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"Emergency Department Preparedness in a Mega Mass Casualty Incident While Under Missile Fire: Lessons Learned from Israel on October 7, 2023"

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Abstract

Introduction On October 7, 2023, approximately 2,500 Hamas terrorists infiltrated southern Israel from Gaza. Over 1,200 people were killed and 1600 were injured in the largest mass casualty incident (MCI) in Israel's history. Emergency departments (EDs)

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throughout the country were overwhelmed with patients and working under missile fire. Injuries included high-velocity gunshot wounds, blast injuries, and burns. The objective of this article is to outline the lessons learned from the response of EDs in Israel to a large, multi-front MCI, in Israel known as a mega MCI, with a specific focus on the clinical care provided to patients in accordance with Israel's National Hospital Disaster Preparedness Plan mandates.

Methods

This is a retrospective descriptive analysis of the implementation of Israel's National Hospital Preparedness Plan to the events of October 7, 2023. The working group that performed this analysis are Israeli and international emergency physicians who are involved in disaster preparedness at either their hospital or on a national level. The study is based on institutional after-action reviews. Any data presented is from the Israel Ministry of Health.

Results A total of 1632 victims from October 7 were seen at 19 EDs throughout the country from the morning of the mega MCI until midnight. The EDs of the Soroka Medical Center, and the Barzilai Medical Center saw the most patients- 624 and 323 respectively. Israel's National Committee for Mass Casualty Incidents (NCMCI) sets comprehensive guidelines and supervises yearly mandatory comprehensive hospital-wide exercises related to MCIs. Based on this, the EDs were able to easily call in additional staff and critical patients were treated using a multidisciplinary approach. Additional patient care areas were opened. There were instances of compromised patient care due to large numbers of arriving patients. Also, there was a need for more secondary transfers.

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Conclusion

Being the largest MCI in Israel's history, October 7tested the performance of the 19 EDs involved. Overall, staffing was sufficient and additional patient care areas were successfully opened. However, there were issues of compromised care and the need for increased numbers of secondary transfers. These lessons are important for the future management of MCIs in Israel and worldwide.

Introduction

On October 7, 2023, approximately 2,500 Hamas terrorists infiltrated southern Israel from Gaza. Over 1,200 people were killed,1632 were injured, and 239 were taken as hostages, resulting in the largest mass casualty incident (MCI) in Israel's history (1). Hospitals throughout the country were alerted, and additional staff were called in. Nineteen hospitals throughout the country received patients. These hospitals ranged approximately 20 to over 170 kilometers from the scene of the MCE. Injuries included high-velocity gunshot wounds, stab wounds, blast injuries, and burns. In Israel, a very large MCI which involves more than 500 patients is referred to as a mega MCI.

Other mega MCIs secondary to terrorism have occurred over the past two decades. The September 11, 2001, World Trade Center attack was the largest MCI in the United States and killed nearly 3,000 (2). However, patients who survived to reach the hospital usually had only minor injuries with only a 10-15% hospital admission rate (3). On March 11, 2004 a series of ten near-simultaneous bombings on four commuter trains in Madrid left 191 dead (177 immediate, 14 delayed deaths) and over 2,000 injured. Approximately 60% of the casualties were brought to the two closest EDs with a critical mortality rate of

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19.5%. (4,5,6), In 2005, simultaneous suicide bombers in the United Kingdom killed 52 and wounded over 700 (7). Unlike these events, the mega MCI on October 7 was ongoing and was accompanied by continuous missile attacks which complicated the medical response. Ashkelon, the city with the hospital closest to the mega MCI, was hit by 160 missiles, 30 within a kilometer of the Barzilai Medical Center (approximately 20 kilometers from Gaza). In Be'er Sheva, location of the Soroka Medical Center (approximately 40 kilometers from Gaza), there were 69 instances of air raid sirens in the first 24 hours, calling for civilians to seek shelter. As such, it was an asymmetric assault with aspects of both a very large terror attack, including indiscriminate violence against unarmed civilians, as well as characteristics of an armed invasion, where the state temporarily was not in control of its territory. October 7 was also distinct in that in a developed country that is part of the Western democratic sphere, soldiers and civilians were treated simultaneously in a civilian trauma system due to injuries sustained by an armed invasion, while the hospitals themselves were at risk of attack. While US and European soldiers have been treated in Western civilian care systems after being evacuated from the Middle Eastern theaters of conflict, this care has never been provided to them in the context of an ongoing large-scale attack on their soil which threatened the facilities in which they received care.

