Physical symptoms that are frequently unexplained among survivors of the Enschede fireworks disaster

This longitudinal study had been performed within the framework of the Enschede Firework Disaster Health Monitoring Project (GGVE –http://www.ggve.nl) and for the Centre for Health Impact Assessment of Disasters (CGOR – http://www.rivm/cgor). Several research institutes co-operated in this project: The National Institute for Public Health and the Environment (RIVM), The Institute for Psychotrauma (IvP), The Netherlands Institute for Health Services Research (NIVEL), and the department of Youth Health Care of the Regional Health Authority (GGD Regio Twente)

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Physical symptoms that are frequently unexplained among
survivors of the Enschede fireworks disaster
Thesis Utrecht University
ISBN: 978-90-393-4490-3

Cover: M. Brouwer
Lay-out: H. Otter
Printed by: Ridderprint, Ridderkerk, the Netherlands

Physical symptoms that are frequently unexplained among survivors of the Enschede fireworks disaster

Fysieke, veelal onverklaarde klachten bij getroffenen van de vuurwerkramp in Enschede
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht
op gezag van de rector magnificus, prof.dr. W.H. Gispen,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen op donderdag 5 april 2007
des middags te 12.45 uur

door

Bellis van den Berg

geboren op 18 december 1977, te Willeskop

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Dr. ir. E. Lebret
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The PhD project described in this thesis was funded by the Ministry of Health, Welfare, and Sport (VWS) in the Netherlands.

Enschede huilt
Een buurt, die wel veel zorgen had,
maar die ook vol verhalen zat,
vol humor en gezelligheid,
die buurt zijn we voor eeuwig kwijt.

Daar waar het vol van kinderen was,
verschillend van geloof en ras,
maar in hun spel gelijkgezind-
loopt nu geen enkel kind.

In de oorlog stond de stad in brand
op Pathmos, Zwik en Hoogeland:
meer dan een halve eeuw nadien
kun je daarvan nog sporen zien.

Nu is, in de heerlijke maand mei,
bij vogelzang, zo vrij en blij,
de stad opnieuw iets aangedaan
dat nooit en nooit voorbij zal gaan.

Arm Enschede, verberg je in
de armen van je koningin
en huil, want daar is reden voor
en huil dan maar aan één stuk door.

Willem Wilmink
17 mei 2000

Contents

		Page
Chapter 1	Introduction	1
Chapter 2	Medically unexplained physical symptoms in the aftermath of disasters.	13
Chapter 3	Symptoms and related functioning in a traumatized community.	43
Chapter 4	Are physical symptoms among survivors of a disaster presented to the general practitioner? A comparison between self-reports and GP data.	59
Chapter 5	Risk factors for physical symptoms after a disaster: a longitudinal study.	75
Chapter 6	Risk factors for medically unexplained symptoms among disaster survivors: a 6-year longitudinal study in general practice.	93
Chapter 7	Selective attrition and bias in a longitudinal health survey among survivors of a disaster.	109
Chapter 8	General discussion	131
Appendix		149
Summary & Samenvatting		153
Dankwoord		163
About the author		165

CHAPTER 1

General introduction

Disasters and their health consequences

Each year, disasters affect large numbers of people throughout the world. In the recent years the number of disasters has increased.[1] Disasters can be defined as acute, collectively experienced traumatic events with a sudden onset. They can be divided into natural disasters such as floods, earthquakes, volcanic eruptions, and hurricanes and man-made disasters such as transportation (e.g. aircraft disasters) and technological disasters (e.g. Chernobyl disaster). What these different events have in common is the potential to affect a large group of people and to engender different types of stressors such as threat to one's life, injury, exposure to death, bereavement, profound loss, and social and community disruption.[2]

Since the Second World War several disasters have occurred in the Netherlands. In 1946, an airplane crashed in a Dutch high school (HBS) in the city of Apeldoorn and killed 23 students. In 1953, a flood occurred in the province Zeeland, which was the largest natural disaster in the Dutch history (1835 victims). Several other transportation disasters occurred, such as a train accident in Harmelen (1962, 93 victims), a collision between a KLM aircraft and a PanAm aircraft on Tenerife, Spain (1977, 264 Dutch victims), and an aircraft disaster in Faro, Portugal (1992, 56 victims). In the longer term, these disasters received relatively little attention from the public or the media. Also, after these disasters no studies, or only small-scale studies, into the health effects of the disasters were performed. This situation was completely different following an airplane crash in the Bijlmermeer in Amsterdam (1992, 43 victims).[3-5] After this airplane crash, survivors reported health problems which they attributed to the disaster and the media gave much attention to conspiracy theories about possible exposure to toxic substances.[3] The public and political unrest resulted in studies into the health effects of the disaster and a parliamentary enquiry in 1998.[4, 5] Factors that may have contributed to this increased attention after the Bijlmer disaster are the emancipation of citizens, changing ideas about grief and responsibilities and a higher level of media focus in general.[6] Studies into the health effects were also performed after the more recent Enschede fireworks disaster (2000, 23 victims) and the café fire in Volendam (2001, 14 victims).[7, 8]

In the past decades, many studies have examined health problems among survivors of different kinds of disasters. The majority of studies have focused on specific psychological problems such as post-traumatic stress disorder (PTSD), depression and anxiety, and have found a positive relationship between disasters and psychopathology.[2, 9, 10] Despite the number of studies, it is difficult to draw general conclusions about the prevalence of mental health problems among survivors since studies were performed after different types of disasters using a variety of designs, time frames, assessment tools and sampling methods.[11] Nevertheless, attempts have been made to gain insight into the prevalence rates of psychopathology among survivors of

disasters. Galea et al. described that the prevalence of PTSD in the first year after man-made disasters is between 25% and 75%.[11] In addition, Norris et al. concluded in their review of 160 studies following mass violence and natural and technological disasters that about 51% of the survivors in those studies showed moderate impairment, 21% severe and 18% very severe impairment, indicative of clinically significant distress. They also concluded that, although the peak of symptoms among survivors will be within the first year after the disaster, the effects of disasters may last for several years.[12]

Besides mental health effects, disasters may have physical health effects as well. Studies that have examined the physical health effects of natural disasters focused predominantly on injuries[13-15] and infectious diseases.[13, 14] In addition, several studies have examined the health effects of exposure to toxic substances after technological disasters such as in Seveso (Italy, 1976),[16] Bhopal (India, 1984),[17] and Chernobyl (Ukrain, 1986).[18]

Health outcomes of disasters can also be the result of the process of attribution, which is often an important problem in the aftermath of man-made disasters.[19] Survivors are likely to attribute their health problems to exposure to toxic substances especially when there is suspicion about the involvement of toxic substances. Attribution may also become a problem in the case of incorrect information about exposure, mistrust of the government or an unresolved question of guilt. In addition, the media can play an important role in the way the disaster-related health risks are perceived by the public.[3] A good example of this phenomenon is the aftermath of the airplane crash in the Bijlmermeer, after which many affected residents and rescue workers reported symptoms such as fatigue, headache and dyspnea.[4, 5, 20] The media strongly reinforced the idea that the health problems were the result of exposure to toxic substances that were released by cargo of the airplane.[3, 4] There was, however, no scientific evidence for the relationship between symptoms and the contents of the cargo.[5, 20] In a study that examined symptoms attributed to the airplane crash, it was shown that there was a large discrepancy between patients and general practitioners (GP) in relating symptoms to the disaster; only 6% of the symptoms that survivors attributed to the disaster were also related to the disaster according to the GP. In addition, the majority of the reported symptoms (57%-93%) could not be explained by a medical disorder and was classified as medically unexplained symptoms (MUS). This study also found that many health complaints (25%) had already been reported to the GP before the disaster took place.[5] These symptoms may have been aggravated by the disaster, or survivors may have begun attributing these symptoms to the disaster.

Because data on the pre-disaster health status are seldom available, it is often very difficult to know whether symptoms are the result of exposure to substances or whether symptoms are the result of distress or attribution to suspected exposure.

Epidemiological studies that include pre-disaster health data and make comparisons possible with populations not exposed to the suspected toxic stressor are very useful in assessing the estimated burden of distress and disease specifically attributable to the exposure.[19]

Medically Unexplained Symptoms

In the last decade, there has been increased awareness that traumatic events can be related to physical symptoms that often remain medically unexplained.[21, 22] The first Gulf War, in particular, has contributed to this awareness.[22] After this war, many veterans complained about symptoms such as fatigue, aching muscles, headache, and difficulty concentrating, which they attributed to exposure to chemical and biological warfare and vaccinations against biological weapons.[23] A large number of epidemiological studies have confirmed an increase of unexplained physical symptoms among military personnel deployed in the Gulf, a phenomenon known as the "Gulf War syndrome".[24]

Medically unexplained symptoms (MUS) and symptom syndromes similar to the Gulf War syndrome are also common in the general population. Studies have shown that physical symptoms such as headache, stomachache and pain in joints and muscles account for approximately 40% of all primary care visits. An estimated 50% to 75% of these symptoms cannot be explained by a medical disorder and are labeled MUS.[25, 26] MUS are important not only because they are very common but also because of the functional impairment, high levels of health care utilization and psychological problems that accompany them.[27-29]

To diagnose patients with a high level of MUS, the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) has defined the Somatization Disorder,[30] but many other labels have been used to describe these symptoms (table 1). The term psychosomatic illness is most often used by the public and is seen as synonymous with the symptoms being 'all in the mind'. Today, terms that pay less attention to the etiological mechanisms are used to describe these symptoms: medically unexplained symptoms; subjective health complaints; and functional symptoms are examples. Multiple MUS and related disability are described as functional somatic syndromes such as chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia. These functional somatic syndromes have a high degree of overlap and common characteristics, and it is unclear whether these syndromes are separate entities or whether they represent one syndrome.[31-34]

Instead of one single cause, it is believed that different factors play a role in the development and course of MUS and functional somatic syndromes. The many biological, psychological and social factors that can affect symptoms are divided into predisposing, precipitating and perpetuating factors, according to their role in the

development and maintenance of the symptoms.[35, 36] Predisposing factors are characteristics of the individual that make him or her more vulnerable for developing symptoms such as childhood adversity or low levels of social support. Precipitating factors are those elements in the individual's life that initiate or trigger the onset or exaggeration of symptoms, such as medical disease or stressful life events. Perpetuating factors are feature of the individual's life that maintain the symptoms.[35] Since the etiology of the symptoms is unknown, treatment of the symptoms and syndromes focuses on management of the symptoms rather than on the cause. Cognitive behavioral therapy (CBT) has shown to be effective in treating patients with MUS.[36, 37] These interventions help patients cope with symptoms by helping them re-examine their health beliefs and expectations and explore the effects of the illness role and of distress on their symptoms.

Table 1: Labels for symptoms that cannot be explained by a medical disorder*

Labels for symptoms	Labels for multiple symptoms
Psychosomatic symptoms	DSM-IV: Somatization disorder
Medically unexplained symptoms (MUS)	DSM-IV: Somatoform pain disorder
Medically unexplained physical symptoms (MUPS)	DSM-IV: Undifferentiated somatoform disorder
Unexplained physical symptoms (UPS)	Abridged somatization disorder
Functional (somatic) symptoms	Multiple symptom syndrome
Unexplained somatic complaints	Physical symptom disorder
Subjective health complaints	Functional somatic syndromes:
Multiple idiopathic physical symptoms (MIPS)	Chronic fatigue syndrome (CFS)
Non-specific physical symptoms	Irritable bowel syndrome (IBS)
Idiopathic physical symptoms	Chronic pelvic pain
	Fibromyalgia
	Multiple chemical sensitivity
	Gulf War syndrome
	Sick building syndrome

* Not exhaustive

Although it is now recognized that traumatic events might result in elevated levels of MUS, these symptoms have seldom been studied after disasters. The majority of studies after disasters have examined mental health problems; especially after the inclusion of PTSD in the DSM-III in 1980, studies have focused on the prevalence and risk factors for PTSD.[38] To date, most studies that have examined MUS after collective traumatic events were only performed once people had started to report symptoms and when media hypes and conspiracy theories had developed, such as happened after the

Gulf War and after the airplane crash in Amsterdam.[3-5, 20] Since these studies were started too late to allow collection of crucial information immediately following the disaster, little is known about the prevalence and course of MUS among survivors of disasters. In addition, little is known about the risk factors for MUS after disasters.

Health consequences of disasters are typically measured by means of questionnaires, which may be one of the difficulties of studying MUS among survivors of disasters. Questionnaires cannot exclude medical disorders; only examination of a physician can rule out medical etiology. For that reason, some authors have argued that MUS cannot be measured by means of questionnaires.[39] To date, the similarities between MUS and self-reported physical symptoms have not been examined and it is not known whether symptoms that are similar to MUS can be measured by means of questionnaires.

Aim of this thesis

In this thesis symptoms are studied that are frequently unexplained among survivors of disasters in general and of the Enschede fireworks disaster in particular.
The main questions are:

1. What is the prevalence of symptoms among survivors?
2. What are risk factors for these symptoms among survivors?
3. Do self-reported symptoms show similarities with medically unexplained symptoms that are presented to the GP?

See box 1 for more information about the Enschede fireworks disaster.

Two data collection methods were used to study symptoms among the survivors of the fireworks disaster: a three-wave longitudinal health survey using self-administered questionnaires, and an ongoing surveillance program in which health problems were registered by GPs in the electronic medical records (EMRs) of survivors. At wave 1 of the health survey, three weeks post-disaster, symptoms were measured using a 13-item symptom scale. At waves 2 and 3 (18 months and nearly four years post-disaster) this scale was expanded with eight symptoms. The health problems presented to the GP were registered according to the International Classification of Primary Care (ICPC) which, for every contact, documents the patient's symptoms, examination findings, diagnosis and interventions.[40] To answer the research questions a cluster was constructed of symptoms that were likely to remain medically unexplained, such as fatigue, abdominal pain, headache, nausea, back pain, and coughing. Table 2 shows the datasets that were used to address the research questions of the different chapters.

Box 1: The Enschede fireworks disaster

On May 13 2000, a fireworks depot exploded in a residential area in the city of Enschede. The explosions and subsequent fire destroyed the surrounding residential area of some 40 hectares. As a result of the explosions, 23 persons of whom four firefighters were killed, and over 900 people were injured. Approximately 1200 people were forced to relocate for a long period because their houses were destroyed or severely damaged. Some 8000 emergency workers were involved into the immediate aid to survivors, evacuation and reconstruction work.

The Dutch government declared the Enschede fireworks disaster a national disaster and several actions were taken: various environmental measures were conducted immediately after the disaster, an information and advice centre was established to supply information to survivors and to coordinate their needs and the Enschede Firework Disaster Health Monitoring Project (GGVE) was started.

The GGVE consisted of a longitudinal health survey and surveillance of the GP records of survivors. The main objective was to acquire information for healthcare workers and policy makers to match interventions to the problems of the survivors. In addition to these policy- and care-directed goals, the project was also aimed to provide new scientific knowledge concerning the clinical course of post-disaster health problems.[7]

Three weeks after the disaster, blood and urine samples of survivors were taken to examine possible exposure to toxic substances.[41] A health survey was performed three weeks (wave 1), 18 months (wave 2) and 45 months (wave 3, nearly four years) after the disaster. A control group was included at waves 2 and 3. In addition to the longitudinal health survey, the electronic medical records (EMRs) of general practitioners were used to study changes in health problems of the survivors. In the Netherlands, every citizen is required to be on the list of one GP, who acts as a gatekeeper to secondary care. For this purpose, all GPs in the city of Enschede were invited to participate in the surveillance program. Data on health problems were extracted from the EMRs of survivors from one year prior to the disaster (May 13, 1999) until five years post-disaster (May 13, 2005).[42]

Table 2: Overview of datasets that are used to address the research questions of the different chapters

Chapter	Longitudinal health survey Survivors	Longitudinal health survey Controls	Surveillance program Electronic Medical Records (EMRs)
Chapter 2 *			
Chapter 3	Waves 2 and 3	Waves 2 and 3	May 13, 2000 until May 13, 2002
Chapter 4	Waves 1 and 2		
Chapter 5	Waves 1, 2 and 3	Waves 2 and 3	May 13, 1999 until May 13, 2004
Chapter 6	Wave 1		
Chapter 7	Waves 1, 2 and 3		

*Not applicable, review of the literature

Outline of this thesis

Chapter 2 starts with an overview of studies, published between January 1983 and December 2003, that reported about physical symptoms or MUS among survivors of disasters. The two questions that are addressed in this chapter are: what is the prevalence rate of physical symptoms reported by survivors of disasters? And, since not all survivors develop these symptoms: what are risk factors for these symptoms after disasters?

In *Chapter 3* the prevalence and course of the self-reported symptoms among survivors of the fireworks disaster are examined. Whether the self-reported symptoms display features similar to those of MUS in the general population (such as functional impairment and psychological problems) are also examined.

Chapter 4 also focuses on the question whether self-reported symptoms show similarities with MUS. It examines whether survivors present their self-reported symptoms to the GP. Furthermore, the proportion of symptoms that are medically unexplained after clinical judgment is described.

Chapter 5 addresses risk factors of self-reported physical symptoms among survivors. Risk factors are divided into predisposing factors, precipitating factors or disaster-related factors, and perpetuating factors. This chapter also examines whether risk factors are similar between survivors and non-traumatized controls.

In *Chapter 6* the course of MUS presented to the GP is evaluated from one year prior to the disaster until four years after the disaster. In addition, risk factors for MUS presented to the GP are examined in this chapter.

Chapter 7 examines selective response at waves 2 and 3 of the longitudinal health survey. Whether possible selective response had biased the prevalence estimates of the health problems among survivors is also studied.

Chapter 8 provides a general discussion of the main findings and examines methodological considerations. In addition, the implications of the findings and recommendations for future studies are described.

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CHAPTER 2

Medically unexplained physical symptoms in the aftermath of disasters

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Published in: Epidemiologic Reviews 2005;27:92-106.

