informed as to the use of this last option.

##### Dissemination

Results will be presented in conferences as well as published in peer-reviewed medical journals. The paper will also be advertised on social media. Since this paper will be published in open access, the public can acquire it freely.

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**Contributors** Study concept and design: SB, JL, PJ. Data acquisition: SB, JR, AK, DB, FL, YF, MD, PJ. Study validation: SB, MD, SS, PJ, JL. Data analysis and interpretation: SB, JR, MD, DB, YF, MD, JL, PJ. Drafting of the manuscript: SB. Critical revision of the manuscript for important intellectual content: SB, DN, FL, HI, SS, JL, PJ. Study supervision: JL, PJ. Accountability: PJ, JC and SB took responsibility for the content of the manuscript, including the data and analysis. The lead author (PJ) affirmed that the manuscript is an honest, accurate and transparent account of the study being reported, and that no important aspects of the study have been omitted.

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**Competing interests** All authors have completed the Unified Competing Interest form at [www.icmje.org/col\\_disclosure.pdf](http://www.icmje.org/col_disclosure.pdf) and declare that no commercial or governmental funding sponsored this project. Jacinthe Leclerc (JC), Philippe Jouvret (PJ), Stephane Bourassa (SB) and Marc Dauphin (MD) have no financial interests that are relevant to the submitted work. Medical Intelligence CBRNE Inc. (also known as MEDINT CBRNE Group) provided a donation for the creation of eCRF. Although SB and MD are MEDINT CBRNE Group founders and shareholders, they have no current financial interests relevant to the submitted work. MEDINT CBRNE Group is a start-up company that was established in 2017 with support from university entrepreneurship services (Laval and Montreal) and the Prince's Trust Canada (<https://www.princesoperationentrepreneur.ca/>). The military expertise that has shaped MEDINT CBRNE Group was developed while serving in the Canadian Armed Forces.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

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