The objective of this article is to describe lessons learned from the response of emergency departments (EDs) in Israel to the October 7 mega MCI. The specific focus of this manuscript is on the clinical care of patients in the treating EDs in the context of the mandates of Israel's National Hospital Disaster Preparedness Plan.

Methods

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Israel's National Hospital Disaster Preparedness Plan: Background

Israel has a current population of 9.5 million. Nationwide, there are 29 hospitals, all of which must have comprehensive disaster preparedness plans, including written protocols and annual training exercises. Each hospital also has a specific trauma designation. There are Supra-Regional Trauma Centers (7), Regional Trauma Centers (13), and Local Trauma Centers (9) (8). Israel's National Health Authority, chaired by the Director General of the Ministry of Health (MOH), coordinates the response to disasters and MCIs. It includes the Surgeon General of the Israel Defense Forces (IDF) and the Director General of Clalit, the country's largest Health Fund.

Subordinate to this is the National Committee for Mass Casualty Incidents (NCMCI), which ensures that hospitals, community medical centers, and emergency medical services (EMS) succeed in the evaluation and treatment of patients in MCIs during both peacetime and wartime (9,10). The 24 NCMCI members are physicians from the disciplines of emergency medicine and surgery, as well as non-physician representatives from the MOH, IDF, EMS, and nurse administrators. The members are appointed to the committee by the MOH. The committee meets quarterly and supervises a training exercise approximately every month at different hospitals throughout the country. This group sets the guidelines to be followed nationwide. Each hospital in the country has its multi-hazard disaster preparedness committee, which is required to participate in mandatory exercises that include an MCI drill once every three years, a mass toxicologic drill once every 3 years, and a war scenario once every four years. These exercises are planned over several months using a strict Gantt chart that is supervised by representatives of the Home Front Command (HFC), the division of the IDF tasked with

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civil protection. This includes meetings on content, logistics, protocol updates, and aligning expectations. The exercises, which can include up to one hundred simulated casualties (whether inexpensive mannequins or soldiers in moulage) usually occur over several hours, after which team and hospital-wide debriefings are conducted. The NCMCI defines a large MCI as including between 100 to 500 victims, while a mega MCI involves over 500 victims.

This is a retrospective descriptive study of the implementation of Israel's National Hospital Preparedness Plan to the mega-terrorist attack that occurred on October 7, 2023. The working group involved in this study are all emergency physicians (BZ, DW, SS, ET, TS, JR, EAA) who are leaders of disaster preparedness at either their individual hospitals, and/or on the NCMCI. MN is an emergency physician and international researcher of conflict-related disaster medicine. The study is based on after-action reviews at their individual institutions. Any data presented is from the Israel Ministry of Health from the day of October 7, 2023. There is no data involving individual patients or their identity.

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Results

ED Visits from the October 7, 2023 Mega MCI

On October 7, 2023, the Gaza envelope region (an area of Israel within 7.2 kilometers of the border with Gaza and with an approximate population of 70,000) was overrun by Hamas terrorists. Those killed included soldiers and civilian inhabitants of multiple kibbutzim (communal settlements) and the cities of Sderot and Ofakim (populations each of over 30,000); (Figure 1 and Table 1). According to the Ministry of Health (MOA), a

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total of 1632 victims from October 7 were seen at 19 EDs throughout the country from the morning of the mega MCI until midnight. The ED of the Soroka Medical Center, one of seven Supra-Regional Trauma Centers, and the closest to the mega MCE (41.6 km) saw the most ED patients (624) (Figure 2). Barzilai Medical Center, the closest hospital to the MCI but a local trauma center, received 323 casualties. After that was the Sheba Medical Center located 70.2 km from the area which received 110 casualties. Sheba although located relatively farther from the site of the mega MCI, is the largest hospital in Israel and has full trauma capabilities, including an active heliport. Other hospitals that received large numbers of casualties included Kaplan Medical Center in Rehovot (98), Shamir Medical Center in Be'er Ya'akov (87), and the Samson Assuta Ashdod University Hospital (87). Other hospitals located between 65.6 and 172 km from the scene received the remainder of the victims. (Table 2).