Introduction

Many studies have examined the health problems among survivors of disasters, showing that the most frequently reported symptoms after disasters are mental health problems, such as posttraumatic stress symptoms, depression, and anxiety.[1,2]

In the last decade, the Netherlands was struck by a few national disasters. On October 4, 1992, an El Al Boeing 747 airplane crashed into two apartment buildings in an Amsterdam suburb. Six years after the airplane crash, a study of the health effects of the crash was conducted. This study showed that, in addition to mental health problems, physical symptoms were very prevalent among the survivors of the plane crash.[3, 4] On May 13, 2000, a fireworks depot exploded in a residential area of the city of Enschede. The explosions and subsequent fire killed 22 people and injured over 900 people, and about 500 homes were severely damaged or destroyed. The Dutch government declared this a national disaster, and the Ministry of Health, Welfare, and Sports decided to launch a study into the health effects of this disaster. This study showed that a substantial proportion of those who were affected by the fireworks disaster suffered from physical symptoms, such as headache, fatigue, and pain in the stomach, chest, joints, and muscles.[5, 6] These symptoms are often labeled as medically unexplained physical symptoms (MUPS), but other labels, such as psychosomatic symptoms or functional somatic syndromes, have been given as well.[7]

Survivors of disasters may attribute these physical symptoms to (suspected) exposure to toxic substances, and this may lead to social unrest and amplification of the health problems.[8, 9] For example, after the Bijlmermeer airplane crash in Amsterdam, many survivors reported health symptoms that they attributed to possible toxic exposures, such as depleted uranium.[3] General practitioners, however, associated only a small proportion (about 20 %) of the most frequently reported symptoms with a diagnosis, and thus the majority of symptoms were unexplained.[4]

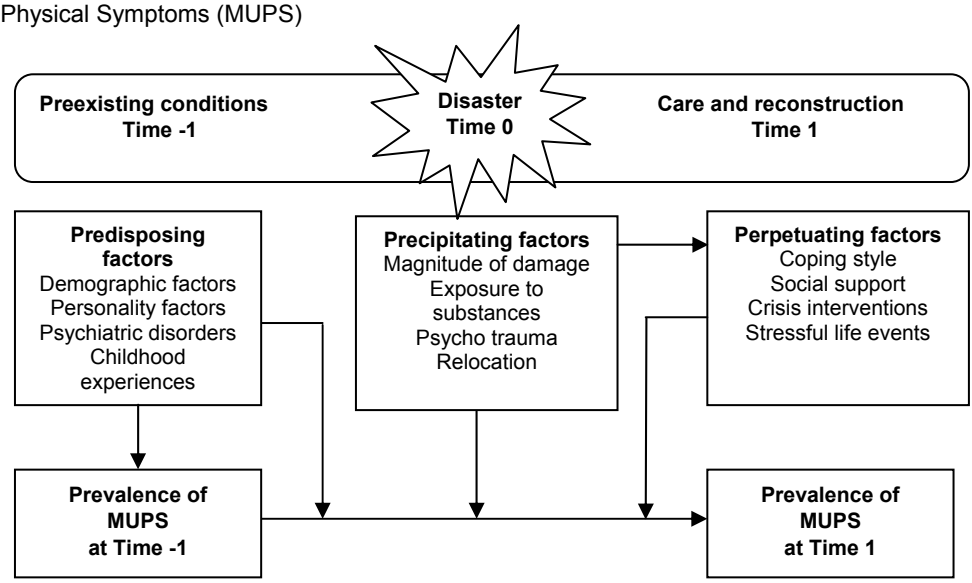
In the nontraumatized general population, MUPS are also very common, with reported prevalence rates ranging from 5 to 35 %.[10, 11] The majority of these symptoms cannot be explained by a medical diagnosis; general population studies have shown that the etiology of 30–75 % of such symptoms as headache, fatigue, and stomachache is unknown.[10, 12, 13]

After disasters, the prevalence rates of MUPS seem to increase. However, since many but not all survivors develop these symptoms, the question arises as to which factors predict who will or will not develop MUPS. Mayou and Farmer divided risk factors into three categories: predisposing, precipitating, and perpetuating factors (which we call the ‘‘3-P model’’).[14] Predisposing factors are factors that already exist before the disaster took place, such as certain demographic characteristics and personality factors. Precipitating factors are directly related to the disaster, for example, injury, relocation, fear, and loss of property. These factors might increase the proportion

of survivors that develops MUPS. After the disaster, perpetuating factors, for example, the coping style of the survivor and lack of social support, are factors that might maintain or exacerbate the symptoms (figure 1).

Since MUPS are associated with impaired emotional and physical functioning,[15, 16] it is useful to identify risk factors that clinicians can use for early screening of MUPS after disasters. More insight into the prevalence rates of and risk factors for MUPS may help clinicians and policy makers to predict symptom outcomes and to optimize aftercare. To get more insight into the prevalence rate of and risk factors for MUPS after disasters, we reviewed the literature that was published in the last two decades. There are two central questions in this review: 1) What is the prevalence rate of MUPS among survivors of disasters at different points in time? and 2) which factors are associated with MUPS among survivors of disasters?

Figure 1: Predisposing, Precipitating and Perpetuating factors for Medically Unexplained Physical Symptoms (MUPS)



Methods

To answer these questions, we reviewed the literature that was published between January 1983 and December 2003. We searched the electronic databases PubMed (US National Library of Medicine, Bethesda, Maryland), PsychInfo (American

Psychological Association, Washington, DC), Embase (Elsevier B.V., Amsterdam, the Netherlands), Biosis (The Thomson Corporation, Stamford, Connecticut), Psyndex (German Institute of Medical Documentation and Information, Cologne, Germany), and SciSearch (Institute for Scientific Information, The Thomson Corporation, Stamford, Connecticut) without any language restriction. The keywords that were used in the searches are shown in table 1. We extended the search by examining the bibliographies of identified review articles and by searching private databases that were available at different research institutes in the Netherlands.

Table 1: Key search terms

Symptoms:	Medically unexplained symptom* (MUS), Medically unexplained physical symptom* (MUPS), Somatic disorder*, Psychosomatic symptom*, Psychosomatic complaint*, Somatic symptom*, Somatic complaint*, Physical symptom*, Physical complaint*, Somatization, Functional somatic symptom*, Stress disorder*, Posttraumatic stress disorder*, Signs and symptoms, Distress, Morbidity, Health, Stress AND
Disaster:	Disaster*, Life event*, Traumatic event*, environmental exposure, NOT Disaster planning AND
Design:	Cross-sectional, Prospective, Case-control, Cohort, Causality, Risk, Determinant*, Predict*

*An asterisk was placed at the and of some words to search for all terms that begin with that word

For the selection of the papers, we used four inclusion criteria: a disaster criterion, a subject criterion, a MUPS criterion, and a report criterion. A *disaster* was defined as a collective stressful experience with a sudden onset. With this definition, publications about natural disasters (e.g., hurricanes, volcanic eruptions) and man-made disasters (e.g., Three Mile Island accident, aircraft disasters) were included, while studies examining survivors of individual traumatic events, such as sexual assault and traffic accidents, were excluded. Although war situations are traumatic and stressful as well, studies about war veterans, survivors of wars, and refugees were excluded because the threat of war and the intention to harm make wartime exposure different from disaster exposure. Subjects had to be directly exposed to the disaster themselves (*subject criterion*). People with close family and personal ties to the primary victims and people whose occupations require them to respond to the disaster, such as relief workers, were excluded. Relief workers were omitted because they are mostly healthy

young men who are selected on the basis of their physical and emotional functioning. In addition, most relief workers are trained to cope with stressful situations, and therefore they may react differently from citizens. The *MUPS criterion* implied that one or more symptoms from a MUPS cluster, based on the International Classification of Primary Care as developed by one of the authors (C.J. Y.), had to be measured (table 2). These symptoms could be measured by self-constructed questionnaires or by validated scales, such as the Symptom Checklist (SCL-90).

Table 2: MUPS cluster based on International Classification of Primary Care

- Pain general/ multiple sites
- Chills
- Weakness/ tiredness general
- Feeling ill
- Fainting/ syncope
- Swelling
- Sweating problem
- Abdominal pain/ cramps general
- Abdominal pain epigastric
- Heartburn
- Rectal/ anal pain
- Perianal itching
- Abdominal pain localized other
- Flatulence/ gas/ belching
- Nausea
- Vomiting
- Diarrhea
- Constipation
- Abdominal distension
- Digestive symptoms/ complaints other digestive organs
- Eye sensation abnormal
- Tinnitus/ ringing/ buzzing ears
- Heart pain
- Pressure/ tightness of heart
- Cardiovascular pain NOS
- Palpitations/ awareness of heart
- Irregular heartbeat other
- Prominent veins
- Swollen ankles/ edema
- Neck symptoms/ complaints
- Back symptoms/ complaints
- Low back symptoms/ compl. without radiation
- Chest symptom/ complaint
- Back symptom/ complaint
- Low back symptom/ complaint
- Chest symptom/ complaint
- Flank/ axilla symptom/ complaint
- Jaw symptom/ complaint
- Shoulder symptom/ complaint
- Arm symptom/ complaint
- Elbow symptom/ complaint
- Wrist symptom/ complaint
- Hand/ finger symptom/ complaint
- Hip symptom/ complaint
- Leg/ thigh symptom/ complaint
- Knee symptom/ complaint
- Ankle symptom/ complaint
- Foot & toe symptom/ complaint
- Muscle pain
- Muscle symptom/ complaint NOS
- Joint symptoms/ complaint
- Headache
- Tension headache
- Pain face
- Restless legs
- Tingling fingers/ feet/ toes
- Disturbance smell/ taste
- Vertigo/ dizziness
- Neurological symptom/ complaint other. neurological system
- Pain respiratory system
- Shortness of breath/ dyspnoea
- Wheezing
- Breathing problem, other
- Cough
- Sneezing/ nasal congestion
- Nose symptom/ complaint other
- Sinus symptom/ complaint
- Throat symptom/ complaint
- Tonsils symptom/ complaint
- Voice symptom/ complaint
- Respiratory symptom/ complaint other respiratory system
- Pain/ tenderness of skin
- Pruritus
- Skin symptom/ complaint other
- Excessive thirst
- Excessive appetite
- Loss of appetite
- Dysuria/ painful urination
- Urinary frequency/ urgency
- Genital pain female
- Menstrual pain
- Pain in penis
- Pain in testis/ scrotum

Although a medical disorder cannot be ruled out for these symptoms, an increase at the population level of these symptoms among survivors of disasters, compared with levels that are found in the general population or a control group, may be assumed to be disaster related. In addition, studies reporting symptoms that were clearly the result of exposure to toxic substances, for example, eye irritation and respiratory symptoms after the Bhopal gas leak,[17] were excluded from this review. To examine prevalence rates of MUPS among survivors of disasters, we included different types of studies (*report criterion*). First, we included studies that reported percentages of MUPS among survivors of disasters. Second, we included studies that reported about a percentage of survivors scoring above a standardized cut-off score. Since cut-off scores are based on scores in a normative population (e.g., those with a score above the 90th percentile have a high score), a control group was not required for these studies. Third, studies were included that reported a mean score on a MUPS scale. For these studies, a control group was required to compare the mean score of survivors with that of control subjects. In addition to these studies that reported about the prevalence of MUPS, we also included studies that did not report about prevalence rates but that did report about risk factors for MUPS.

The titles and/or abstracts of the identified studies were screened by one of the authors to evaluate whether they met both the disaster criterion and the subject criterion (B. v. d. B.). When there was any doubt about the disaster criterion or the subject criterion, we asked for a full-text version of that study. In addition, we took a random sample of 50 studies that were rejected because of the disaster criterion or the subject criterion to evaluate whether they were indeed not relevant for the review. None of the rejected articles satisfied the criteria. Hard copies of publications that met the disaster criterion and the subject criterion were reviewed by two authors to evaluate whether MUPS was measured (B.v.d.B., L.G.). When there was no consensus between the two authors about the MUPS criterion, a third reviewer did an additional evaluation.

Results

The database searches yielded 3,290 citations: 1,474 from PubMed and 1,816 from the other databases that were searched (figure 2). The citations from PubMed were complete with title and abstract; for the citations from the other databases, only a title was available. In total, 2,817 articles were excluded because they did not meet the disaster criterion, and 52 articles were excluded because of the subject criterion. The search for citations in the bibliographies of identified review articles yielded an additional 26 studies, and 22 eligible articles were found in private databases. We evaluated 469 hard copies with regard to the MUPS criterion (figure 2), of which 32 studies were also evaluated by a third reviewer. Most studies reported only psychological problems among survivors of disasters, such as posttraumatic stress

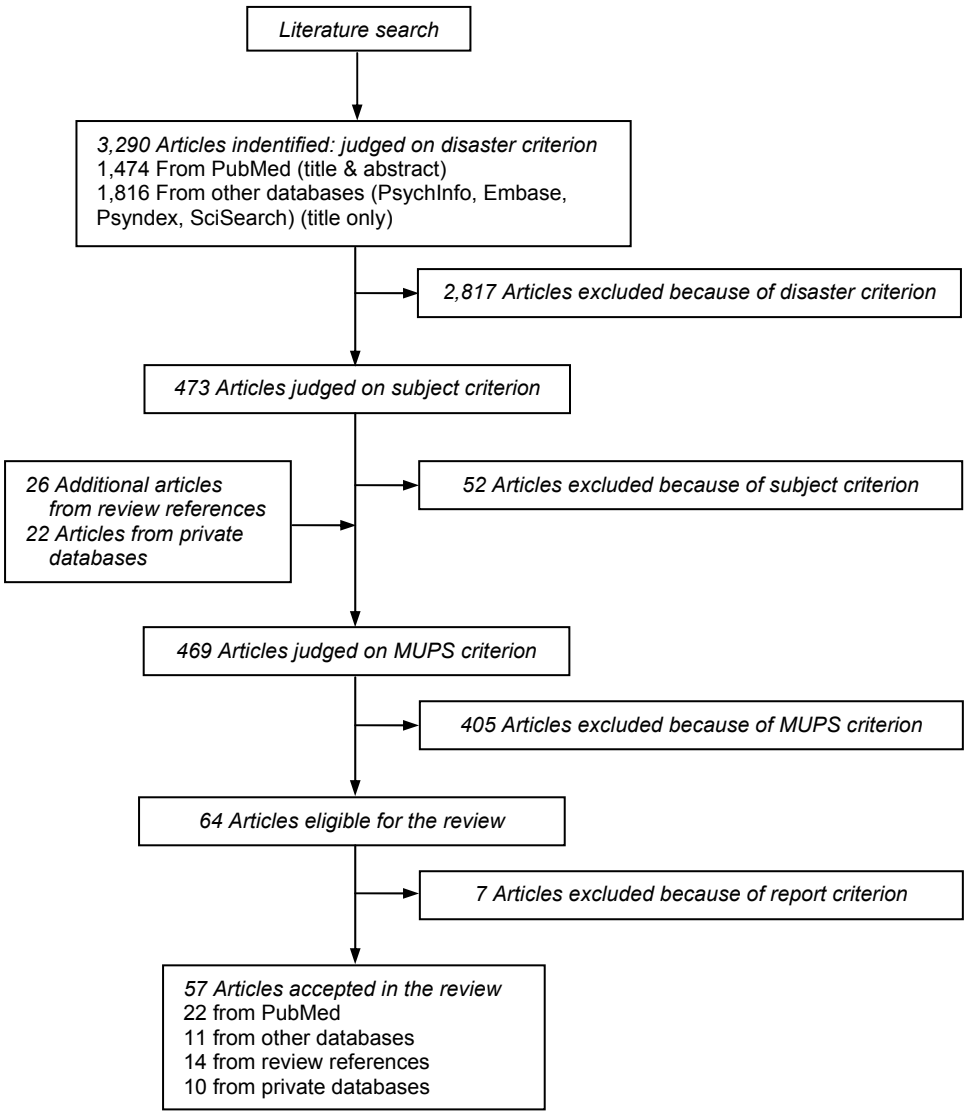
symptoms or anxiety. Sixty-four studies were eligible for the review, of which seven were excluded because of the report criterion. Finally, we accepted 57 studies for this review: 33 cross-sectional studies mostly with a control group and 24 longitudinal studies of which most were retrospective, with four of the latter having a control group. Thirty-seven studies reported about MUPS among survivors of natural disasters, and 20 studies reported about those affected by man-made disasters (table 3). Some study populations were reported in different publications (18–29), but we considered these studies as one study; as a consequence, risk factors examined in these studies will be reported once as well.

Response rates were given in 33 studies, ranging from 12 % to 100 %. In the 57 relevant studies, 21 different questionnaires were used to measure MUPS. The SCL-90 somatization subscale was used most often (16 studies). It measured headache, dizziness, pain in the chest or heart, pain in the lower back, nausea or upset stomach, soreness of muscles, difficulty breathing, hot or cold spells, numb or tingling feelings, lump in the throat, feeling bodily washed out, and having a heavy feeling in the arms or legs. In nine studies, MUPS was measured by self-constructed questionnaires.

What is the prevalence rate of MUPS among survivors of disasters at different points in time?

Percentages. Fifteen studies, primarily after natural disasters, examined the percentage of survivors that reported MUPS.[4, 25, 30-42] Table 3 shows for each study the range of the different symptoms that were measured. The prevalence rates of the individual symptoms that were measured are shown in figure 3. The majority of symptoms were measured 3 months after the disaster. This figure shows that there is large variation in the prevalence of different symptoms at the same measurement time, as well as in the prevalence of the same symptoms at different measurement times. For example, the prevalence rate of headache, which was measured in eight studies, varies considerably, with 36 % three months after an earthquake in Ecuador,[33] 58 % four months after a hurricane in Honduras,[36] and 18 % six years after a plane crash in the Netherlands.[4] Fatigue was measured in seven studies; 44 % of survivors in the United States,[30] and 48 % of survivors in Japan reported fatigue one week after an earthquake.[34] Five years after a volcanic eruption in Colombia, 13 % of survivors reported fatigue.[25] Some symptoms, such as eye irritation and skin problems, were rarely measured, and thus little is known about the prevalence rates of these symptoms.

Figure 2: Literature search to search for articles on Medically Unexplained Physical Symptoms (MUPS) in survivors of disasters



Mean score. Twenty-two studies compared mean scores on scales of MUPS between survivors and controls. Of these studies, 14 were performed after man-made disasters, and the SCL-90 somatization subscale was used most often to measure MUPS (11 studies). In 18 studies, survivors reported a significantly higher mean score than control subjects did,[29, 37, 42-57] with risk ratios ranging from 1.1 for the Chernobyl accident after 10 years[44] to 10.6 for the attack on the World Trade Center in New York after three months.[42] Compared with control subjects, survivors reported more MUPS both shortly after disasters and during a longer term; 11 years after the Chernobyl accident, affected mothers perceived their children as substantially more symptomatic than did mothers in the comparison group.[52] The mothers themselves were also more symptomatic than mothers in the control group (odds ratio = 2.4).[53] Three studies did not find a difference in MUPS between survivors and controls, of which two studies were performed about 1 year after a natural disaster,[58, 59] and one study was performed 14 years after the Buffalo Creek dam collapse.[60] In contrast, in one study five years after a flood, less MUPS were found among survivors compared with controls.[61]

Course over time. Although figure 3 might suggest that MUPS became less prevalent as the time after the disaster increased, some prevalence rates of MUPS were still high years after a disaster.[4] Follow-up studies show inconsistent results about the course of MUPS over time; MUPS significantly decreased between one week and four months after an earthquake,[30] and between seven months and five years after a volcanic eruption.[25] In addition, the percentage of survivors reporting MUPS after an earthquake in Japan seemed to decrease as well.[34] In contrast, after the Australian bushfires, the percentage of children with MUPS scores above a cut-off value increased between two and eight months after the disaster.[62] The prevalence of MUPS did not change among child survivors of an earthquake between one and two years after the earthquake,[32] and among adult survivors of an earthquake between three and nine months.[43] Finally, there was no change in the prevalence of MUPS between eight and ten years after the Chernobyl accident.[44]

Which factors are associated with MUPS among survivors of disasters?

In this section, we will describe factors that were associated with MUPS in the reviewed studies. Biologic markers, such as cortisol level, that cannot be measured by means of questionnaires, will not be described in this section. Most factors were examined in just one single study; in this section, we report on factors that were examined in at least two different studies, using a model with predisposing, precipitating, and perpetuating factors (the 3-P model) (table 4).

Table 3: Characteristics and findings of studies examining MUPS

First author and year of publication (reference no.)	Disaster and Country	N	Response rate* (%)	Measure †	Time since disaster				Findings			Risk factors
					Pre-disaster	< 1 month	1 month – 1 year	> 1 year	Prevalence range (%) ‡	Δ Control group§	Δ Time¶	
Anderson, 1994 (64)	Earthquake, USA	211	90	SCL-90-R		24 hour						Yes
Bland, 1996 (70)	Earthquake, Italy	772	80	SCL-90-R				7 years				Yes
Cardena, 1993 (30)	Earthquake, USA	98	20 & 90	Self-constructed		1 week	4 months		3 symptoms: Time 1: 30-44; Time 2: 13-28		- -	No
Chen, 2001 (31)	Earthquake, Taiwan	525		CHQ-12			1 month		3 symptoms: 51-53			No
Karanci, 1995 (58)	Earthquake, Turkey	461/ 129#		SCL-40				1⅓ years		ND		Yes
Kitayama, 2000 (32)	Earthquake, Japan	258**		Self-constructed			12 months	2 years	3 symptoms: Time 1: 7-30; Time 2: 6-24		ND	No
Lima, 1989 (33)	Earthquake, Ecuador	150	100	SRQ			3 months		6 symptoms: 17 – 43			No
Najarian, 2001 (45)	Earthquake, Armenia	49/ 25#		SCL-90-R				2½ years		++		Yes
Pynoos, 1993 (67)	Earthquake, Armenia	231**	100	CPTSD-RI				1½ years				Yes
Tainaka, 1998 (34)	Earthquake, Japan	2,555				1 week	3 months	1½ years	6 symptoms: Time 1: 8-80, Time 2: 69-5, Time 3: 39-2			Yes
Wang, 2000 (43)	Earthquake, China	335/ 172#		SCL-90			3 & 9 months			++	ND	Yes

Bravo, 1990 (18); Canino, 1990 (19)	Flood, Puerto Rico	912	93	DIS/DS	- 1 year			2 years			Yes
Cook, 1990 (74)	Flood, USA	96	98	BSI		1 week	1¼, 3, 4 & 5 months				Yes
Escobar, 1992 (35)	Flood, Puerto Rico	375		DIS/DS	- 1 year			2 years	12 symptoms: 4 -36		No
Melick, 1985 (61)	Flood, USA	122/ 45#		SCL-90				5 years		- -	No
Phifer, 1988 (20); Phifer, 1989 (21)	Flood, USA	222	70	Self-constructed	- 3 months		3 & 9 months	1¼, 1¾ & 4¼ years			Yes
Phifer, 1990 (63)	Flood, USA	222	64	Self-constructed	- 1 year			1½ years			Yes
Smith, 1996 (22); Smith, 2000 (23)	Flood, USA	131	27	PSI			1½ & 6 months				Yes
Solomon, 1987 (59)	Flood, USA	360 / 183#	84	DIS/DS				1¼ years		ND	Yes
Fairley, 1986 (46)	Hurricane, Fiji	75 / 64#	99	GHQ & SSI			2½ months			GHQ: ++ SSI: ++	Yes
Guill, 2001 (36)	Hurricane, Honduras	110		Self-constructed			4 months		Headache: 58		No
Lutgendorf, 1995 (68)	Hurricane, USA	49	58	CFIDS			3 months				Yes
Shannon, 1994 (65)	Hurricane, USA	5,687**		RI			3 months		13% above cut-off		Yes
Shaw, 1995 (71)	Hurricane, USA	106**		TRF			2 months	2½ years			Yes

Table 3 (continued): Characteristics and findings of studies examining MUPS

First author and year of publication (reference no.)	Disaster and Country	N	Response rate* (%)	Measure †	Time since disaster				Findings			Risk factors
					Pre-disaster	< 1 month	1 month – 1 year	> 1 year	Prevalence range (%) ‡	Δ Control group§	Δ Time ¶	
Cowan, 1985 (66)	Volcanic eruption, USA	119	85	SCL-90-R			12 months					Yes
Lima, 1987 (24); Lima, 1993 (25)	Volcanic eruption, Colombia	113		SRQ			7 months	5 years	6 symptoms: Time 1: 20-60; Time 2: 13–36		- -	No
Murphy, 1984 (26); Murphy, 1988 (27)	Volcanic eruption, USA	155	80	SCL-90-R			11 months	3 years				Yes
Clayer, 1985 (37)	Bushfires, Australia	1,526 / 100#	52	Self-constructed			12 months		Nerve problems: 30, palpitations: 7	++		No
Maida, 1989 (38)	Bushfires, USA	25		DIS/DS			3 months		3 symptoms: 8 – 20			No
McFarlane, 1987 (62)	Bushfires, Australia	808** / 734#,**	43	RQ			2 & 8 months	2¼ years	Above cut-off: Time 1: 1;Time 2: 5; Time 3: 7		++	No
McFarlane, 1997 (47)	Bushfires, Australia	1,526 / 1,439#	77	GHQ			12 months			++		Yes
Dollinger, 1986 (39)	Lightning strike, USA	29**		MCBC (expansion)			2 months		7 symptoms: 3 – 31			No

Baum, 1983 (48)	TMI, USA	38 /83#	70	SCL-90		1½ years		++		No
Davidson, 1986 (49)	TMI, USA	52 35#	70	SCL-90-R		4⅔ years		++		Yes
Cleary, 1984 (50)	TMI, USA	403 / 1,506#		Self-constructed	4 months 10 months			++		Yes
Prince-Embury, 1988 (51)	TMI, USA	108 / 974#	51	SCL-90-R		6 years		++		No
Bromet, 2000 (52)	Chernobyl accident, USSR	300** / 300**	92 / 85††	CSI & CBCL		11 years		CSI: ++ CBCL:++		Yes
Bromet, 2002 (53)	Chernobyl accident, USSR	300 / 300#	92 / 85††	SCL-90-R		11 years	55% above cut-off	++		No
Cwikel, 1997 (44)	Chernobyl accident, USSR	374 / 334#	91	SCL-90		8 years 10 years		++	ND	Yes
Havenaar, 1997 (54)	Chernobyl accident, USSR	265 / 184#	92 / 88††	BrSI		6½ years	51% above cut-off	++		No
Holen, 1990 (28); Holen, 1991 (29)	Industrial disaster, Norway	73 /89#		Self-reported symptoms	5 weeks	8 years		++		No

Table 3 (continued): Characteristics and findings of studies examining MUPS

First author and year of publication (reference no.)	Disaster and Country	N	Response rate* (%)	Measure †	Time since disaster				Findings			Risk factors
					Pre-disaster	< 1 month	1 month – 1 year	> 1 year	Prevalence range (%) ‡	Δ Control group§	Δ Time ¶	
Weisaeth, 1989 (40)	Industrial disaster, Norway	246	98	PTSS-30			1 month 7 months		Time 2: muscle pain: 5 – 35 fatigue: 3 – 33			Yes
Grace, 1993 (60)	Buffalo Creek dam collapse, USA	199 / 50#	39	PEF & SCL-90-R				14 years		ND		No
Shariat, 1999 (41)	Terrorist attack, USA	494	54	HSQ				2⅔ years	5 symptoms: 22 – 44%			Yes
Trout, 2002 (42)	Terrorist attack, USA	191 / 155#	68 / 47††	Self-constructed			3 months		12 symptoms: 10 – 66%	++		No
Yokoyama, 1998 (55)	Terrorist attack, Japan	18 / 15#	12	POMS			7 months			++		Yes
Creamer, 1990 (56)	Multiple, shooting, Australia	446 / 338#	53 / 57††	SCL-90-R			4 months			++		No
Chung, 1999 (72)	Aircraft disaster, UK	82	55	GHQ			6 months					Yes
Donker, 2002 (4)	Aircraft disaster, Nether lands	533		Self-reported symptoms				6 years	6 symptoms: 9 - 45%			No

Livingston, 1992 (69)	Aircraft disaster, UK	55		GHQ	12 months			Yes
Tyano, 1996 (57)	Bus-train collision, Israel	306 / 83#	68/ 82††	SCL-90		7 years	++	Yes

* Response rates of the first measurement time are reported for longitudinal studies. When response rates of different exposure groups were given, the lowest percentage is reported.

† SCL-90 (SCL-90-R/ SCL-40) = Symptom Checklist somatization sub-scale; CHQ-12 = Chinese Health Questionnaire; SRQ = Self Reporting Questionnaire; CPTSD-RI = Children's Post-traumatic Stress Disorder Reaction Index; DIS/DS = Diagnostic Interview Schedule/ Disaster Supplement; BSI = Brief Symptom Inventory; PSI = Physical Symptoms Index; GHQ = General Health Questionnaire; SSI = Somatic Symptom Inventory; CFIDS = Chronic Fatigue Immune Dysfunction Symptoms; RI = Frederick Reaction Index for Children; TRF = Teacher's Report Form; RQ = Rutter Questionnaire (parent & teacher); MCBC = Missouri Children Behaviour Checklist; CSI = Children's Somatization Inventory; CBCL = Child Behaviour Checklist; HSQ = Health Status Questionnaire; BrSI = Bradford Somatic Inventory; PTSS-30 = Posttraumatic Stress Scale 30; PEF = Psychiatric Evaluation Form; POMS = Profile of Mood States fatigue sub-scale.

‡ Prevalence range of group of medically unexplained symptoms.

§ Statistical significant difference in score on scale between survivors and controls; ++ means survivors reported more MUPS than controls, -- means survivors reported less MUPS than controls, ND means there is no difference in reported MUPS between survivors and controls.

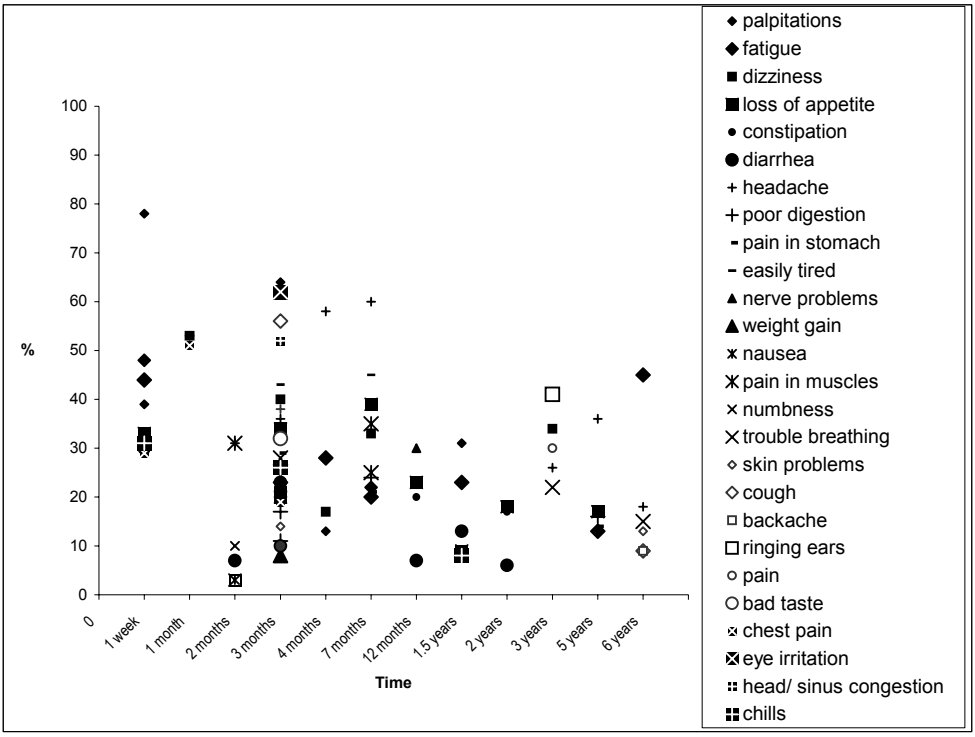
¶ Statistical significant difference in reported MUPS between two time points; ++ means survivors reported more MUPS at the second assessment compared to the first assessment, -- means survivors reported less MUPS at the second assessment compared to the first assessment, ND there is no difference in reported MUPS between the two assessments.

Control group.

** Children.

††Reference data.

Figure 3: Prevalence rates of individual Medically Unexplained Physical Symptoms (MUPS)



Predisposing factors. Predisposing factors already exist before the disaster and are typically risk factors for MUPS in the general population (figure 1). A group that might be at relatively greater risk for MUPS after disasters would be those with pre-existing MUPS; three flood studies found, after controlling for demographic characteristics and level of exposure, a positive association between pre- and post flood symptoms.[18, 20, 63]

In line with general population studies, women reported higher rates of MUPS in seven studies after natural disasters in which this association was examined.[18, 47, 58, 59, 64-66] Three studies did not find an association between reported MUPS and gender.[22, 63, 67]

High age, examined in eight studies, was not consistently found to be a risk factor for MUPS. One study among earthquake survivors showed that older subjects reported more MUPS.[58] After a hurricane, older survivors reported a greater worsening of chronic fatigue symptoms compared with younger survivors.[68] A study among child

survivors of a hurricane showed that late adolescents reported less MUPS compared with younger groups.[65] Five studies did not find any association between age and MUPS.[18, 22, 63, 66, 69]

Education, occupational status, and income are often considered to be indicators of socioeconomic status; these factors were not often examined as a risk factor for MUPS in the reviewed literature. A low educational level was found to be positively associated with MUPS in three studies after natural disasters,[58] of which two adjusted for other demographic characteristics, pre-disaster symptoms, and level of exposure.[18, 63] One study did not find this association.[22]

Precipitating factors. Involvement in the disaster can manifest itself in different ways. One way is the magnitude of physical damage to oneself, loved ones, and/or property. Another way may consist of exposure to toxic agents, radiation, or biologic agents. A third way is the possible psychological trauma experienced. High involvement in the disaster defined as the magnitude of damage seems to be an important risk factor for the development of MUPS. Fifteen studies examined this association: 11 studies showed that a high degree of physical damage was positively associated with MUPS,[18, 20, 22, 26, 34, 40, 45, 57, 63, 68, 70] and four studies did not find such an association.[59, 67, 68, 71]

Three studies that examined the association between relocation and MUPS did not find higher levels of MUPS among those who were relocated.[45, 50, 70] In one study, relocated subjects reported less MUPS than those who were not relocated.[43] Important to consider in this study was that those who were not relocated experienced significant aftershocks when they returned to their damaged houses, and they received less social support from agencies than did those who were relocated.

Perpetuating factors. Psychological problems are common after disasters and might be important risk factors for MUPS in those affected by disasters. For example, posttraumatic stress symptoms were positively associated with MUPS in five cross-sectional studies,[49, 55, 72] of which two were performed among children.[52, 67] In addition, two studies found a positive association between psychological distress and MUPS.[23, 68]

Coping styles, which refer to the specific way people act in a stressful situation, might be associated with MUPS as well. Two general coping strategies have been distinguished: 1) problem-focused coping or active coping involves the effort to do something active to alleviate stressful circumstances and 2) emotion-focused coping involves the effort to regulate the emotional consequences of stressful events.[73] The association between MUPS and active coping was considered in two studies, but no association was found.[22, 57] Avoidant coping, engaging in a substitute task, was found to be associated with MUPS among those affected by the Three Mile Island accident[50] but not among survivors of a flood.[22]

Table 4: Predisposing, precipitating and perpetuating factors for Medically Unexplained Physical Symptoms (MUPS) in survivors of disasters

	Positive association		Negative association	No difference	
	Ref. No.*	Adjustment(s)	Ref. No.*	Ref. No.*	Adjustment(s)
Predisposing factors					
Pre-disaster symptoms	18†	Gender, age, education, report effect, exposure level			
	20†	Gender, age, education, employment, marital status			
	63†	Gender, age, education, employment, marital status, exposure level			
Female gender	18	Age, education, pre-disaster symptoms, report effect, exposure level		22†	Age, education, income, church attendance, religious salience
	47			63	Age, education, employment, marital status, pre-disaster symptoms, exposure level
	58	Age, education, feel secure at home		67	
	59				
	64				
	65				
	66	Age, stressful life events, social support			
High age	58	Gender, education, feel secure at home	65	18	Gender, education, pre-disaster symptoms, report effect, exposure level
	68			22†	Gender, education, income, church attendance, religious salience
				63	Gender, education, employment, marital status, pre-disaster symptoms, exposure level
				66	Gender, stressful life events, social support
Married				63	Gender, age, education, employment, pre-disaster symptoms, exposure level

Low income	22†	Gender, age, education, church attendance, religious salience		
Low occupational status			63	Gender, age, education, marital status, pre-disaster symptoms, exposure level
Low education	18	Gender, age, pre-disaster symptoms, report effect, exposure level	22†	Gender, age income, church attendance, religious salience
	58			
	63	Gender, age, employment, marital status, pre-disaster symptoms, exposure level		
Church attendance			22†	Gender, age, education, income, religious salience
			50	MUPS at previous measurement time
Religious salience			22†	Gender, age, education, income, church attendance
Precipitating factors				
High physical damage	18	Gender, age, education, pre-disaster symptoms, report effect	59	Pre-disaster symptoms
	20†	Gender, age, education, employment, marital status, pre-disaster symptoms	67	
	22†	Gender, age, education, employment, income, church attendance, religious salience	68	
	26		71	
	34			
	40†			
	45			
	57	Education, income		
	63	Gender, age, education, employment, marital status, pre-disaster symptoms		
	68	Age		
	70			

Table 4 (continued): Predisposing, precipitating and perpetuating factors for Medically Unexplained Physical Symptoms (MUPS) in survivors of disasters

	Positive association		Negative association	No difference	
	Ref. No.*	Adjustment(s)	Ref. No.*	Ref. No.*	Adjustment(s)
High exposure to substances	44†				
High disruption				68	age
Importance of deceased person	66	Gender, age, social support, self-efficacy			
Preventability of death	66	Gender, age, social support, importance of deceased person			
Hospitalized/ treated	40				
Financial loss				70	Exposure level
Relocation			43	45	
				50	MUPS at previous measurement time
				70	Exposure level
Perpetuating factors					
PTSD symptomatology	49				
	52				
	55	Gender, age, education, alcohol consumption, smoking, serum cholinesterase activity			
	67				
	72				
Depression	66			68	
Psychiatric morbidity	46				
Psychological distress	23				
	68	Age, level of disruption			

Active coping			22†	Gender, age, education, income, church attendance, religious salience, exposure level, avoidant coping
			57	
Avoidant coping	50	MUPS at previous measurement time, self-esteem, psychotropic drug use	22†	Gender, age, education, income, church attendance, religious salience, exposure level, active coping
Optimism			68	Age, psychological distress, level of disruption
Introspection			50	MUPS at previous measurement time
Low self-esteem			50	MUPS at previous measurement time, psychotropic drug use, avoidant coping
Heavy social burden	59	Pre-disaster symptoms		
Low social support	59	Pre-disaster symptoms	27	Level of exposure, self-efficacy
			50	MUPS at previous measurement time
			66	Gender, age, stressful life events
			68	Age, psychological distress, level of disruption
			73	
Low self-efficacy	27	Exposure level, social support	50	MUPS at previous measurement time
Psychotropic drug use	50	MUPS at previous measurement time, self-esteem, avoidant coping		
Drinking			50	MUPS at previous measurement time
Smoking			50	MUPS at previous measurement time
Bad physical health	66			
Stressful life events	66	Gender, age, social support		

* Risk factors reported in the accepted studies, reference numbers correspond with reference numbers in Table 3 and list of references.

† Factors were longitudinally analyzed

A study among survivors of a severe flood showed that those who experienced low social support reported more MUPS.[59] Five other studies that examined social support did not, however, find this association.[27, 50, 66, 68, 74]

Discussion

This review showed that MUPS are common in survivors of disasters and are more prevalent in those affected by disasters compared with the general population. Regardless of the type of disaster, a higher proportion of survivors compared with controls suffer from MUPS both immediately after and in the years following a disaster. In addition, a few consistent risk factors for MUPS, such as female gender as a predisposing factor, high physical damage as a precipitating factor, and posttraumatic stress symptoms as a perpetuating factor, were identified.