Israel National Hospital Disaster Preparedness Plan: Guidelines and Standards

Activation of an MCI Protocol

According to the standards of the NCMCI, an MCI protocol can only be activated by the hospital director, deputy director, or one of their designees. Each hospital then calls in the necessary staff. The method of notification is not standardized but usually involves short message service (SMS).

Once an MCI is declared, several procedures occur in parallel as team members arrive at predesignated sites in the hospital. The physicians in the ED immediately begin to either admit, discharge, or shift patients to 'flex' areas that are generally not in use. Any

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unstable patients are supposed to have a verbal report given to the accepting department and be escorted by trained medical personnel. At the same time, identification vests and walkie-talkies are distributed in addition to MCI equipment carts that are rolled to predesignated areas. Staff are given checklists to verify that all necessary tasks are expedited. Hospital security services cordon off the ED and place signs designating the specific treatment areas. If the hospital comes under missile fire, all patients need to be moved to protected areas.

In general, most of the EDs in Israel were able to quickly clear room for incoming casualties by discharging or admitting patients. One factor that worked in their favor was that the mega MCI occurred on a Saturday morning (Shabbat in Hebrew), which is the Jewish day of rest, and simultaneously Simchat Torah, a Jewish holiday. Thus, there were fewer patients present in the ED than usual

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Triage

While most EDs in Israel triage patients according to either the Emergency Severity Index (11), the Canadian Triage and Acuity Scale (12), or the Australasian Triage Scale (13), there is no standard nationwide protocol for hospital-based triage for an MCI. However, there is a national standard for the patients to be divided into the categories of “immediate,” or “ambulatory.” Many hospitals divide the “immediate” category into those who are unstable and need to be resuscitated in the hospital’s trauma bay and those more stable, who can be treated in an acute care area.

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In routine times, critically wounded patients are triaged to designated trauma bays, however, due to the overwhelming number of casualties, many were intubated and had invasive ED procedures such as the insertion of chest tubes or central lines outside of these areas.

Patient Care

Throughout the EDs in Israel, care for patients, especially in the trauma bays and any unstable patients, is based on the team approach and usually involves emergency physicians, surgeons, and anesthesiologists– depending on the hospital. All care is based on the international Advanced Trauma Life Support (ATLS) protocols. The ATLS course is mandatory for all EM, anesthesia, and surgical residents.

No patient is to be discharged directly from the ED. Rather, all patients destined to be released are transferred to an area known as "observation before discharge." The assigned staff of physicians, nurses, and social workers review the patient's chart to ensure that the patient was appropriately assessed and considered suitable for discharge. They also verify that any necessary procedures or tests were performed and that proper follow-up is in place.

Patient flow in a large or mega MCI is unidirectional. Once a patient leaves the ED, they either go to the imaging department, or are admitted to one of the surgical or orthopedic wards, the intensive care unit, the operating room, or "observation before discharge." Each area of the ED, whether trauma, acute care, ambulatory, or "observation before discharge," has an administrative director who is a senior physician. This director verifies that the necessary documentation, tests, and procedures were performed before leaving

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the department. The administrators each have a checklist detailing their required activities.

Secondary Transfers

Part of the training mandated by the NCMCI is for hospitals to practice either the secondary transfer of patients to other medical centers or to practice being a receiving hospital. *Deceased Patients*

The NCMCI mandates defining designated areas beyond the hospital morgue if there is a surplus of deceased patients. Many patients were brought in from the field by EMS or even private vehicles who were deceased. The catastrophic events of October 7 resulted in a massive influx of casualties, many with severe trauma that complicated identification and management.

Surge Capacity

Increasing staff surge capacity consists of calling in all relevant employees including physicians, nurses, and ancillary services. Staff surge capacity was successful as physicians, nurses, and ancillary staff quickly reported to their hospitals. In terms of workspace, one hospital was able to quickly set up trauma bays in buildings outside the main ED (14). Lists of required equipment are standardized by the NCMCI. Representatives of the committee periodically check the supplies. As per protocol, all hospitals must pre-designate appropriate protected areas for an MCI. These spaces may be different from those used daily and are required to have appropriate signage. Many institutions increase their ambulatory ED capacity using clinic space in protected areas. There may also be different areas designated for an MCI versus a mega MCI, or when the

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hospital is under missile attack. These areas are officially approved in advance by the NCMCI.