Since there is no clear-cut distinction between a major incident and a disaster, we included the keywords ‘‘traumatic events’’ and ‘‘life events’’ in our search strategy. The search identified 3,290 articles: 1,474 in PubMed and 1,816 in other databases. As a result of using the disaster criterion, 86 % of the studies, mostly performed after individual traumatic events or after war situations, were excluded. This indicates that keywords such as ‘‘life events’’ and ‘‘traumatic events’’ were too general. This was confirmed by a replication of the search in PubMed in which we included solely the keyword ‘‘disasters,’’ without ‘‘life events’’ and ‘‘traumatic events’’; this search yielded 671 papers.

The prevalence rates of MUPS in the reviewed studies are in accordance with results of studies among people affected by individual traumatic events,[75, 76] and among war veterans[15, 77] it is therefore not likely that the results of this review would have been different when we included studies about individual traumatic events and war situations. Studies about relief workers were excluded on the basis of the subject criterion. Because relief workers, like war veterans, are predominately young (male) adults and more healthy compared with residents, it is likely that studies among relief workers would have yielded lower prevalence rates of MUPS. We accepted studies about child survivors of disasters. Since children seem to report the same symptom patterns as their parents,[78] the inclusion of these studies would probably not have affected the results of this review. Finally, 469 studies were judged on the MUPS criterion. The majority of these studies measured psychological problems, such as posttraumatic stress disorder and depression; we found 57 articles in which MUPS were measured. We excluded studies in which symptoms were likely to be the result of exposure to toxic substances. However, information on dose-response relations for the substance is typically insufficient to make a clear distinction between symptoms from toxicologic effects and MUPS. Therefore, MUPS may also be prevalent after exposure to toxic substances.[9, 79]

Few consistent risk factors were observed in the reviewed studies. It is unclear how our selection criteria may have affected the answers to our second research question. The literature on risk factors for MUPS after disasters was even more limited than that on the prevalence rate of MUPS; most risk factors were examined in only one study. However, the identified risk factors for MUPS after disasters were similar to those found in studies among the general population, Gulf War veterans, and victims of sexual assault. For example, female gender was found to be a risk factor for MUPS in the general population,[10, 16] and in studies among Gulf War veterans.[77, 80] The perpetuating factors posttraumatic stress symptoms and psychological distress were associated with MUPS among survivors of disasters, and this association has also been found in community studies,[10, 13] among Gulf War veterans,[81, 82] and among victims of sexual assault.[76] This indicates that, in particular, predisposing and perpetuating risk factors for MUPS are likely to be similar across different kinds of traumatic events. Precipitating factors might, however, differ across different kinds of traumatic events, and therefore we excluded studies among survivors of individual traumatic events and wartime exposure.

Although this review shows that survivors of disasters report more MUPS compared with controls, we found substantial variation in the reported prevalence rates of MUPS. This variation might have resulted from differences in study characteristics, which make adequate comparison difficult. First, the time of measurement since the disaster differed among studies. Some studies measured MUPS in the months after the disaster, but other studies were performed for the first time years after the disaster. Second, the number of participants as well as the response rate differed among studies. The majority of studies reporting prevalence rates had a low response rate (<60 %) or did not report any rate. For interpreting the prevalence rate, a high response rate is needed, so that selection bias is limited. Third, the study populations were often not chosen randomly, which might have introduced some bias. However, the use of a random sample is difficult in studies that are performed shortly after a disaster, and therefore convenience samples are frequently used. For convenience samples, information about who did or did not participate in the study is often lacking, and thus the results can either be an under- or overestimation of the true health problems. However, selective participation can also occur in studies that used random sampling. Moreover, after disasters, it is difficult to identify all the eligible survivors, since the affected area as well as the denominator of the affected population cannot always be defined. Fourth, many different questionnaires were used to measure MUPS: 21 different questionnaires in 57 accepted studies. As a result, the number and the type of symptoms that were measured differed among studies. Because of these limitations in the study designs, we cannot draw a definite conclusion about the prevalence rates of MUPS in survivors of disasters.

In contrast to risk factors for MUPS, risk factors for posttraumatic stress disorder have often been studied. Low socioeconomic status, history of psychiatric disorders, and stressful life events have been shown to be risk factors for posttraumatic stress disorder,[83] but such an association with MUPS has rarely been studied. In addition, little is known about how different factors interact over time. Nevertheless, three factors seem to be associated with MUPS: the predisposing factor female gender, the precipitating factor high physical damage, and the perpetuating factor posttraumatic stress symptoms. Since female gender is also a risk factor for MUPS in the general population, the question is whether female gender modifies the effect of the disaster by increasing MUPS after the disaster or whether females already reported more MUPS before the disaster. Because most accepted studies were retrospective, this question cannot be answered; more prospective studies, preferably with a pre-disaster measurement, are needed to answer this question.

Damage to house or property, injury to oneself or others, serious threat to one's own or one's family member's life, and loss of a loved one were, in most studies, combined into a single exposure variable. Therefore, we reported these factors as the precipitating factor high physical damage in this review. However, the individual exposure variables might be associated with MUPS differently. Future research should consider these factors as different precipitating factors.

Since most studies that examined risk factors for MUPS were cross-sectional or used cross-sectional analyses, we cannot draw a conclusion about causality. For the identification of perpetuating factors (such as posttraumatic stress symptoms and depression) in particular, more longitudinal studies after disasters are needed to answer the question about whether these factors are risk factors or intermediate factors for MUPS.

In conclusion, this review shows that survivors of disasters report more MUPS compared with controls. However, since there is much diversity in study designs among studies, no definite conclusion can be drawn about the prevalence rate of MUPS at different time points after disasters. In addition, a few possible risk factors for MUPS were identified: female gender, high physical damage, and posttraumatic stress symptoms. Many risk factors for MUPS, such as a history of psychiatric disorders and stressful life events, were often studied among the general population or Gulf War veterans, but these factors were rarely studied in survivors of disasters. Therefore, more epidemiologic research after large-scale disasters is needed. To facilitate and prepare epidemiologic studies after disasters, the Dutch Ministry of Welfare, Public Health, and Sports set up the Centre for Health Impact Assessment of Disasters at the National Institute for Public Health and the Environment. Since MUPS impair people's functioning and can be very persistent over time, these future studies must focus on risk factors for MUPS, such as pre-disaster MUPS or mental health problems and the

contribution of individual disaster-related factors, so that survivors at risk for the development of MUPS can be more easily identified.

Acknowledgements
The authors thank Wim ten Have for helping them with the development of the search strategy and for searching the different databases. They would like to thank Dr. Anja Dirkzwager for evaluating studies on which no consensus could be reached. They would also like to thank Dr. Marc Ruijten for his advice on the studies in which survivors were possibly exposed to toxic substances.

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CHAPTER 3

Symptoms and related functioning in a traumatized community

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Published in: Archives of Internal Medicine 2005;165:2402-2407

Abstract

Background: Traumatic events are described as precipitating factors for medically unexplained symptoms. The aim of this study was to examine the prevalence and course of symptoms reported by disaster survivors and to assess whether the symptoms have features similar to those of medically unexplained symptoms.

Methods: A 3-wave longitudinal study was performed after an explosion of a fireworks depot. As a result of the explosion, 23 people were killed, more than 900 people were injured, and about 500 homes were damaged or destroyed. Respondents completed a set of validated questionnaires measuring their health problems 3 weeks (wave 1), 18 months (wave 2), and 4 years (wave 3) after the disaster. A comparison group was included at waves 2 and 3.

Results: The study population included 815 survivors who participated in the 3 waves. The mean number of symptoms was higher among survivors compared with control subjects at wave 2 (7.5 vs 5.8 symptoms) and at wave 3 (6.1 vs 4.9 symptoms) (p <.001 for both). Survivors and control subjects with more symptoms reported significantly lower mean scores on all scales of the Dutch version of the RAND 36-item health survey. Illness behavior and depression and anxiety were associated with the number of symptoms. For example, more than 60% of survivors with 10 or more symptoms reported depression and anxiety, compared with 2.4% of survivors with 0 to 1 symptoms (p <.001).

Conclusions: Up to 4 years after the disaster, symptoms were more prevalent among survivors than controls. Although medical disorders cannot be excluded, the reported symptoms showed several features similar to those of medically unexplained symptoms in the general population.

Introduction

Symptoms such as headache, stomachache, fatigue, and pain in joints or muscles are common in the general population. An estimated 80% of the general population experiences at least one of these symptoms in any given month.[1, 2] When disclosed to a general practitioner (GP), many symptoms cannot be explained by a medical diagnosis and are considered medically unexplained.[3]

Traumatic events such as natural and man-made disasters are often described in the literature as precipitating factors for elevated levels of unexplained physical symptoms.[4-6] A prospective study of a severe flood in Puerto Rico showed a higher number of new physical symptoms among survivors compared with control subjects one year after the flood.[7] After disasters, survivors may attribute physical symptoms to suspected exposure to toxic substances, which can lead to amplification of health problems.[8] After an airplane crash in Amsterdam, the Netherlands, many survivors attributed their physical symptoms to the harmful effect of substances from the wreck or cargo such as depleted uranium.[9] Donker et al. reported that GPs could not associate most of these symptoms with a medical disorder.[10]

Medically unexplained symptoms (MUS) are seldom studied in the aftermath of disasters.[6] Instead, the literature on traumatic events focuses on mental health problems such as posttraumatic stress disorder (PTSD), depression, and anxiety. Almost all disaster investigations that examined physical symptoms used questionnaires.[6] Only examination by a physician can rule out an underlying medical explanation for reported symptoms; this is one of the difficulties of studying MUS by means of a questionnaire.[11] To get more insight into the similarities between MUS observed in medical practice and the physical symptoms reported on questionnaires, other characteristics of MUS have to be considered. In the general population, features associated with MUS are functional impairment and increased illness behavior such as sick leave, health care, and medication use.[12-14] In addition, studies[13, 14] have shown that patients with MUS have more comorbid psychiatric disorders, especially major depression and anxiety disorder.

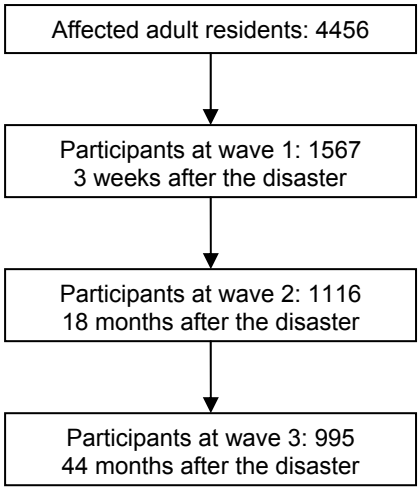
To better understand the physical symptoms after disasters and their similarities with MUS in the general population, we explored the data of a longitudinal study that was performed after a man-made fireworks disaster.[15] The following research questions were addressed: (1) What is the course of symptoms over time among survivors of the fireworks disaster? (2) Are symptoms more prevalent among survivors compared with controls? (3) Do the symptoms reported by survivors and controls have features similar to those of MUS in the general population, such as functional impairment, increased illness behavior, and psychological symptoms?

Methods

Participants and procedure

As a result of the explosion of a fireworks depot in a residential area in Enschede, the Netherlands, on May 13, 2000, and the subsequent fire, 23 persons were killed, more than 900 people were injured, and about 500 homes were severely damaged or destroyed. The Dutch government declared this a national disaster and began a longitudinal study of the health consequences of the disaster. An initial survey (wave 1) was commenced 3 weeks after the disaster. On the basis of the list of addresses at the registry office of Enschede, it was confirmed that the total affected group consisted of 4456 adult residents. All adult residents were invited to participate. Data collection took place at an air force base close to Enschede. In total, 1567 survivors (response rate, 35.2%) completed a questionnaire (figure).

Figure. Flowchart of the study. Sixteen of 1567 participants at wave 1 were lost to follow-up at wave 2, and 51 of 1567 were lost to follow-up at wave 3.



Approximately 18 months after the disaster, in November 2001, a second survey (wave 2) was conducted. All wave 1 participants who had given informed consent for future contact received an announcement letter. In addition, a sample of 1600 residents was drawn from the registry office at Tilburg, the Netherlands, to serve as a control group. Tilburg was comparable to the affected area in Enschede with

regard to the composition of the population and their general health status. The control sample was stratified according to sex, age, and country of origin to make it comparable to the survivors from wave 1.

To stimulate participation, survivors and controls were telephoned at home after the announcement letter was sent. If a respondent agreed to participate, a questionnaire was sent to his or her home address in the preferred language (Dutch, German, English, or Turkish). Interpreters were available at a community center to assist in completing the questionnaires. In total, 1116 of 1551 survivors (response rate, 72.0%) and 821 controls (response rate, 51.3%) completed a questionnaire at wave 2.

In January 2004, almost 4 years after the disaster, a third survey (wave 3) was taken. Except for participants who were lost to follow-up because we were unable to locate them, all participants of wave 1 who had given written informed consent for future contact received an announcement letter. In the control group, only a small proportion of immigrants (immigrants were defined as respondents who were born in a foreign country of whom at least 1 parent was also born in a foreign country or respondents whose parents were both born in a foreign country) had agreed on the informed consent form to be contacted again. To avoid differences between the two groups, 184 immigrants in the original sample who did not participate in the first control survey also received an announcement letter.

Participation was stimulated by means of home visits and telephone calls. If a respondent agreed to participate, a questionnaire in his or her preferred language was sent or hand delivered. As at wave 2, interpreters were available at the community center to assist in completing the questionnaires. In total, 995 of 1516 survivors (response rate, 65.6%), 587 of the 793 controls who were lost to follow-up (response rate, 74.0%), and 53 of 184 immigrants (response rate, 28.8%) completed a questionnaire at wave 3. Details of the study population, participation, and procedures in the 3 waves have been described elsewhere.[15-19] In this article, we describe 815 survivors who participated in the three surveys vs 821 controls at wave 2 and 640 controls at wave 3. The survivors and the control groups were similar in demographic characteristics.[18, 19]

Measures

The questionnaires were comparable in the three surveys for the survivors and in the two surveys for the controls. The questionnaires primarily included scales that had been previously validated in the Dutch population, as described in the next subsections.

Symptoms – At wave 1, symptoms were measured by the 13-item Vragenlijst voor Onderzoek naar de Ervaren Gezondheid (VOEG) (Questionnaire into Subjective Health Complaints) scale, a validated questionnaire that has often been used for studies in the Dutch population.[20] The items of this scale ask respondents whether they

regularly have symptoms such as stomachache, fatigue, pain in the region of the heart or chest, and pain in the bones and muscles. At the second and third waves, 12 symptoms were added to the questionnaire.

While most symptoms were asked about only once, gastrointestinal and fatigue symptoms were asked about in three different ways. In the analysis, these were treated as one gastrointestinal symptom and one fatigue symptom to avoid giving these two symptoms more weight compared with the other symptoms. Therefore, 21 different symptoms were used for the analyses of the symptoms at waves 2 and 3 (table 1).

Functional status – Participants completed the validated Dutch version of the RAND 36-item health survey (RAND-36).[21] This questionnaire comprises the nine scales of Physical Functioning, Social Functioning, Physical Role Limitations, Emotional Role Limitations, Mental Health, Vitality, Bodily Pain, General Health Perceptions, and Change in Health. All scales were scored from 0 to 100, with higher scores indicating better health.

Illness behavior – Participants were asked whether they were currently on sick leave and whether they were currently receiving disability benefits. Participants were asked about their use of any prescription medication from a GP. In addition, participants were asked about the number of visits to their GP in the past two months, a period that was chosen to avoid recall bias. The number of visits in the past year was estimated using the two months' figures.

Psychological symptoms – Depression and anxiety were measured by the Dutch version of the Symptom Checklist 90.[22] Responses were based on a 5-point Likert scale and assessed the degree of depression and anxiety during the past week.

Statistical analysis

t Tests were used to test differences in the mean numbers of symptoms reported by survivors at the three waves. The prevalence of symptoms among survivors and controls were compared by calculating crude odds ratios and 95% confidence intervals.

To evaluate the associations among the number of symptoms and functional status, illness behavior, and psychological problems, we added the 21 symptoms together and, using cutoff values, categorized the totals into four ranges. The cutoffs were based on the distribution of the symptoms reported by the control group at wave 2 and on cutoffs that were previously used for other scales, such as the Symptom Checklist 90.[22] The first range was 0 to 1 symptoms, the second was 2 to 9 symptoms, the third was 10 to 14 symptoms (80th percentile), and the fourth was 15 or more symptoms (95th percentile).

Scores on the depression and anxiety subscales of the Symptom Checklist 90 were dichotomized using the sex-specific normal values for the healthy Dutch

population. According to these tables, 20% of the Dutch population scores “high” to “extremely high” on the subscales.[22]

Analysis of variance and X^2 tests were used to evaluate the associations among the 4 symptom ranges and the 9 scales of the RAND-36, illness behavior, depression, and anxiety. Logistic regression analyses were used to calculate group effects for illness behavior, depression, and anxiety. To determine whether chronic diseases and associated symptoms affected the results, the analyses were repeated for survivors (361 at wave 2 and 402 at wave 3) and for controls (435 at wave 2 and 341 at wave 3) without self-reported chronic diseases.

Results

Symptoms over time

Three weeks after the disaster, survivors reported a mean±SD number of 5.6±3.3 symptoms on the 13-item VOEG scale. Eighteen months after the disaster, the mean±SD number of symptoms on this 13-item scale was comparable (5.5±3.7 symptoms). Almost 4 years after the disaster, the mean±SD number of symptoms had decreased significantly (4.6±3.6). On the 21-item scale of symptoms, survivors reported a mean±SD of 7.5±4.9 symptoms at wave 2, which was significantly higher than that at wave 3 (6.1±4.7 symptoms).

Symptoms among survivors and controls

Symptoms were prevalent among survivors and controls. However, 18 months after the disaster, the mean number of symptoms was higher among survivors than controls (7.5 vs. 5.8; p <.001, t-test). Fifteen of 21 symptoms were significantly more prevalent among survivors (table 1). The most prevalent symptoms were similar among survivors and controls, with higher prevalence rates among survivors for fatigue (70.1% vs. 49.9%), pain in the neck and shoulders (56.9% vs. 48.0%), and pain in the bones and muscles (52.9% vs. 42.4%).

At wave 3, survivors reported a mean number of 6.1 symptoms, which was higher than the mean number of 4.9 symptoms among controls (p <.001). Twelve of the 21 symptoms were significantly more prevalent among survivors. The most prevalent symptoms were similar among survivors and controls, with higher prevalence rates among survivors.

Table 1: Prevalence of 21 symptoms among survivors and control subjects at wave 2 and wave 3*

Symptom	Wave 2			Wave 3		
	Survivors (n= 815)	Controls (n= 821)	OR (95% CI)	Survivors (n= 815)	Controls (n= 640)	OR (95% CI)
	N = 815	N = 821		N = 815	N = 640	
Listlessness	48.6	25.5	2.8 (2.2 – 3.4)	37.9	21.9	2.2 (1.7 – 2.8)
Fatigue	70.1	49.9	2.4 (1.9 – 2.9)	61.1	44.2	2.0 (1.6 – 2.5)
Forgetfulness	46.0	29.2	2.1 (1.7 – 2.5)	38.2	24.3	1.9 (1.5 – 2.4)
Ringing in the ears	25.6	16.1	1.8 (1.4 – 2.3)	20.8	13.8	1.6 (1.2 – 2.2)
Pain in chest & the region of the heart	26.4	17.5	1.7 (1.3 – 2.2)	18.7	17.8	1.1 (0.8 – 1.4)
Lump in throat	14.9	9.9	1.6 (1.2 – 2.2)	11.3	5.6	2.1 (1.4 – 3.2)
Stomachache	45.6	34.2	1.6 (1.3 – 2.0)	36.4	31.6	1.2 (1.0 – 1.6)
Pain in bones and muscles	52.9	42.4	1.5 (1.3 – 1.9)	43.8	37.1	1.3 (1.1 – 1.6)
Nausea	19.3	13.7	1.5 (1.2 – 2.0)	12.7	11.3	1.1 (0.8 – 1.6)
Dizziness	27.8	20.9	1.5 (1.2 – 1.8)	22.9	16.0	1.6 (1.2 – 2.0)
Pain in neck and shoulders	56.9	48.0	1.4 (1.2 – 1.7)	50.6	41.7	1.4 (1.2 – 1.8)
Cold fingers, hand and feet	43.0	34.4	1.4 (1.2 – 1.8)	35.9	32.8	1.1 (0.9 – 1.4)
Excessive sweating	29.2	22.7	1.4 (1.1 – 1.8)	21.8	16.1	1.5 (1.1 – 1.9)
Pain in back	49.2	41.6	1.4 (1.1 – 1.7)	45.6	39.1	1.3 (1.1 – 1.6)
Headache	46.7	39.0	1.4 (1.1 – 1.7)	39.3	30.4	1.5 (1.2 – 1.9)
Deafness	19.4	15.3	1.3 (1.0 – 1.7)	17.5	13.4	1.4 (1.0 – 1.9)
Tight feeling in the chest	24.0	20.3	1.3 (1.0 – 1.6)	19.5	16.2	1.3 (1.0 – 1.7)
Tingling in arms and legs	38.1	32.4	1.3 (1.0 – 1.6)	32.3	25.6	1.4 (1.1 – 1.8)
Poor vision	25.9	22.0	1.2 (1.0 – 1.6)	20.6	18.6	1.1 (0.9 – 1.5)
Shortness of breath	33.3	28.8	1.2 (1.0 – 1.5)	24.6	21.1	1.2 (1.0 – 1.6)
Fainting	17.0	20.7	0.8 (0.6 – 1.0)	15.4	12.7	1.2 (0.9 – 1.7)

Abbreviations: CI, confidence interval; OR, odds ratio

* Data are given as percentages unless otherwise indicated.

Table 2: Association between the number of symptoms and functional impairment at wave 2 for survivors and control subjects*

	No. of symptoms†			
RAND-36 scale	0 - 1	2 – 9	10 – 14	≥ 15
Physical functioning				
Survivors	97.0	86.0	67.5	53.4
Controls	95.2	83.9	64.0	55.0
Social functioning‡				
Survivors	94.5	80.9	58.5	41.7
Controls	94.7	84.2	67.5	52.6
Physical role limitations‡				
Survivors	95.2	73.0	41.8	19.9
Controls	96.2	80.3	54.2	26.5
Emotional role limitations‡				
Survivors	96.4	76.1	47.3	24.0
Controls	97.4	86.6	59.1	32.3
Mental health‡				
Survivors	84.9	72.2	52.1	40.5
Controls	85.2	77.1	59.0	49.1
Vitality‡				
Survivors	75.2	60.3	40.8	31.3
Controls	79.6	66.5	44.6	39.9
Pain				
Survivors	92.8	79.2	58.6	39.7
Controls	94.2	78.9	62.7	49.7
General health				
Survivors	82.7	67.6	46.1	31.4
Controls	81.7	68.6	47.0	36.6
Health change				
Survivors	57.6	53.3	42.9	28.9
Controls	54.1	51.1	46.0	37.2

* Data are given as mean scores on the RAND-36-item health survey (RAND-36) (score range, 0 [poor health] to 100 [good health]). $p < .001$ for all comparisons across rows;

† The numbers of survivors and control subjects are as follows: *0 to 1 symptoms*, 86 survivors (11.0%) and 134 controls (16.8%); *2 to 9 symptoms*, 436 survivors (55.8%) and 499 controls (62.6%); *10 to 14 symptoms*, 181 survivors (23.1%) and 121 controls (15.2%); and *15 or more symptoms*, 79 survivors (10.1%) and 43 controls (5.4%). To categorize the number of symptoms, we added the 21 symptoms together and subsequently divided this scale into 4 categories. Survivors who had 2 or more items on the 21-symptom scale missing were excluded from the analyses involving the associations among the 4 symptom ranges and the 9 scales of the RAND-36, illness behavior, depression, and anxiety;

‡ Mean score of control subjects greater than that of survivors, $p < .001$.

At wave 2, 33.3% of survivors reported 10 or more symptoms compared with 20.6% of controls (p <.001, X^2 test). At wave 3, the proportion of survivors who reported 10 or more symptoms was still higher than among controls (26.2% vs. 17.7%; p <.001, X^2 test).

Associated features

The symptoms reported at wave 2 were associated with functional impairment. With increasing numbers of symptoms, the mean scores of all nine scales of the RAND-36 decreased considerably for survivors and controls. Despite reporting the same number of symptoms, survivors had significantly lower mean scores than controls on five of the nine scales of the RAND-36 (table 2).

Table 3: Association between the number of symptoms and increased illness behavior at wave 2 for survivors and control subjects*

	No. of symptoms†			
Behavior	0 - 1	2 – 9	10 – 14	≥ 15
Currently on sick leave				
Survivors	1.3	7.2	20.0	31.0
Controls	1.8	5.9	14.4	18.5
Currently receiving disability benefits				
Survivors	1.2	3.8	18.9	28.4
Controls	< 1.0	4.5	14.7	30.0
Painkillers				
Survivors	6.0	17.5	37.7	62.5
Controls	4.6	19.7	37.7	51.3
Sedative use‡				
Survivors	3.6	7.0	24.2	41.2
Controls	< 1.0	3.5	23.2	31.6
Visits to general practitioner in the past year, mean no.				
Survivors	2.6	7.3	12.5	17.5
Controls	3.1	6.6	14.1	18.4

* Data are given as percentages unless otherwise indicated. p <.001 for all comparisons across rows.

† The numbers of survivors and control subjects are the same as in table 2.

‡ Percentage of survivors greater than that of control subjects, p <.05.

In Table 3, the association between symptoms at wave 2 and increased illness behavior is summarized. Among survivors and controls, a higher number of symptoms was associated with a higher proportion of participants currently on sick leave. For both groups, having more symptoms was associated with receiving disability benefits. Moreover, the use of medication increased significantly with an increasing number of symptoms, with a stronger association among survivors for the use of sedatives. The number of symptoms was also associated with health care use. For the survivors and controls, the mean number of visits to the GP increased from 3.1 visits a year for those with 0 to 1 symptoms to 18.4 visits a year for those with 15 or more symptoms.

Participants reporting more symptoms had significantly more depression and anxiety (table 4). This association was stronger for survivors. Compared with controls, survivors with 10 or more symptoms had high scores 1.3 times more often on the depression subscale and 1.5 times more often on the anxiety subscale. Exclusion of respondents with chronic diseases did not change the odds ratios or any of the associations (data not shown).

Table 4: Association between the number of symptoms and the prevalence of depression and anxiety at wave 2 among survivors and control subjects*

	No. of symptoms*†			
	0 - 1	2 – 9	10 – 14	≥ 15
Depression‡				
Survivors	2.4	19.4	68.4	89.0
Controls	6.2	17.3	52.1	71.4
Anxiety§				
Survivors	2.4	16.1	62.3	86.7
Controls	2.3	6.7	41.2	59.5

* Data are given as percentages. p <.001 for all comparisons across rows.

† The numbers of survivors and control subjects are the same as in table 2.

‡ Percentage of survivors greater than that of control subjects, p <.05.

§ Percentage of survivors greater than that of control subjects, p <.001.

Comment

In contrast to many studies in the aftermath of disasters, this study focused on physical symptoms among survivors rather than on mental health problems. Symptoms were more common among survivors compared with controls. Eighteen months after the

disaster, 33.3% of survivors reported 10 or more symptoms compared with 20.6% of controls. Although the results showed a gradual decrease in the number of symptoms, survivors reported significantly more symptoms than controls four years after the disaster. Despite the elevated number of symptoms among survivors, no theories about possible exposure to toxic substances developed in the aftermath of the fireworks disaster. The absence of such a theory might be explained by the reassuring results of the blood and urine samples that were obtained three weeks after the disaster, in which no elevated body burden was detected.[16]

Symptoms in this study were similar to MUS in the general population.[12-14] With increasing numbers of symptoms, we found a decrement of ten points or more among the scores on the nine scales of the RAND-36. This decrement is similar to that seen with chronic disorders such as arthritis, diabetes mellitus, and gastrointestinal disorders,[23] as well as with MUS observed in general population studies.[12, 13] Respondents with increasing numbers of symptoms also reported increased use of sick leave, health care, and medications.

The symptoms in this study were strongly associated with depression and anxiety, which is also similar to MUS in the general population.[13, 14] The association was stronger for survivors than controls, despite their reporting the same number of symptoms. This effect was also found for five of the nine scales of the RAND-36 and for the use of sedatives. These stronger effects among survivors may reflect the higher level of distress due to the traumatic event. They might also suggest worse severity of symptoms in the survivor group, which was not measured in our study.

Because only 35.2% of all affected residents participated in the first wave of the survey, participation may have been biased toward those with or without health problems. Shortly after the disaster, all affected adult residents registered at an information and advice center that was established to supply information to survivors and to coordinate their needs. To detect possible selection bias, the database of the information and advice center was used to compare demographic characteristics of the participants with those of the nonparticipants. The analysis showed that participation was somewhat biased. Fewer men and fewer younger (18-24 years) and older (≥ 65 years) residents but more immigrants participated at the first wave.[17, 24] To study the magnitude of the selection bias, analyses of multiple imputations were used to fill in missing data of nonparticipants. The prevalence estimates of postdisaster health problems were unaffected.[25] At wave 2, fewer men, fewer younger survivors, and fewer survivors with more health problems at wave 1 participated. Despite this selection bias, no significant differences in the estimated prevalence rates of health problems were observed after multiple imputations.[18, 26] Analyses indicate that the effect of the selection bias on the outcomes of interest was limited. Although the prevalence rates of symptoms among controls decreased between wave 2 and wave 3, additional analysis

showed that this was not the result of nonparticipation at wave 2 among controls with high symptom levels.

As in most disaster studies, physical symptoms were based on self-reporting rather than physical examination; therefore, we could not assess the presence of medical disorders. However, excluding the respondents with self-reported chronic diseases did not affect our results. In addition, analyses of the blood and urine samples demonstrated no elevated body burden due to the fireworks disaster.[16] This makes it unlikely that the higher prevalence of symptoms among survivors is the result of exposure to toxic substances. In addition, many survivors and controls reported 10 or more symptoms in different organ systems, making it unlikely that all of these symptoms were the result of a medical disorder or toxic exposure. The study of the airplane crash in Amsterdam confirmed that GPs associated only 40% of reported symptoms with a medical diagnosis, leaving 60% unexplained.[9] The reported symptoms in this study show many similarities with MUS. Therefore, the term *medically unexplained symptoms* may be used to refer to symptoms that are common, persistent, and related to functional impairment, increased illness behavior, and comorbid psychological symptoms.

Because only a few disaster studies have focused on MUS, little is known about the contribution of precipitating factors, such as damage to house and property, and perpetuating factors, such as lack of social support and mental health problems, to the development and persistence of MUS after disasters.[6] Because knowledge of these factors may facilitate detection of vulnerable individuals and optimize care delivery by clinicians after a disaster, future studies should focus on factors that might be responsible for MUS among survivors of disasters.

Acknowledgments

We thank Hendriek Boshuizen, PhD, for her statistical advice and Peter Van der Velden, PhD, for his critical review of the manuscript.

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CHAPTER 4

Are physical symptoms among survivors of a disaster presented to the general practitioner? A comparison between self-reports and GP data

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Submitted

Abstract

Background: Most studies that examined medically unexplained symptoms (MUS) have been performed in primary or secondary care and have examined symptoms for which patients sought medical attention. Disasters are often described as precipitating factors for MUS. However, health consequences of disasters are typically measured by means of questionnaires, and it is not known whether these self-reported physical symptoms are presented to the GP. Also it is not known whether the self-reported symptoms are related to a medical disorder or whether they remain medically unexplained. In the present study, it was examined whether disaster survivors presented self-reported symptoms to the general practitioner (GP). Also, it was assessed whether presenting symptoms to the GP was associated with functional impairment and distress. Finally, the proportion of symptoms that are medically unexplained after clinical judgment was examined.

Methods: Survivors of a man-made disaster (N= 887) completed a questionnaire 887, 3 weeks (T1) and 18 months (T2) post-disaster. This longitudinal health survey was combined with an ongoing surveillance program of health problems registered by GPs.

Results: The majority of self-reported symptoms was not presented to the GP and survivors were most likely to present persistent symptoms to the GP. For example, survivors with stomachache at T1 and T2 were more likely to report stomachache to their GP (28%), than survivors with stomachache at either T1 (6%) or T2 (13%). Presenting symptoms to the GP was not consistently associated with functional impairment and distress. 56 – 91% of symptoms was labeled as MUS after clinical examination.

Conclusion: These results indicate that the majority of self-reported symptoms are not a reason to seek medical care and that the decision to consult with a GP is not dependent on the level of impairment and distress. Also, self-reported physical symptoms are likely to be similar to MUS.

Introduction

Symptoms such as fatigue, stomachache, and headache are very common;[1] an estimated 80% of the general population experiences at least one symptom in any given month.[2, 3] Primary care studies have also shown that, when presented to the general practitioner (GP), at least one-third of these symptoms cannot be related to a medical disease after clinical judgment, and are labeled as medically unexplained symptoms (MUS).[1, 4] MUS are strongly associated with a high level of functional impairment and psychological problems such as depression and anxiety,[4, 5] Because MUS are defined as physical symptoms that have no clinically determined pathogenesis after an appropriate thorough diagnostic evaluation,[6] most studies examined MUS among primary or secondary care patients.

Although these symptoms are a major reason to seek medical care,[3, 4] the majority of symptoms are transient and not considered severe enough to seek medical attention and are not presented to the GP.[2, 3] This results in a large reservoir of symptoms in the general population that has not been studied in primary and secondary care studies.[7] Although these symptoms can be studied by means of questionnaires in epidemiological studies, questionnaires have some difficulties as well. Firstly, it is not known whether the reported symptoms are transient or whether they are of clinical pertinence and a reason to seek medical care. Secondly, because only examination of a physician can exclude medical disorders, it is unclear whether self-reported symptoms are similar to MUS.[8]

Although traumatic events such as disasters have often been described as important precipitating factors for MUS, MUS are not often studied after disasters.[9-12] Despite this, some previous studies have shown elevated levels of physical symptoms among survivors.[12] However, health consequences of disasters and other collective stressful events are typically measured by means of questionnaires, and it is not known whether these self-reported physical symptoms among survivors are similar to MUS.

In the present study among survivors of a man-made disaster, we compared self-reported symptoms with symptoms registered in the electronic medical systems of GPs. Three research questions were addressed. Firstly, were self-reported symptoms among survivors presented to the GP? Secondly, were survivors who presented their symptoms to the GP more impaired and more distressed compared to those who did not present their symptoms to the GP? Thirdly, what was the GPs clinical judgment to the presented symptoms, i.e. were the symptoms related to a medical diagnosis or could they be labeled MUS?

Methods

Study design and participants

We combined two data collection methods: a longitudinal health survey among survivors using self-administered questionnaires and an ongoing surveillance program in which health problems were registered by GPs in the electronic medical records (EMRs) of survivors.

The first health survey was performed 3 weeks (T1) after the explosion of a fireworks depot in a residential area in the city of Enschede, the Netherlands (13 May 2000). As a result of the explosions and the subsequent fire, 23 people were killed, over 900 people were injured and approximately 1200 people were forced to relocate because their houses were destroyed or severely damaged. All residents of the affected area were invited to participate in the health survey by means of announcements in the local media and letters. In total, 1567 affected residents (estimated response ≈ 30%) completed a questionnaire at wave 1. Approximately 18 months after the disaster, in November 2001 a second survey (T2) was conducted. Affected residents (i.e. survivors) who had completed a questionnaire at T1 and who had given informed consent for future contact received an announcement letter (N= 1551). In total, 1116 survivors (response 72.0%) participated at T2. The Medical Ethical Testing Committee (TNO-Leiden-The Netherlands) approved the study protocol. Details of the study population, non-response and procedures of the surveys have been described elsewhere.[13-16]

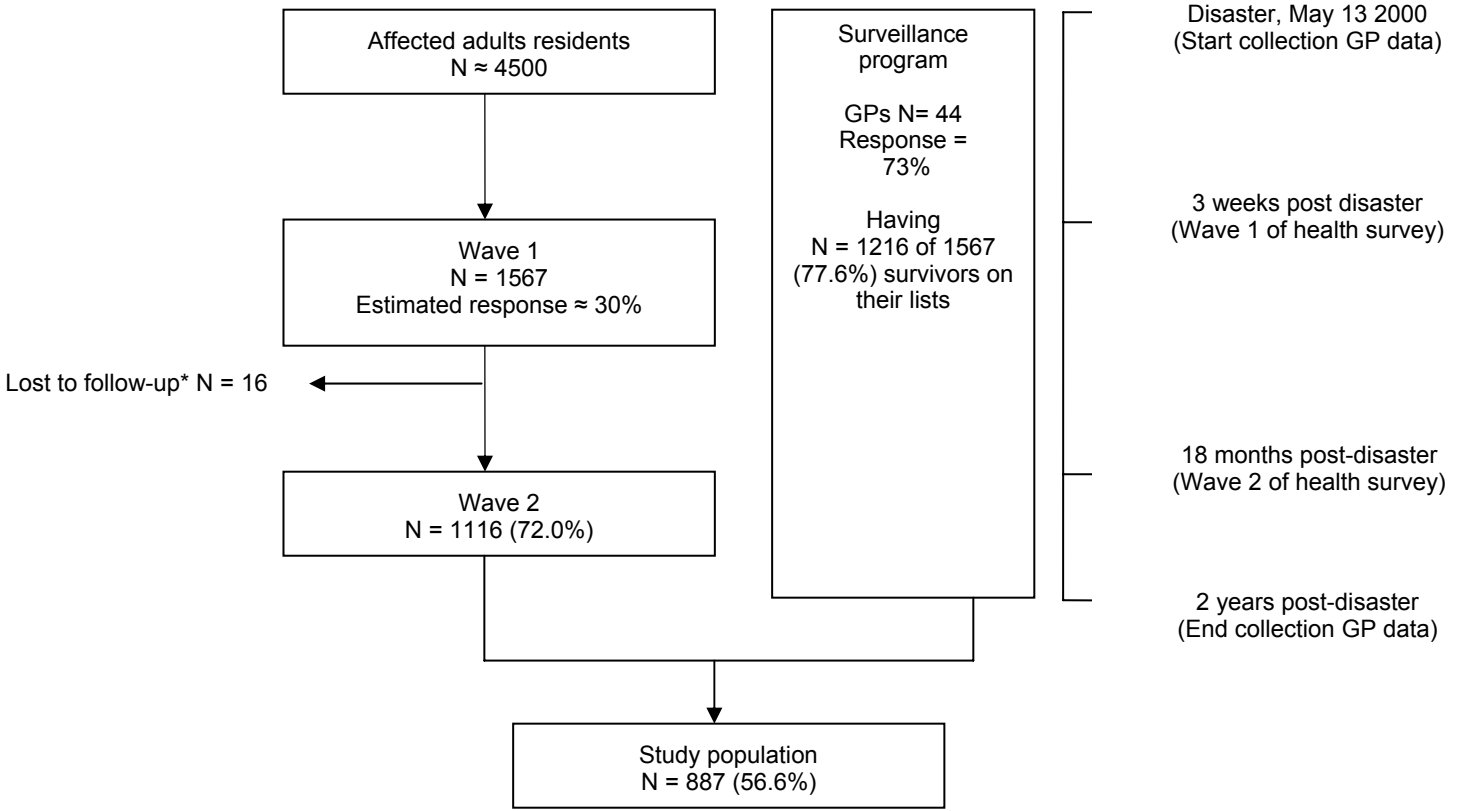
In addition to the health survey, all GPs in Enschede were invited to participate in the surveillance program. Dutch citizens are required to be registered at one general practice, and the GP serves as the gatekeeper for secondary care. In total, 44 out of 60 GPs agreed to participate (73%). Of the non-participating GPs, nine did not have affected residents in their practice. Patients were informed about the participation of their GP in the surveillance program, and nobody denied access to their medical information.