DISCUSSION

Activation of an MCI Protocol

The method of activation of the staff for an MCI is not standardized. Most activate via SMS while many hospital teams additionally send WhatsApp messages Following the Beirut Port Blast in 2020, it was recommended to use WhatsApp messaging to activate an MCI and remove previously required lengthy approval to prevent delays. This protocol allowed the activation plan to be in effect 17 minutes after the Beirut explosion occurred (15). The critique is that especially during the night when the staff is asleep, this method may be ineffective as WhatsApp messages can be missed. Many hospitals in Israel are currently moving to a proprietary communication system that simultaneously sends SMS and voice activation. This voice activation can be adjusted to repeat itself a set number of times until the receiver acknowledges the message. The advantage of continuous dialing is that the service calls at predesignated intervals and times until the responder answers, which is critical during weekends and nights.

October 7 underscored the severe challenges associated with the administration of inpatients while under direct attack from missiles. Hospitals that were under missile attacks from Gaza needed to provide care in protected areas both for the wounded as well as those patients who were already admitted. The distance from Gaza to hospitals in southern and central Israel ranges from 20 km to 75 km, allowing people 30 - 90 seconds to run into designated shelters when the air raid siren is activated (16). While the majority

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of hospitals have areas that are built as bomb shelters and most EDs are in areas protected from missiles, other patient spaces are unprotected. During this attack, relocating patients from vulnerable areas of hospitals, such as wards and intensive care units, to safer, underground facilities was a paramount priority. This process required meticulous coordination to ensure that patients, particularly those who were bedridden or critically ill, were transferred swiftly and safely. This was challenging and required additional staff resources. Despite the pre-established protocols and the use of underground facilities, hospitals encountered significant difficulties in evacuating patients due to the simultaneous need to protect these individuals from ongoing missile attacks. The successful evacuation was largely attributed to the pre-event drills and the presence of trained volunteers and nursing students, which facilitated rapid and efficient transfers. However, the need for a more robust, adaptable evacuation strategy that can handle the unpredictability of simultaneous threats and patient needs was highlighted as a critical area for future improvement. Another important lesson was the need to have a functional multi-use area so that when not being used for emergencies it can serve other purposes. This is more feasible financially and allows for constant upkeep of these areas.

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Triage

There is much literature on prehospital triage for an MCI although the evidence is limited (17). One simulated study compared the Canadian Triage and Acuity Scale to Simple Triage and Rapid Treatment (START) and found that the START method was significantly faster (18). It should be noted that those performing the triage in this study

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were experienced nurses. While in Israel, daily, triage is performed by nurses, by protocol during an MCI, triage can also be performed by a paramedic or physician. One hospital had an issue where a heliport located on the roof of the hospital brought patients directly to the trauma bays. In the chaos of October 7, some patients weren't adequately registered or triaged. On a daily basis, this hadn't been an issue as the hospital always received advanced notice of helicopter transports.

Patient Care

According to the Israel National Trauma Registry which includes only patients who arrived in the ED, over 90% of the injuries were penetrating and 19% were caused by explosives. Of the 630 patients who were hospitalized on October 7 and 8 from the areas that Hamas infiltrated, 44% were civilians with similar injury patterns to the soldiers (19). Due to the overwhelming number of patients, many hospitals reported that the trauma bays were full, and even unstable patients were seen in other areas of the ED. For example, Soroka Medical Center received over 600 injured within the first 24 hours, with the peak rate at 83 injured per hour. Of the injured, 102 (15.2%) were classified as major trauma (20,21).

Overall, the EDs practiced unidirectional flow and the patients who went on to imaging did not return. Unidirectional flow has been identified as a preferred practice in MCIs, including in non-conflict settings; the U.S. Department of Health and Human Services recommends that patients do not return to the ED from the CT as this causes clogging and unnecessary occupation of space in the ED (22).