The study population in the present study consisted of 887 survivors who participated at T1 and at T2 of the health survey, and who were registered in one of the participating general practices at the time of the disaster (figure 1).

Measures

Self-reported symptoms – Symptoms were measured at T1 and T2 by the 13-item VOEG scale (Questionnaire into Subjective Health Complaints), a validated questionnaire which has often been used for studies in the Dutch population.[17] The items of this scale ask respondents whether or not (yes/no) they regularly suffer from symptoms such as headache, back pain, and fatigue (table 1).

Figure 1: Flowchart of the study population.



* Lost to follow-up: deceased or emigrated

To make the symptoms compatible with the International Classification of Primary Care (ICPC),[18] the classification system used by the GPs, different stomach and fatigue items were grouped. In addition, listlessness and tingling in arms and legs were excluded because they were not compatible with one of the ICPC codes.

Functional impairment – Participants completed the validated Dutch version of the RAND-36.[19] This questionnaire measures different concepts of functional status. We examined functional status at 18 months post-disaster (T2) because this gives more insight into the true impairment of survivors than the functional status measured three weeks post-disaster. The physical and mental health summary scales were calculated using the means scores of the US population, cut-off scores were based on the standardized mean score minus one standard deviation.[20]

Psychological distress – Feelings of depression and anxiety were measured by the Dutch version of the SCL-90,[21, 22] which assesses the degree of depression and anxiety during the past week. We dichotomized the scales into 'very high' and 'high' versus 'above average', 'average', and below 'average', according to established references for the healthy Dutch population.[21]

Symptoms presented to the GP – We used all information on symptoms and diagnoses that was registered in the EMRs of survivors from the day after the disaster until two years post-disaster, which was half a year after T2. Symptoms and diagnoses were registered by the GP in accordance with the ICPC.[18]

To examine whether survivors presented their self-reported symptom to the GP, we compared self-reported symptoms with corresponding symptoms in the EMRs of survivors. For example, headache on the symptom-scale was compared with the ICPC codes N01 (headache) and N02 (tension headache). We compared the VOEG items with one to four corresponding ICPC codes, except for the item 'pain in bones and muscles', which we compared with 21 different ICPC codes (table 1).

To evaluate the GPs clinical judgment of the symptoms, we used 'episodes of care', that were constructed by GPs. An episode of care is the period from the first presentation of a health problem to a health care provider until the completion of the last encounter for that same health problem.[23] Symptoms were labeled as MUS if they were not associated with a medical diagnosis at some point during the episode.

Statistical analyses

Information from the health survey and the surveillance program was summarized and analyzed by using SAS version 9.1. The percentages of survivors who presented symptoms to the GP were examined for various groups: survivors without self-reported symptoms at T1 and T2 (no symptoms), survivors with self-reported symptoms at T1 but not at T2 (T1 only), survivors self-reported symptoms at T2 but not at T1 (T2 only), and survivors with self-reported symptoms both at T1 and T2 (persistent symptoms).

Table 1: Number of survivors who presented symptoms to the GP that correspond with self-reported symptoms*

Symptoms on symptom-scale (corresponding ICPC codes)	Self-reported symptoms at T1 and/or T2	No. of survivors with self-reported symptom (%)	No. of survivors who presented symptom to the GP (%) †	Risk ratio ‡
Fatigue	No symptoms	93 (11.4)	3 (3.2)	1.0
(ICPC codes: A04, P06)	T1 only	158 (19.3)	22 (13.9)	4.3
	T2 only	0 (0.0)	0 (0.0)	0
	T1 and T2	568 (69.4)	162 (28.5)	8.9
Pain in bones and muscles	No symptoms	278 (35.2)	127 (45.7)	1.0
(ICPC codes: L01 – L20, L29)	T1 only	85 (10.7)	46 (54.1)	1.2
	T2 only	163 (20.6)	104 (63.8)	1.4
	T1 and T2	265 (33.5)	169 (63.8)	1.4
Back pain	No symptoms	318 (40.5)	31 (9.8)	1.0
(ICPC codes: L02, L03)	T1 only	65 (8.3)	10 (15.4)	1.6
	T2 only	150 (19.1)	44 (29.3)	3.0
	T1 and T2	252 (32.1)	73 (29.0)	3.0
Stomachache	No symptoms	366 (41.3)	21 (5.7)	1.0
(ICPC codes: D01 – D03, D06)	T1 only	122 (13.8)	16 (13.1)	2.3
	T2 only	141 (15.8)	29 (20.6)	3.6
	T1 and T2	258 (29.1)	73 (28.3)	5.0
Headache	No symptoms	271 (34.2)	12 (4.4)	1.0
(ICPC codes: N01, N02)	T1 only	146 (18.4)	9 (6.2)	1.4
	T2 only	97 (12.3)	13 (13.4)	3.1
	T1 and T2	278 (35.1)	59 (21.2)	4.8
Shortness of breath	No symptoms	446 (56.2)	10 (2.2)	1.0
(ICPC codes: R02 – R04, R29)	T1 only	71 (9.0)	0 (0.0)	0
	T2 only	118 (14.9)	13 (11.0)	5
	T1 and T2	158 (19.9)	34 (21.5)	9.8
Dizziness	No symptoms	459 (58.2)	15 (3.3)	1.0
(ICPC code: N17)	T1 only	103 (13.0)	3 (2.9)	0.9
	T2 only	62 (7.9)	4 (6.5)	2.0
	T1 and T2	165 (20.9)	26 (15.8)	4.8
Pain in chest and region of heart	No symptoms	501 (64.1)	23 (4.6)	1.0
(ICPC codes: L04, K01 – K03)	T1 only	66 (8.5)	10 (15.2)	3.3
	T2 only	96 (12.3)	17 (17.7)	3.9
	T1 and T2	118 (15.1)	32 (27.1)	5.9

GP: general practitioner; ICPC: International Classification of Primary Care;

* Due to missing values on T1 and T2, N-values differ from the total study population (N= 887);

† Survivors with a symptom (ICPC code) corresponding with the self-report symptom in their (EMR);

‡ Risk ratio: % of survivors with self-reported symptoms who presented symptoms to the GP / % of survivors without self-reported symptoms who presented symptoms to the GP.

Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for the associations between medical care seeking for symptoms reported at T2 and functional impairment and distress reported at T2. We controlled for sex, age, educational level, and immigrant status.

Finally, we calculated the percentages of the symptoms that could not be related to a medical diagnoses in the episodes of care.

Results

Table 1 shows the ICPC codes that correspond with the self-reported symptoms. Survivors were most likely to seek medical care for persistent self-reported symptoms. Except for pain in bones and muscles, about 25% of the persistent symptoms (T1 and T2) were also found in the medical records of survivors. Survivors with self-reported symptoms only at T2 were more likely to present their symptoms to the GP than survivors with self-reported symptoms only at T1. For example, survivors with stomachache at T1 and T2 were five times more likely to seek medical care for their symptom than survivors without stomachache at both waves. In addition, survivors with stomachache at T1 were 2.3 times, and those with stomachache at T2 were 3.6 times more likely to visit the GP with stomachache compared to survivors who did not report this symptom on the symptom-scale.

Table 2 shows the percentage of survivors who reported a high level of functional impairment, depression, anxiety and physical symptoms at T2. Percentages are compared between survivors who did or did not present self-reported symptoms at T2 to the GP in the two years post-disaster. Survivors who sought medical care for fatigue were more likely to have poor mental and physical health as reported on the RAND-36 summary scales and a high level of psychological distress and physical symptoms at T2 than survivors who did not present fatigue to the GP. In addition, survivors who presented pain in bones and muscles, pain in back and stomachache to the GP were somewhat more likely to report poor physical health on the RAND-36 summary scale and a high level of physical symptoms at T2. This pattern was not found for headache, shortness of breath, dizziness, and pain in chest and region of the heart.

Table 3 shows the number of survivors that presented their self-reported symptom to the GP, and the number of symptoms presented to the GP, showing that many survivors presented the same symptom several times to the GP in the two years post-disaster. The majority of symptoms was not related to a diagnosis in an episode of care, and was labeled as MUS. Fatigue was unexplained most often (90.9%), followed by headache (85.6%). Shortness of breath and pain in the chest and the region of the heart were least often labeled as MUS (both 55.8%).

Table 2: Functional status and distress among survivors who did and did not present self-reported symptoms at T2 to the GP

	Presented self-reported symptom to GP (%)	Did not present self-reported symptom to GP (%)	Adjusted OR (95% CI)*
Fatigue	N = 162	N = 406	
Poor physical health †	42.3	25.3	1.9 (1.2-3.1)
Poor mental health †	59.4	39.2	2.4 (1.5-3.7)
Feelings of depression (high)	61.0	44.3	2.1 (1.4-3.2)
Feelings of anxiety (high)	56.4	40.2	2.0 (1.3-3.0)
Physical symptoms (high) ‡	81.5	65.3	2.1 (1.3-3.4)
Pain in bones and muscles	N = 273	N = 155	
Poor physical health †	46.7	19.2	3.5 (2.0-6.4)
Poor mental health †	44.1	37.6	1.3 (0.8-2.1)
Feelings of depression (high)	54.2	47.6	1.3 (0.8-2.1)
Feelings of anxiety (high)	49.0	41.3	1.3 (0.8-2.1)
Physical symptoms (high) ‡	75.5	64.5	1.6 (1.0-2.7)
Back pain	N = 117	N = 285	
Poor physical health †	41.1	27.7	1.9 (1.1-3.3)
Poor mental health †	42.1	41.1	1.0 (0.6-1.7)
Feelings of depression (high)	48.6	51.5	0.8 (0.5-1.3)
Feelings of anxiety (high)	44.4	42.5	0.8 (0.5-1.3)
Physical symptoms (high) ‡	75.2	69.8	1.4 (0.8-2.3)
Stomachache	N = 102	N = 297	
Poor physical health †	43.6	28.5	1.6 (0.8-2.9)
Poor mental health †	50.0	47.4	1.1 (0.6-1.9)
Feelings of depression (high)	57.8	53.7	1.0 (0.6-1.6)
Feelings of anxiety (high)	61.1	46.2	1.6 (0.9-2.7)
Physical symptoms (high) ‡	86.3	77.1	1.8 (0.9-3.6)
Headache	N= 72	N= 303	
Poor physical health †	36.4	29.1	0.9 (0.4-1.8)
Poor mental health †	58.2	47.3	1.2 (0.6-2.3)
Feelings of depression (high)	56.9	51.2	0.9 (0.5-1.7)
Feelings of anxiety (high)	52.9	51.9	0.8 (0.4-1.4)
Physical symptoms (high) ‡	81.9	75.9	1.0 (0.5-2.0)
Shortness of breath	N= 47	N= 229	
Poor physical health †	48.4	41.1	0.8 (0.3-2.1)
Poor mental health †	48.4	52.0	0.6 (0.2-1.5)
Feelings of depression (high)	56.1	60.0	0.6 (0.3-1.5)
Feelings of anxiety (high)	54.8	54.2	0.8 (0.4-1.8)
Physical symptoms (high) ‡	70.2	82.1	0.4 (0.2-0.9)

Table 2 (continued): Functional status and distress among survivors who did and did not present self-reported symptoms at T2 to the GP

	Presented self-reported symptoms to GP (%)	Did not present self-reported symptoms to GP (%)	Adjusted OR (95% CI)*
Dizziness	N= 30	N= 197	
Poor physical health †	52.9	44.3	1.1 (0.4-3.5)
Poor mental health †	52.9	55.0	0.9 (0.3-2.8)
Feelings of depression (high)	53.9	64.5	0.7 (0.3-1.7)
Feelings of anxiety (high)	67.9	60.4	1.5 (0.5-3.8)
Physical symptoms (high) ‡	93.3	87.8	1.5 (0.3-7.6)
Pain in chest and region of heart	N= 49	N= 165	
Poor physical health †	37.5	39.5	0.6 (0.2-1.4)
Poor mental health †	68.8	58.9	1.5 (0.6-3.8)
Feelings of depression (high)	64.3	62.9	0.8 (0.3-1.7)
Feelings of anxiety (high)	73.3	60.8	1.2 (0.5-2.7)
Physical symptoms (high) ‡	87.8	82.4	1.3 (0.5-3.6)

GP = general practitioner;

* Adjusted for possible confounders, sex, age, educational level and ethnicity;

† A low score on the physical and mental component score of the RAND-36;

‡ Six or more symptoms on the 13-item symptoms scale, which is one standard deviation above the reference mean.

Discussion

The majority of symptoms reported by survivors of the fireworks disaster was not presented to the GP. Survivors with persistent symptoms, reported at T1 and T2, were more likely to seek medical care for their symptoms than survivors with self-reported symptoms only at T1 or only at T2. Presenting symptoms to the GP was not consistently associated with a high level of functional impairment and distress. When presented to the GP, the majority of symptoms could not be related to a medical disorder in the episode of care.

To our knowledge, this is the first study that compared self-reported symptoms among survivors of a disaster with the symptoms that are registered in the medical records. Despite this, some potential limitations of the present study deserve attention. Firstly, since only 35.2% of all affected residents participated at T1, participation may have been biased. Shortly after the disaster, all affected residents were registered; this database was used to detect possible demographic differences between participants and non-participants at T1.

Table 3: Diagnoses most frequently associated with symptoms presented to the GP and percentage of symptoms labeled as MUS

Self-reported symptom	No. of survivors that presented self-reported symptom to the GP	No. of symptoms presented to the GP	Diagnosis after clinical judgment of the GP	%
Fatigue	180	420	Various diagnoses	9.1
			No diagnosis/ MUS	*90.9*
Pain in bones and muscles	319	1102	Musculoskeletal disease, other	3.5
			Back syndrome with radiating pain	3.0
			Various diagnoses	21.8
			No diagnosis/ MUS	*71.7*
Back pain	127	268	Back syndrome with radiating pain	13.4
			Arthrosis spinal column	5.6
			Various diagnoses	5.6
			No diagnosis/ MUS	*75.4*
Stomachache	118	317	Esophagus disease	11.0
			Peptic ulcer other	5.4
			Irritable bowel syndrome	3.2
			Stomach function disorder	3.2
			Various diagnoses	13.2
			No diagnosis/ MUS	*64.0*
Headache	81	139	Migraine	7.2
			Various diagnoses	7.2
			No diagnosis/ MUS	*85.6*
Shortness of breath	47	95	Asthma	14.7
			Acute bronchitis	10.5
			Various diagnoses	18.8
			No diagnosis/ MUS	*55.8*
Dizziness	33	46	Vertiginous syndrome	10.9
			No diagnosis/ MUS	*89.1*
Pain in chest and region of the heart	59	95	Various diagnoses	44.2
			No diagnosis/ MUS	*55.8*

GP = general practitioner; MUS = medically unexplained symptoms.

Analysis showed that participation was somewhat selective: women, those living with a partner, those aged 45- 64 years, and immigrants were more likely to participate. To study the magnitude of selection bias, analysis of multiple imputations were used to fill in missing data of non-participants. The results showed that the prevalence estimates of health problems were hardly affected.[15] In addition, there was some selective response at T2; fewer men, fewer younger survivors, and fewer survivors with high levels of health problems at T1 participated. Despite this, no significant differences in the estimated prevalence rates of health problems were observed after multiple imputation.[24]

Secondly, we compared self-reported symptoms with ICPC codes.[18] Therefore, we have to consider the sensitivity and specificity of the ICPC codes that correspond with the self-reported symptoms. The GP might not register all symptoms that the patient presents or the GP might have used an ICPC code that we did not consider as corresponding with the self-reported symptom. This means that there may be some false negatives and thus the percentage of survivors presenting their self-reported symptoms may be slightly higher. In addition, table 1 shows percentages of survivors who had a self-reported symptom neither at T1 nor at T2 but for whom symptoms were registered in the EMRs. These cases are not necessarily false positives, since the symptoms can be correctly registered when survivors had these symptoms only between the two waves.

To date, most studies that examined MUS have been performed in primary or secondary care and have examined symptoms for which patients sought medical attention. The present study examined whether self-reported symptoms among survivors of a man-made disaster were presented to the GP. The majority of self-reported symptoms was not presented to the GP. Apparently, most of the symptoms were self-limiting or not considered severe enough to seek medical attention. Symptoms that were reported only at T1 were less often presented to the GP than symptoms reported at T2 or persistent symptoms (T1 and T2). It is possible that, shortly after the disaster, survivors were mostly impaired by psychological problems such as anxiety and depression, and they only sought medical help for physical symptoms after a longer period when these symptoms became persistent and disabling. It can also be speculated that symptoms at T1 were likely to be transient or were explained by the survivors as a normal reaction to the disaster. Indeed, cognitions about the symptoms affect medical care seeking decisions. For example, Sensky et al. found that frequent attenders to general practice had less normalizing explanations for their symptoms than the comparison group.[25] In addition, Cameron et al., found that symptoms that were attributed to stress rather than to illness, were less likely to be presented to the GP.[26]

In a recent study among survivors of the fireworks disaster, we showed that the self-reported symptoms are strongly related with a high level of functional

impairment and psychological problems.[27] For that reason, we examined whether survivors with a high level of functional impairment and psychological distress were more likely to seek medical care for their symptoms. Survivors who presented fatigue to the GP were significantly more likely to have a high level of impairment and distress. Survivors who presented pain in bones and muscles, pain in back and stomachache to the GP were more likely to report a poor physical health and a have a high level of physical symptoms at T2 compared to those who did not present these symptoms to the GP. This pattern was, however, not found for the other symptoms. Apparently, a high level of impairment and distress were not the major reasons to seek medical care and it is likely that the decision to consult a GP was based on other factors such as perceived susceptibility to illness, perceived severity of symptom and beliefs about the cause of the symptoms.[25, 26, 28, 29]

Of the self-reported symptoms that were also presented to the GP, 56% to 91% remained medically unexplained in the episode of care. This finding is consistent with a study among survivors of an airplane crash in Amsterdam in which it was shown that 57% to 85% of symptoms presented to the GP remained unexplained.[30] These results suggests that physical symptoms among survivors of disasters such as headache, stomachache and fatigue are likely to be similar to MUS.

In conclusion, the majority of symptoms reported by the survivors of the fireworks disaster was not presented to the GP. On the one hand, this indicates that not all symptoms reported in epidemiologic studies after traumatic events are of clinical pertinence. On the other hand, this study shows that the symptoms presented to the GP are only the tip of the iceberg and GPs will not see all survivors who suffer from physical symptoms in their practice. Also, the survivors who present their symptoms to the GP are not always those who have a high level of functional impairment and distress. When presented to the GP, most symptoms could not be related to a medical disorder, and were labeled as MUS. This result indicates that physical symptoms reported in a questionnaire are likely to be medically unexplained.

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CHAPTER 5

Risk factors for physical symptoms after a disaster: a longitudinal study

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Submitted

Abstract

Objective: Although symptoms such as fatigue, headache and pain in bones and muscles are common after disasters, risk factors for these symptoms among disaster survivors have rarely been studied. We examined predisposing, precipitating and perpetuating factors for these physical symptoms among survivors of a man-made disaster. In addition, we examined whether risk factors for physical symptoms differ between survivors and controls.

Methods: Survivors completed a questionnaire three weeks after the disaster (N= 1567), 18 months after the disaster, and four years post-disaster. Symptoms and risk factors were measured using validated questionnaires. A comparison group was included at waves 2 and 3 (N= 821). Random coefficient analysis was used to study risk factor for symptoms.

Results: Female gender (Beta (B)= 1.0, 95% confidence interval (CI): 0.6, 1.4), immigrant status (B= 1.0, 95% CI: 0.6, 1.4), cigarette smoking (B= 0.5, 95% CI: 0.1, 0.8) and pre-disaster psychological problems (B= 0.8, 95% CI: 0.1, 1.4) were predisposing factors for symptoms. Although disaster-related factors were predictors, the magnitude of this association was reduced when perpetuating factors were added. Intrusions and avoidance, depression, anxiety and sleeping problems were perpetuating factors for physical symptoms among survivors and mediated the relation between traumatic stress and physical symptoms. Risk factors for symptoms were comparable between survivors and controls.

Conclusion: The results indicate that health care workers should be alert for physical symptoms among individuals with a high level of psychological problems.

Introduction

Traumatic life events have been described as important precipitating factors for medically unexplained symptoms (MUS) such as stomachache, headache and fatigue.[1-3] Most of the studies that relate trauma to MUS have been performed among Gulf War veterans and have found higher prevalence rates of unexplained symptoms among veterans than among control groups.[4-6] The majority of studies after disasters have focused on mental health problems such as post-traumatic stress disorder (PTSD), depression and anxiety but a few have also examined physical symptoms comparable to MUS and found elevated levels among survivors.[7-9]

Although high levels of symptoms are found among survivors, not every survivor develops symptoms, implying that some survivors are more at risk than others. Risk factors for physical symptoms among survivors of disasters have not often been studied; only a few potential risk factors such as female gender and high levels of damage have been consistently identified in disaster studies.[7] Risk factors for symptoms that are often referred to as MUS have been studied most frequently among the general population and among war veterans, showing that female gender,[4, 5, 10-15] low socioeconomic status,[12-14] living alone,[11, 12, 14] and older age have found to be risk factors for symptoms.[5, 11, 14] In addition to these predisposing factors, comorbid psychological problems such as PTSD and anxiety have been described as perpetuating factors that maintain and exacerbate symptoms.[5, 10, 11, 13, 14] Several studies among war veterans have indicated that these psychological problems, especially PTSD, mediate the relation between traumatic exposure and physical symptoms. [16, 17]

Insight into factors that predict symptoms among survivors of disasters is useful to better understand the relation between traumatic exposure and physical symptoms. In addition, information about risk factors could be important for health care workers and policy makers since it facilitates both the detection of those at risk and the implementation of preventive interventions to reduce risk. It is, however, not known whether the risk factors that have been found in studies among the general population and among war veterans are similar for survivors of disasters. Also, precipitating factors such as destroyed house and peritraumatic dissociation, which has been described as a potential risk factor for symptoms,[1] have not been examined in previous studies. In the present longitudinal study, we address two research questions. First, what are predisposing (e.g. gender), precipitating (e.g. house destroyed) and perpetuating (e.g. anxiety) factors for physical symptoms (e.g. headache, fatigue) among survivors of a man-made disaster? Second, are risk factors for symptoms comparable between survivors and non-traumatized controls?

Methods

Study design and participants

On May 13, 2000 a fireworks depot exploded in a residential area in the city of Enschede, the Netherlands. As a result of the explosion and subsequent fire, 23 persons were killed, more than 900 people were injured and about 1200 people were forced to relocate because their houses were severely damaged or destroyed. The Dutch government declared this a national disaster and started a longitudinal study into the health consequences of the disaster.

Details of the study population and procedures have been described elsewhere.[9, 18-20] In summary, the first wave (T1) of this study was performed three weeks post-disaster. Residents of the affected area were invited to participate in the health survey by means of letters and announcements in the local media. In total, 1567 affected residents (estimated response ≈ 30%) completed a questionnaire at T1.

Approximately 18 months post-disaster, from November 2001 to January 2002, the second wave (T2) was performed. All T1 participants who had given informed consent for future contact received an announcement letter. In addition, a sample of 1600 residents was drawn from the registry office in the city of Tilburg, the Netherlands, to serve as a control group. The control group was stratified according to sex, age, and country of origin to make it comparable to the survivors who participated at T1.

To stimulate participation, survivors and controls were telephoned at home after the announcement letter was sent. If a respondent agreed to participate, a questionnaire was sent to his or her home address in the preferred language (Dutch, German, English or Turkish). Interpreters were available at a community center to assist in completing the questionnaires. In total, 1116 survivors (response 72%) and 821 controls (response 52%) completed a questionnaire at T2.

Nearly four years post-disaster, (January-March 2004) a third survey (T3) was performed. Except for participants who were lost to follow-up, all survivors of T1 and all controls from T2 who had given written informed consent for future contact were invited to participate. Participation was stimulated by means of home visits and telephone calls. As at T2, interpreters were available at the community center to assist in completing the questionnaires. In total, 995 survivors (response 66%) and 589 controls (response 74%) completed a questionnaire at T3.

Measures

The questionnaires were comparable for survivors and controls, but disaster-related questions were not included in the control questionnaire.

Physical symptoms. At T1, symptoms were measured by a 13-item questionnaire into subjective health complaints (VOEG-13),[21] a validated scale that has

often been used for studies in the Dutch population. The items asked respondents whether they regularly have symptoms such as headache and stomachache. At T2 and T3, this questionnaire was extended to 21 different symptoms (VOEG-21). In this study, the extended scale measured at T2 and T3 was used as the outcome variable.[9] The following symptoms were measured: listlessness, fatigue, forgetfulness, ringing in the ears, pain in the chest and the region of the heart, lump in the throat, stomachache, pain in the bones and muscles, nausea, dizziness, pain in the neck and shoulders, cold fingers, hand and feet, excessive sweating, pain in the back, headache, deafness, tight feeling in the chest, tingling in arms and chest, poor vision, shortness of breath, and fainting.

Predisposing factors. The following demographic and lifestyle characteristics were measured: sex, age, educational level, occupational status (having a paid job), cigarette smoking and immigrant status (first and second generation, mainly of Turkish origin). For survivors, self-reported pre-disaster psychological and relational problems reported at T1 were included.

Precipitating factors. Several experiences during or shortly after the disaster were measured at T1: relocation due to severely damaged or destroyed house; the loss of loved ones (family, colleagues, friends); injury requiring medical treatment. In addition, several questions asked about what survivors had seen, heard and felt during the disaster. A scale was made for the 29 items; survivors with 18 or more experiences (80^{th} percentile) were defined as having a high disaster exposure. Finally, the extent to which survivors had experienced peritraumatic dissociation during or immediately after the disaster was measured by the Peritraumatic Dissociative Experiences Questionnaire. The total score of this scale ranges from 10 to 50. Survivors with a score higher than 35 (80^{th} percentile) were defined as having high levels of peritraumatic dissociation.[22]

Perpetuating factors. Several mental health problems were measured at all waves of the health survey. For the survivors, the impact of event scale (IES) was used to measure intrusions and avoidance reactions which serve as an indication for a clinical level of PTSD.[23,24] Survivors with an overall score above 25 were defined as having a high level of intrusions and avoidance reactions. Among survivors and controls, feelings of depression, anxiety and hostility were measured by the Dutch version of the Symptom Checklist (SCL-90).[25] We dichotomized the scales into high (80^{th} percentile) versus low scores, according to established references for the healthy Dutch population.[26] Sleeping difficulties were measured by the Groninger Sleep Quality Scale;[27] the scale ranges from 0 to 10, respondents with a score above four were defined as having severe sleeping difficulties.

Statistical analysis

For both survivors and controls, all wave completers had different characteristics than non-respondents at follow-up.[28] Since deleting the incomplete cases might lead to biased results, we corrected for this selective response by means of multiple imputation (MI).[29] This statistical method makes use of the intercorrelations of variables from the non-missing data to estimate plausible values for the data that is missing. MI is considered a superior method for dealing with missing data than other more commonly used methods such as mean imputation.[29, 30] The outcome of interest (physical symptoms) and all risk factors, measured at the different waves, were included in the MI model. In addition, variables that highly correlated with the potential risk factors and with the symptom scale were selected since this increases the power of the multiple imputation model.[30] Table 1 describes the additional variables included in the MI model. We did not dichotomize any of the continuous variables entered in the model. We applied an adapted version of predictive mean matching using a SAS macro that makes partial use of the SAS (version 9.1) multiple imputation (MI) procedure.[37] Five datasets were generated in which the non-missing data are the same and the values imputed for the missing data vary between datasets. We analyzed these datasets separately and combined the results using the 'MIANALYZE' procedure in SAS, which produces valid confidence intervals by taking the uncertainty due to missing data into account.

Pearson correlation analysis was performed to get insight into the relationships between the precipitating factors, perpetuating factors and reported symptoms.

Because the survey data were collected longitudinally, with three measurements times for the survivors, random coefficient analysis (RCA) was used to examine risk factors for symptoms among survivors. RCA takes into account the correlation between repeated measurements on a subject and both subject-level (e.g. gender) and time-varying (e.g. depression) variables can be included simultaneously in the model. In the current analyses, random intercept models were used, which means that each subject has his own intercept.[38] Before performing RCA, multiple regression analyses were performed for symptoms at T2 and T3 separately to confirm that the direction and strength of associations between the risk factors and symptoms were similar for the two waves. RCA proceeded in four steps. In the first model we studied whether predisposing factors predicted symptoms at T2 and T3. In the second model, we added the precipitating factors to the model. In the third model, perpetuating factors at an earlier point in time (T-1) then the reported symptoms were added. Finally, concurrent perpetuating factors were added to the model.

Since disaster-related factors were not measured in the control survey, considerably fewer risk factors were examined for controls. The control group was included only at T2 and T3, and therefore, risk factors could only be studied for symptoms reported at T3. For these reasons, multiple regression models were used to

compare risk factors between survivors and controls. The survivor and control group were analyzed separately to determine whether the direction and strength of associations between the risk factors and symptoms reported at T3 were similar.

Table 1: Variables used in the multiple imputation model, in addition to the 21-item symptom scale and the selected potential risk factors *

Description of variable	Survivors	Controls
	Available at waves †	Available at waves
13-item VOEG scale [21]	T1	NA
Optimism sub-scale [31]	T2, T3	T2, T3
Social support scale [32]	T2, T3	T2, T3
Distrust sub-scale [33]	T2, T3	NA
Physical functioning sub-scale [34, 35]	T2, T3	T2, T3
Physical role limitations sub-scale [34, 35]	T1, T2, T3	T2, T3
Emotional role limitations sub-scale [34, 35]	T1, T2, T3	T2, T3
Energy/ fatigue sub-scale [34, 35]	T2, T3	T2, T3
Mental well-being sub-scale [34, 35]	T2, T3	T2, T3
Social functioning sub-scale [34, 35]	T1, T2, T3	T2, T3
Pain sub-scale [34, 35]	T1, T2, T3	T2, T3
General health sub-scale [34, 35]	T1, T2, T3	T2, T3
Health change sub-scale [34, 35]	T1, T2, T3	T2, T3
Somatization sub-scale [25, 26]	T1, T2, T3	T2, T3
Obsessive-compulsive sub-scale [25, 26]	T1, T2, T3	T2, T3
Sleeping problems sub-scale [25, 26]	T1, T2, T3	T2, T3
Phobic anxiety sub-scale [25, 26]	T1, T2, T3	T2, T3
Interpersonal sensitivity sub-scale [25, 26]	T1, T2, T3	T2, T3
State anger sub-scale [36]	T2	NA
Anger expression sub-scale [36]	T2	NA
5 items of the IES [23, 24] ‡	T1, T2, T3	NA
4 items of the SCL-90 depression sub-scale [25, 26] ‡	T1, T2, T3	T2, T3
3 items of the SCL-90 anxiety sub-scale [25, 26] ‡	T1, T2, T3	T2, T3
2 items of the SCL-90 hostility sub-scale [25, 26] ‡	T1, T2, T3	T2, T3

* Additional scales and items correlated r > .50 with the 21-item symptom scale and the selected potential risk factors;

† To be included in the random coefficient analyses (RCA), scales had to be available at all three wave of the health survey;

‡ The IES was missing when 2 or more items were missing and the SCL-90 sub-scales were missing when 3 or more items were missing. Since the individual items were less often missing and highly correlated with the sub-scales, these items were included in the imputation model;

NA, not available.

These stratified analyses revealed that risk factors for symptoms among survivors and controls were comparable. The two groups were thus analyzed in one model, with an indicator for 'disaster exposure' (survivors versus controls). Although the confidence intervals were overlapping, some factors appeared to differ between survivors and controls. For these factors, interaction effects were tested in the combined model.

Because respondents with chronic diseases could have symptoms that are associated with their disease, all results were adjusted for concurrent chronic diseases such as diabetes, cancer, asthma, and chronic stomach disorders.

Results

Correlation analysis

Table 2 shows the Pearson correlation coefficients among precipitating factors, perpetuating factors and physical symptoms reported by survivors at T2 and T3 and shows that these factors were strongly related to physical symptoms. The correlation coefficients were comparable for the control group (data not shown).

Risk factors for symptoms reported by survivors

Table 3 presents the results of the RCA for symptoms reported by survivors at T2 and T3. Model 1 shows that female survivors reported on average 1.2 symptoms more on the 21-item symptoms scale than male survivors (B= 1.2, 95% CI= 0.8, 1.6). In addition, the mean number of symptoms was higher for survivors with a low educational level, without a paid job, for immigrants, cigarette smokers, and those with pre-disaster psychological and pre-disaster relational problems. These associations remained when precipitating factors were added (model 2). Model 2 shows that disaster-related factors were associated with a higher mean number of symptoms among survivors. For example, survivors who had lost a loved one reported on average one symptom more than those who had not (B= 1.0, 95% CI= 0.2, 1.8).

This association diminished after entering perpetuating factors into the model (models 3 and 4). With the exception of gender, the associations between predisposing factors and symptoms also diminished after adding perpetuating factors. All distress reactions measured at an earlier time point, with the exception of feelings of hostility (B= 0.2, 95% CI= -0.3, 0.6), were positively associated with a higher mean number of symptoms (model 3). This relation diminished when concurrent perpetuating factors were added (model 4), indicating stronger associations between concurrent distress and symptoms.

The full model showed that female gender, older age, an immigrant status, smoking cigarettes, pre-disaster psychological problems, physical symptoms, intrusions and avoidance reactions, feelings of depression, and feelings of anxiety measured at

an earlier time point as well as concurrent intrusions and avoidance, feelings of depression, anxiety and sleeping problems were associated with a higher mean number of symptoms among survivors at T2 and T3 of the health survey.

Risk factors for symptoms reported by survivors and controls

Table 4 shows the results of the multiple regression analysis in which potential risk factors for symptoms among survivors and controls were analyzed together. When predisposing factors were controlled for, survivors of the disaster reported on average 1.1 symptoms more (B= 1.1, 95% CI= 0.7, 1.4) at T3 than control subjects (model 1). When psychological problems were entered in the model (models 2 and 3), the associations between predisposing factors and symptoms diminished and the effect of disaster exposure disappeared (B= -0.1, 95% CI= -0.4, 0.2 in model 3). Model 4 showed that among survivors and controls, female gender, no paid job, immigrant status, physical symptoms at an earlier point in time, as well as concurrent feelings of depression, anxiety, and sleeping problems were associated with physical symptoms at T3. There was an interaction effect between disaster survivor and concurrent sleeping problems (B= 0.8, 95% CI= 0.1, 1.6) indicating that survivors with a high level of sleeping problems at T3 reported on average nearly one symptom more at T3 than did controls with a high level of sleeping problems. The associations between the other risk factors and symptoms were similar between survivors and controls.

Discussion

In the present longitudinal study, we examined predisposing, precipitating and perpetuating factors for physical symptoms reported by survivors of a fireworks disaster. Random coefficient analysis (RCA) showed several predisposing factors for symptoms among survivors: female gender, older age, immigrant status, cigarette smoking and pre-disaster psychological problems were associated with an increase in the mean number of symptoms reported 18 months and four years post-disaster. In addition, physical symptoms, intrusions and avoidance, depression and anxiety measured at an earlier point in time as well as concurrent intrusions and avoidance, depression, anxiety and sleeping problems were risk factors for symptoms among survivors. Risk factors were comparable between survivors and non-traumatized controls.

Correlation analyses showed associations between precipitating factors, especially house destroyed and disaster exposure, and physical symptoms at T2 and T3. This finding is consistent with other disaster studies, showing that high levels of damage due to the disaster was a risk factor for physical symptoms.[7]

Table 2: Pearson correlation coefficients among precipitating factors and perpetuating factors selected for random coefficients analyses for physical symptoms reported by survivors (N= 1567) at T2 and T3*

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.	19.	20.	21.	22.	23.
1. House destroyed	-																						
2. Lost a loved one	.01	-																					
3. Injury self	.12	.02	-																				
4. Disaster exposure	.22	.06	.16	-																			
5. Dissociation	.23	.07	.10	.37	-																		
6. PTSD symptoms T1 †	.18	.06	.10	.35	.67	-																	
7. PTSD symptoms T2 †	.21	.07	.11	.29	.42	.54	-																
8. PTSD symptoms T3 †	.24	.08	.12	.32	.43	.50	.73	-															
9. Depression T1	.27	.08	.13	.33	.62	.67	.55	.53	-														
10. Depression T2	.19	.08	.14	.27	.39	.43	.64	.57	.63	-													
11. Depression T3	.18	.07	.13	.29	.36	.42	.57	.65	.60	.79	-												
12. Anxiety T1	.23	.08	.13	.34	.61	.65	.55	.54	.89	.60	.56	-											
13. Anxiety T2	.20	.06	.13	.28	.39	.43	.66	.60	.53	.89	.74	.62	-										
14. Anxiety T3	.17	.06	.13	.28	.37	.42	.59	.68	.55	.75	.90	.58	.79	-									
15. Hostility T1	.21	.07	.14	.28	.49	.52	.43	.43	.78	.56	.53	.75	.53	.49	-								
16. Hostility T2	.17	.07	.13	.25	.34	.34	.54	.52	.53	.83	.70	.52	.80	.68	.60	-							
17. Hostility T3	.16	.07	.12	.27	.33	.34	.48	.56	.51	.70	.84	.49	.67	.80	.54	.73	-						
18. Sleeping problems T1	.18	.04	.09	.37	.46	.54	.46	.44	.57	.42	.41	.56	.42	.41	.44	.33	.33	-					
19. Sleeping problems T2	.19	.02	.08	.27	.33	.39	.33	.46	.44	.53	.43	.43	.53	.42	.35	.41	.37	.53	-				
20. Sleeping problems T3	.19	.03	.08	.29	.31	.40	.31	.55	.48	.48	.56	.46	.48	.54	.37	.41	.46	.53	.61	-			
21. Symptoms (V13) T1 ‡	.16	.06	.07	.32	.46	.51	.46	.37	.62	.42	.44	.61	.43	.41	.51	.36	.36	.55	.35	.43	-		
22. Symptoms (V13) T2 ‡	.17	.09	.08	.28	.39	.45	.39	.47	.54	.62	.55	.53	.60	.54	.43	.50	.45	.49	.56	.51	.61	-	
23. Symptoms (V21) T2 ‡	.19	.07	.11	.28	.41	.46	.41	.52	.57	.67	.61	.57	.67	.61	.45	.55	.52	.48	.55	.52	.59	.90	-
24. Symptoms (V21) T3 ‡	.18	.05	.13	.29	.37	.44	.37	.57	.56	.63	.70	.57	.62	.68	.46	.52	.59	.44	.46	.60	.57	.70	.75

* Continuous variables were used in the correlation analysis, except for house destroyed, lost a loved one and injury self.