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However, because of the overwhelming number of patients, care was sometimes compromised. For example, one hospital reported that one of the first wounded that was received was a 26-year-old female police officer who arrived with gunshot wounds to the face and arm. She had a bullet lodged in her right maxillary sinus next to the orbit. She signed an agreement for surgery, but before going down to the operating room, the wounded began to pour in and the MCI was announced. She went from being the most urgent to the least, and was operated on over 72 hours later. In addition, some patients who were intubated and kept in a holding area were not sedated adequately because that zone area was not supplied with medication nor staffed by a nurse (only a ED physician).

Secondary Transfers

The secondary transfer of patients from frontline hospitals to tertiary care centers emerged as a significant challenge during the October 7 attacks. As hospitals near the conflict zones reached their capacity quickly, the necessity for secondary transfers became apparent to provide specialized care for critically injured patients or for those for whom it was anticipated that there would be no room to operate on them in the near future. The transfers were managed by the national control room jointly staffed by members of the MOH and HFC. This transfer process was complicated by the logistics of moving patients to safer facilities. MDA played a crucial role in coordinating these transfers, but the hostile environment posed risks to both patients and EMS personnel. On October 7, MDA conducted 64 secondary transfers by ambulance from the two hospitals closest to Gaza (23). Other patients underwent secondary transfer by other ambulance services or by army helicopter. The IDF and other ambulance services secondarily transferred dozens more.

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To mitigate the issues, it became clear that a national mechanism for managing secondary transfers should be established, incorporating real-time tracking and communication systems to ensure the timely and safe relocation of patients. Additionally, hospitals must develop contingency plans that include alternative routes and methods of transportation, such as helicopters, to facilitate rapid transfers under adverse conditions. This experience has underscored the need for improved coordination and flexibility in managing secondary transfers during an MCI, particularly when faced with ongoing threats.

Deceased Patients

Hospital facilities were rapidly overwhelmed, revealing critical gaps such as insufficient morgue space, inadequate body cooling, and limited pathology support. These deficiencies created significant challenges in handling and preserving the deceased, raising concerns about maintaining dignity and proper care.

Despite the overwhelming number of casualties, there is no evidence that ethical standards were compromised or that patients declared deceased were incorrectly assessed as having no pulse. This adherence to proper triage practices, even under extreme pressure, suggests that established protocols were followed.

To address these challenges, future strategies should include developing mobile mortuary units with advanced cooling systems and forensic capabilities. Forming partnerships with local and international organizations to provide temporary morgue facilities can help manage sudden surges in casualties. Additionally, implementing cutting-edge identification technologies, such as biometric systems, can improve the accuracy and efficiency of identifying victims. Preparing for such emergencies through simulation

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drills and innovative resource planning is essential for enhancing future crisis responses (24).

Surge Capacity

Surge capacity in the disaster literature refers to "staff," "stuff," "space," and "system" (25,26,27,28). Staff surge capacity was successful as physicians, nurses, and ancillary staff quickly reported to their hospitals, including those under bombardment. Ashkelon, the location of the Barzilai Medical Center was Ashkelon was hit by 160 rockets on October 7 including, 30 within a kilometer of the hospital, yet 80% of the entire hospital staff arrived to care for the injured.

Space was created initially by clearing the ED. Any patients who can be admitted were sent upstairs even in mid-workup. This is a drill that is practiced annually in EDs throughout Israel and was successful in all but one department. The second part of clearing the ED- sending patients home, was limited in most departments due to the ongoing missile attacks. Some hospitals expanded their treatment areas based on preplanned protocols. The Soroka Medical Center converted an area in the ED generally used for orthopedic and minor procedures, into a space to care for the critically ill. Many of the spaces in this area already have monitors in preparation for an MCI. In addition, they used the same day surgery site as a holding area for those awaiting discharge or secondary transfer. Although the literature discusses using nonclinical areas such as waiting rooms for patient care, many hospitals such as Soroka chose to essentially readjust their ED for more critical patients (29,30)

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Despite repeated annual large-scale drills, one of the major challenges that arose from the October 7 attacks was the large number of patients seen at the hospitals located close to the event. This surge in patient intake generated overload in the hospitals, creating potential treatment delays for those less critically injured. The lessons included sending directly from the field non-critical patients to more distant hospitals and increasing the number of secondary transfers.

Limitations:

There are several limitations to this study. The goal of this paper is to describe and analyze the implementation of Israel's robust system of ED preparedness for an MCI. While all of the physician authors are emergency medicine specialists who work clinically as well as take an active administrative role in disaster preparedness, whether on a hospital or national level, there are other physicians in the country who are also involved in hospital disaster preparedness who were not consulted. They may have also provided important lessons that were learned. Another limitation is data that was presented for numbers of victims seen at 19 different EDs does not include severity scores or outcomes. Although interesting and important, this data is not yet available on a national level, and the scope of this paper is on lessons learned from the events in relation to Israel's national disaster preparedness program. An important additional study would be to analyze the trauma severity and outcomes.

Future Directions

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The MOH is now developing a national computerized Homefront Command and Control platform that will function across ministries. This includes the MOH, the HFC, hospitals, and any governmental office. The platform includes maps that can identify incoming threats and the ability to send assignments via SMS. It allows chat and “carousels” to enter into local platforms while on the National Command and Control System. The platform can work on stationary computers, laptops, or cell phones.

Conclusion

On October 7 the effectiveness of the NCMCI protocols was rigorously tested, revealing both successes and critical areas for enhancement. The committee's established procedures for emergency response, resource allocation, and inter-agency coordination were initially effective but faced challenges due to delays in real-time data sharing and communication bottlenecks. One particular area of improvement included the need for more secondary transfer of patients. However, the October 7 events demonstrated that despite this rigorous training framework, there remain significant opportunities to refine protocols and improve real-time coordination to enhance overall response efficiency in future crises.

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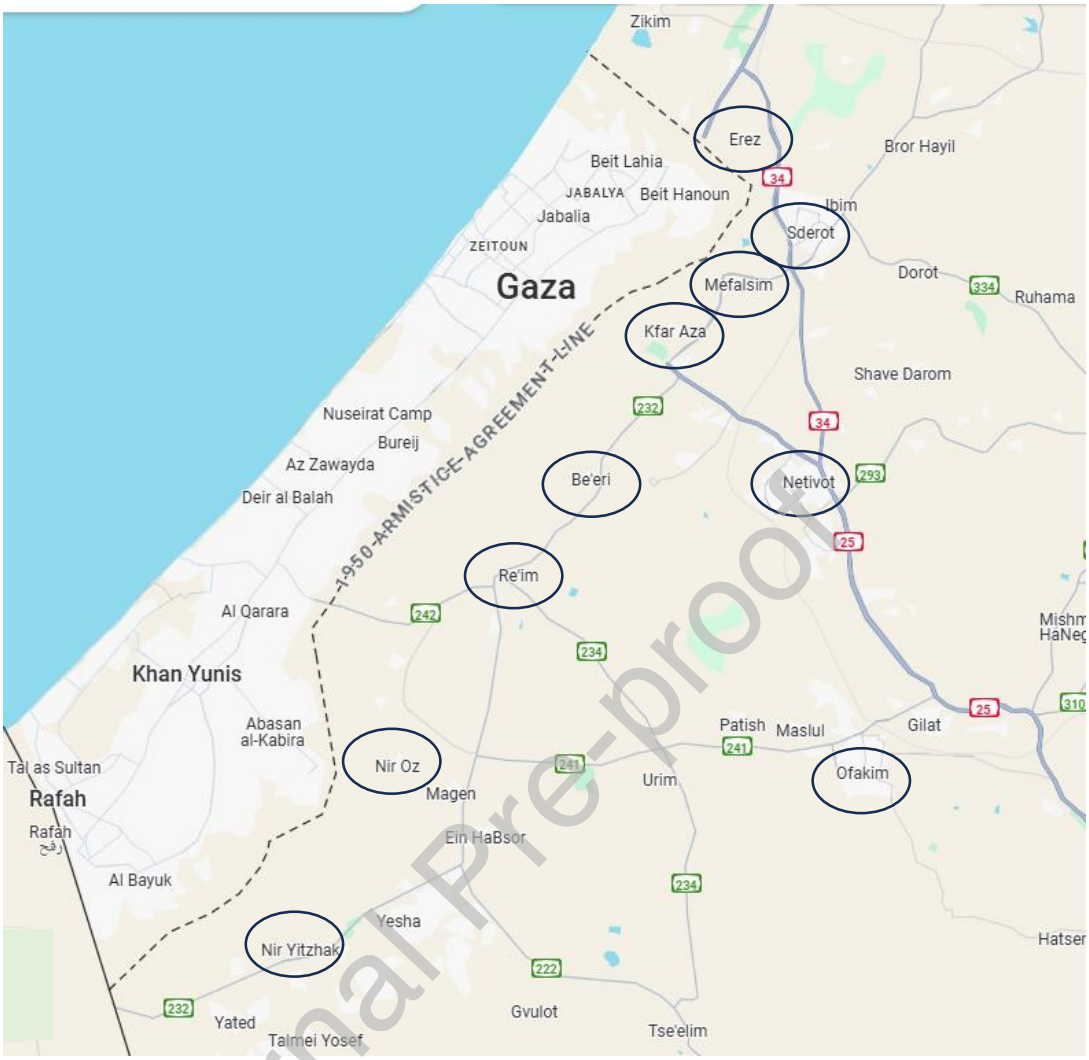

Figure 1: Location of casualties in Gaza Envelope communities on October 7, 2023 (Based on Google Maps)

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Figure 2: Helicopter landing with casualties at the Soroka Medical Center in Be'er Sheva on October 7, 2023

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Table 1: Locations of casualties during the October 7, 2023 Mega MCI

Location of fatalities	**Location type**	**Total population**
Alumim	Kibbutz	531
Be'eri	Kibbutz	1,071
Ein HaShlosha	Kibbutz	353
Holit	Kibbutz	210
Kfar Aza	Kibbutz	787
Kissufim	Kibbutz	294
Nahal Oz	Military Base	162
Nahal Oz	Kibbutz	479
Netiv HaAsara	Moshav	1278
Nir Am	Kibbutz	726
Nir Oz	Kibbutz	380
Nir Oz and Nirim (area between)	Music Festival	~100
Nirim	Kibbutz	416
Nir Yitzhak	Kibbutz	633
Ofakim	City	35,506
Re'im- Nova	Music Festival	~350
Re'im	Military Base/ Kibbutz	422
Sderot	City	33,002
Sufa	Kibbutz	233
Zikim	Military Base	141
Zikim	Kibbutz	918

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Table 2: Number of Casualties Arriving at Emergency Departments in Israel on October 7, 2023. Distances are general distances from Gaza and not from a specific area of the MCI.

	Hospital/Medical Center	**City**	**Number of casualties in ED (MOH)**	**Distance from Gaza**
1.	Soroka Medical Center	Be'er Sheva	624	41.6 km
2.	Barzilai Medical Center	Ashkelon	323	19.9 km
3.	Sheba Medical Center (Tel Hashomer)	Ramat Gan	110	70.2 km
4.	Kaplan Medical Center	Rehovot	98	52.7 km
5.	Shamir Medical Center (Assaf Harofeh)	Be'er Ya'akov	87	62.5 km
6.	Samson Assuta Ashdod University Hospital	Ashdod	87	35.7 km
7	Tel Aviv Sourasky Medical Center (Ichilov)	Tel Aviv	66	71.2 km
8.	Wolfson Medical Center	Holon	49	65.6 km
9.	Hadassah University Hospital- Ein Kerem	Jerusalem	43	70.9 km
10.	Meir Medical Center	Kfar Saba	43	85.7 km
11.	Rabin Medical Center- Beilinson Hospital	Petah Tikva	33	75.6 km
12.	Shaare Zedek Medical Center	Jerusalem	16	74.4 km
13.	Laniado Hospital	Netanya	16	101 km
14.	Hillel Yaffe Medical Center	Hadera	15	113 km
15.	Hadassah University Hospital- Mount Scopus	Jerusalem	7	80.4 km
16.	Carmel Medical Center	Haifa	6	151 km
17.	Rambam Health Care Campus	Haifa	5	156 km
18.	Rabin Medical Center- HaSharon Hospital	Petah Tikva	2	75.2 km
19.	Baruch Padeh Medical Center	Poriya	2	172 km
	Total		1632	

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Declaration of Interest Statement

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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