† Intrusions and avoidance reactions measured by the Impact of Event Scale (IES)

‡ V13: 13-items VOEG-scale; V21: 21-item VOEG-scale.

Table 3: Associations between predisposing, precipitating and perpetuating factors and physical symptoms among survivors (N=1567) reported at T2 and T3 of the longitudinal health survey *

	Model 1: Predisposing factors only		Model 2: Model 1 + precipitating factors		Model 3: Model 2 + perpetuating factors T-1		Model 4: Model 3 + concurrent perpetuating factors	
	B	95% CI	B	95% CI	B	95% CI	B	95% CI
Intercept	6.3	5.5, 7.0	6.6	5.7, 7.4	3.6	2.8, 4.4	1.8	1.1, 2.5
Female	1.2	0.8, 1.6	1.1	0.7, 1.6	0.8	0.4, 1.2	1.0	0.6, 1.4
Age	0.01	-0.004, 0.03	0.02	0.001, 0.03	0.01	-0.002, 0.03	0.02	0.004, 0.03
Low educational level	0.7	0.2, 1.2	0.5	0.1, 1.0	0.3	-0.1, 0.7	0.1	-0.3, 0.5
No paid job T-1	0.9	0.4, 1.3	0.8	0.3, 1.2	0.7	0.3, 1.1	0.3	-0.1, 0.7
Immigrant	3.5	3.0, 4.0	2.9	2.4, 3.4	2.0	1.6, 2.4	1.0	0.6, 1.4
Smoker T-1	0.9	0.3, 1.4	0.8	0.2, 1.3	0.6	0.1, 1.0	0.5	0.1, 0.8
Pre-disaster psychological problems	2.0	1.1, 3.0	1.8	0.9, 2.7	1.1	0.3, 1.8	0.8	0.1, 1.4
Pre-disaster relational problems	1.8	0.4, 3.2	1.4	0.1, 2.8	0.9	-0.1, 2.0	0.4	-0.4, 1.2
House destroyed			1.0	0.5, 1.5	0.5	0.1, 0.8	0.2	-0.2, 0.5
Lost a loved one			1.0	0.2, 1.8	0.5	-0.2, 1.2	0.4	-0.3, 1.0
Injury self			1.2	0.5, 1.9	0.8	0.2, 1.4	0.6	-0.001, 1.2
High disaster exposure			1.1	0.5, 1.6	0.5	0.1, 1.0	0.2	-0.2, 0.6
Peritraumatic dissociation			1.7	1.2, 2.1	0.7	0.3, 1.1	0.3	0.1, 0.7
Physical symptoms T-1 †					1.4	1.0, 1.9	1.0	0.6, 1.5
Intrusions and avoidance T-1					0.8	0.5, 1.1	0.5	0.2, 0.8
Depressive feelings T-1					1.0	0.5, 1.5	0.5	0.02, 1.0
Feelings of anxiety T-1					0.9	0.5, 1.4	0.5	0.1, 1.0
Feelings of hostility T-1					0.2	-0.3, 0.6	-0.1	-0.5, 0.4
Sleeping problems T-1					0.6	0.2, 1.0	0.3	0.04, 0.7
Intrusions and avoidance (concurrent)							0.8	0.3, 1.3
Depressive feelings (concurrent)							1.5	1.1, 2.0
Feelings of anxiety (concurrent)							1.3	0.9, 1.7
Feelings of hostility (concurrent)							0.4	-0.002, 0.9
Sleeping problems (concurrent)							1.6	1.1, 2.0

* The regression coefficient (B) is adjusted for concurrent chronic diseases and represents the increase or decrease of symptoms reported on the 21-item symptom scale for survivors with that characteristic;

† 13-item symptom scale (VOEG-13).

Previous studies did however, not adjust for distress after the disaster. In our study, the association between disaster-related factors and physical symptoms diminished considerably after adding distress reactions such as feelings of depression and anxiety to the model. In addition, peritraumatic dissociation, which has been proposed as a potential risk factor for physical symptoms and other distress reactions was associated with physical symptoms but this association also disappeared after adjusting for psychological distress.[1, 39]

These results support the hypothesis that distress following traumatic exposure mediates the relation between exposure and physical health problems.[16, 17] Schnurr and Green proposed PTSD as the primary pathway through which trauma leads to physical health problems.[16] In our study, the associations between depression and anxiety and symptoms were as strong or even stronger than the association between symptoms of PTSD and physical symptoms. This suggests that PTSD might not be the primary pathway, but that other post-disaster distress reactions also mediate the relation between exposure and physical symptoms.

In the analyses comparing survivors and controls, the effect of disaster exposure disappeared after adding perpetuating factors. This result supports the hypothesis that physical symptoms are more strongly related to distress than to the traumatic exposure and confirms previous findings that psychological problems are important risk factors for physical symptoms. [5, 10, 11, 13, 14]

Risk factors for physical symptoms among survivors were also comparable with the risk factors for symptoms that are referred to as MUS among the general population and war veterans and were similar between survivors and controls.[4, 5, 10-15] This indicates that risk factors for symptoms among disaster survivors are similar to risk factors for physical symptoms among other populations.

High correlations were found among the different perpetuating factors and between the perpetuating factors and physical symptoms. High correlations between factors might result in unstable estimates and high standard errors. Collinearity diagnostics indicated that collinearity was not a problem in our regression models. However, the strong correlations do indicate a high level of comorbidity among the disaster survivors. Previous studies among the general population and war veterans also found a high levels of depression, anxiety and PTSD among individuals with MUS.[11, 14] In addition, we found that about 65% of survivors with 10 to 14 symptoms and about 85% of survivors with 15 or more symptoms on the symptom scale reported high levels of depression and anxiety, suggesting that symptoms are related to, but not fully dependent on psychological problems.[9]

Table 4: Associations between possible risk factors and physical symptoms among survivors (N= 1567) and controls (N= 821) reported at T3 of the longitudinal study *

	Model 1: Predisposing factors only		Model 2: Model 1 + perpetuating factors T-1		Model 3: Model 2 + concurrent perpetuating factors		Model 4: Model 3 + interaction terms	
	B	95% CI	B	95% CI	B	95% CI	B	95% CI
Intercept	1.4	0.8, 2.2	0.7	0.1, 1.3	0.6	-0.02, 1.3	0.6	-0.1, 1.2
Female	0.8	0.4, 1.3	0.8	0.4, 1.3	0.9	0.4, 1.3	0.9	0.4, 1.3
Age	-0.01	-0.02, 0.06	0.01	-0.003, 0.02	0.01	-0.001, 0.02	0.01	-0.001, 0.02
Low educational level	0.3	-0.1, 0.7	-0.1	-0.5, 0.2	-0.1	-0.4, 0.2	-0.1	-0.4, 0.2
No paid job	1.5	1.1, 2.0	0.9	0.4, 1.3	0.6	0.3, 0.9	0.6	0.2, 0.9
Immigrant	3.2	2.7, 3.7	1.7	1.0, 2.3	1.1	0.5, 1.7	1.1	0.4, 1.7
Smoker	1.0	0.4, 1.6	0.5	0.02, 1.1	0.4	-0.1, 0.8	0.4	-0.1, 0.8
Survivor of fireworks disaster	1.1	0.7, 1.4	-0.1	-0.4, 0.3	-0.1	-0.4, 0.2	-0.4	-0.5, 0.4
Physical symptoms T-1 †			2.9	2.5, 3.4	2.6	2.1, 3.0	3.1	2.4, 3.7
Feelings of depression T-1			0.9	0.3, 1.5	0.3	-0.2, 0.8	0.3	-0.3, 0.8
Feelings of anxiety T-1			1.5	0.9, 2.1	0.7	0.1, 1.4	-0.03	-1.0, 1.0
Feelings of hostility T-1			0.6	0.1, 1.2	0.2	-0.3, 0.7	0.5	-0.2, 1.2
Sleeping problems T-1			0.7	0.3, 1.0	0.02	-0.5, 0.5)	0.4	-0.5, 1.2
Feelings of depression (concurrent)					1.4	0.8, 2.0	1.4	0.8, 2.0
Feelings of anxiety (concurrent)					1.1	0.6, 1.5	1.1	0.6, 1.6
Feelings of hostility (concurrent)					0.5	-0.002, 1.0	0.5	-0.003, 1.0
Sleeping problems (concurrent)					1.6	1.1, 2.2	1.0	0.3, 1.7
Survivor*physical symptoms t-1							-0.7	-1.5, 0.1
Survivor*feelings of anxiety t-1							1.0	-0.01, 2.0
Survivor*feelings of hostility t-1							-0.5	-1.5, 0.5
Survivor*sleeping problems t-1							-0.4	-1.4, 0.5
Survivor*sleeping problems (concurrent)							0.8	0.1, 1.6

* The regression coefficient (B) is adjusted for chronic diseases and represents increase or decrease in symptoms on the 21-item symptom scale for survivors with that characteristic;

† 13-item symptom scale (VOEG-13).

This study has several strengths. Firstly, information about disaster exposure was obtained three weeks post-disaster. Delay in data collection may introduce recall bias and important data may be lost forever. Secondly, we included a control group at T2 and T3, which gave us the opportunity to compare risk factors for symptoms between survivors and controls. Thirdly, in contrast to most of the previous disaster studies that examined risk factors for physical symptoms, we were able to longitudinally analyze the risk factors, showing that, in addition to concurrent distress, distress reactions reported at an earlier point in time were risk factors for symptoms. This information is useful for screening of people at risk for developing symptoms.

Despite these strengths, some potential limitations should be considered. Firstly, the response rate among residents at T1 was low (about 30%), and participation was somewhat selective: women, those living with a partner, those aged 45-64 years and immigrants were more likely to participate. However, further analyses indicated that the prevalence estimates of health problems were barely affected by this selective participation.[40] In addition, there was some selective response at T2 and T3. Among survivors all wave completers (N= 815) were more likely to be female, middle aged, highly educated, native Dutch and to have a paid job than survivors who did not participate at all three surveys. Among controls, those who participated at both surveys (N= 793) were younger, more highly educated, and more likely to have a paid job than controls who participated only at the first survey. To overcome possible bias, we corrected for selective response by means of multiple imputation (MI). We believe that the MI model was adequate for predicting the missing data because it included variables related to missingness (e.g. gender, age, education). We also expect that the inclusion of additional variables in the imputation model (table 1) that were strongly correlated with the variables of interest (containing missing values), increased the power of the multiple imputation model.[31] The results of RCA and multiple regression analysis with and without imputed data were comparable, indicating that selective response hardly biased the associations between the risk factors and symptoms.

A second limitation of the current study is that symptoms were measured by means of a questionnaire. Since only examination by a physician can exclude medical disorders, it is not known whether the symptoms reported by survivors and controls are medically unexplained (MUS) or can be explained by a medical disorder. However, in a recent study, we found that symptoms reported by the survivors showed features similar to those of MUS, such as associations with functional impairment and high levels of psychological problems.[9] Also, when presented to the GP, the majority of symptoms (56% – 91%) reported by survivors could not be explained by a medical disorder and were labeled as MUS.[28, 41]

To our knowledge, this was the first study that thoroughly studied risk factors for physical symptoms among survivors of a disaster. Psychological problems such as

PTSD and depression were important perpetuating factors for symptoms and mediated the relation between traumatic exposure and symptoms that are often referred to as MUS. The risk factors were similar between survivors and controls and were comparable with risk factors that have been found in studies among the general population and war veterans. These results indicate that health care workers should be alert for physical symptoms especially among individuals with psychological problems and might prevent the development of physical symptoms by treating these psychological problems.

Acknowledgements
We gratefully thank Dr. S. van Buuren and G. Jacobusse (TNO Quality of Life) for their statistical advice and Dr. H. Boshuizen (RIVM) for the use of her SAS macro for predictive mean matching.

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CHAPTER 6

Risk factors for symptoms after traumatic stress: a 5-year longitudinal study in general practice

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Submitted

Abstract

Background: Traumatic events such as disasters have been described as an important precipitating factor for medically unexplained symptom (MUS). However, MUS have not often been studied among survivors of disasters. This study examines the course of MUS presented to the general practitioner (GP) in the one year before the disaster and in the first four years after a man-made disaster and studies the risk factors for MUS among survivors. This information may help GPs to identify individuals at risk for MUS.

Method: Data were extracted from the electronic medical records of survivors (N=1216) and survivors completed a questionnaire 3 weeks after the disaster.

Results: Compared to the year prior to the disaster, the mean number of MUS was increased in the first two years after the disaster. Several risk factors for MUS were identified by using generalized estimating equations such as female gender (OR= 1.4, 95% CI: 1.1, 1.8), immigrant status (OR= 1.9, 95% CI: 1.5, 2.5), a high level of pre-disaster MUS (OR= 5.5, 95% CI: 4.1, 7.4) and concurrent psychological problems (OR= 3.9, 95% CI: 3.1, 5.0). Disaster-related factors were not directly related to MUS. Our model could not predict all survivors with a high level of symptoms.

Conclusions: The number of MUS was increased after the disaster. Several important risk factors for MUS were identified in this study. Although these factors are easy to recognize by GPs, they were insufficient to identify all survivors who will report a high level of MUS to the GP.

Introduction

Medically unexplained symptoms (MUS) are a common reason to seek medical care. When presented to the GP more than three quarters of symptoms such as stomachache, headache, and pain in bones and muscles can not be explained by a medical disorder.[1] Despite the lack of a medical diagnosis, these symptoms are associated with impairment in functioning that is similar to that of patients with medical disorders.[2, 3]

Patients who present these symptoms to their general practitioner (GP) may undergo extensive medical investigations, mostly without any result.[4, 5] Therefore, knowledge of factors that characterize patients with MUS is useful for identification of these individuals before costly test are done. Factors associated with MUS can be divided into predisposing, precipitating and perpetuating factors.[6] Predisposing factors are patient characteristics that make them more at risk for developing symptoms such as female gender,[7-9] lower educational level,[8] unemployment,[7, 9] childhood medical illness and maltreatment.[10, 11] Precipitating factors are events in the person's life such as stressful life events and psychological problems that precipitate symptoms. Finally, perpetuating factors are those that maintain or exaggerate symptoms (e.g. financial problems and lack of social support).[6]

Although disasters have been described as an important precipitating factor for MUS,[12] studies that focus on MUS among survivors of disasters are rare.[13] Some health surveys after disasters have reported elevated levels of self-reported physical symptoms among survivors,[13, 14] but only one study have examined MUS in general practice after a disaster. This study, that was performed six years after an airplane crash in Amsterdam has shown that 57% to 93% of symptoms presented to the GP could not be explained by a medical disorder.[15] Risk factors for MUS presented to the GP have not been studied before among survivors of disasters.

On May 13, 2000 a fireworks depot exploded in a residential area in the city of Enschede, the Netherlands. As a result of the explosion and subsequent fire, 23 people were killed, more than 900 people were injured and approximately 1200 people were forced to relocate because their houses were destroyed or severely damaged. To study the course of health problems among survivors, the electronic medical records (EMRs) of GPs were used. In the present study, the course of MUS presented to the GP in the one year before the disaster and in the first four years after the disaster is examined among the total group of survivors and among several subgroups. In addition, risk factors are studied for a high level of MUS presented to the GP. Finally, the extent to which the identified risk factors predicted survivors with a high level of symptoms is examined. This information may help GPs to identify individuals at risk for developing MUS.

Methods

Study design and study population

Two data collection methods were combined: a surveillance program in which the electronic medical records (EMRs) of survivors were used and a health survey that was performed three weeks post-disaster.[16-18] The Medical Ethical Testing Committee (TNO-Leiden-The Netherlands) approved the study protocol.

All GPs in the city of Enschede were invited to participate in the surveillance program. Dutch citizens are required to be registered at one general practice, and the GP serves as the gatekeeper for secondary care. In total, 44 out of 60 GPs agreed to participate (73%). The participating GPs had 89% of all survivors of the fireworks disaster on their list.[16]

Three weeks after the disaster a health survey was performed in which survivors were asked about their exposure to the disaster and their health problems. All residents of the affected area were invited to participate in the health survey by means of announcements in the local media and letters. In total, 1567 affected residents (estimated response ≈ 30%) completed the questionnaire.[17, 18]

The study population of the present study consisted of 1216 survivors who participated in the health survey and who were registered in one of the participating general practices at the time of the disaster.

Measures

Medically Unexplained Symptoms - Data on health problems were extracted from the EMRs of survivors from one year prior to the disaster (May 13, 1999) until four years post-disaster (May 12, 2004). The registration systems of the participating general practices document the patient's symptoms, examination findings, diagnosis and interventions in accordance to the International Classification of Primary Care (ICPC) which is compatible with the ICD-10.[19] A cluster of symptoms that are likely to remain medically unexplained, such as fatigue, abdominal pain, headache, nausea, and back pain was constructed by one of the authors (CJY). Symptoms in this cluster were defined as MUS when during one month after presenting the symptom no medical diagnosis had been registered, as an explanation for the symptom. The study period was divided into six years: from one year before until the date of the disaster (year -1), from the date of the disaster until one year post-disaster (year 1), continuing up to four years after the disaster (years 2 to 4).

Potential risk factors – Data on potential risk factors were also available from the EMRs. Firstly, gender, age and type of health insurance (private versus public) which was used as an indication for socioeconomic status since higher income is related to private health insurance. Secondly, the number of GP visits in the year prior

to the disaster. Male survivors with 8 or more visits and female survivors with 11 or more (80th percentile) visits in the year prior to the disaster were defined as having a high level of health care utilization. Also, a high level of MUS (≥ 5 symptoms, 90th percentile) in the year prior to the disaster and any psychological problem presented to the GP in the year prior to the disaster as well as any concurrent psychological problems were selected.

From the health survey, data on educational level, employment status (having a paid job) and immigrant status were available. Disaster-related factors were also available from the health survey: relocation due to a severely damaged or destroyed house; the loss of loved ones; injury due to the disaster. In addition, several questions were asked about what survivors had seen, heard and felt during the disaster. A scale was made for the 29 items; survivors with 18 or more experiences (80th percentile) were defined as having a high level of disaster exposure. Finally, the extent to which survivors experienced psychological distress during or shortly after the disaster was measured by the Peritraumatic Dissociative Experiences Questionnaire,[20] the depression and anxiety sub-scales of the Symptoms Checklist-90 (SCL-90),[21, 22] and the Impact of Event Scale (IES).[23, 24] Survivors who had a high score on three or four of these scale were considered as having a high level of self-reported distress after the disaster.

Data analysis

Of the 1216 survivors in the study population, 160 survivors (13.2%) had one or more missing values on the variables selected from the questionnaire. Since deleting the incomplete cases might lead to biased results, we corrected for this selective response by means of multiple imputation (MI).[25] This statistical method makes use of the intercorrelations of variables from the non-missing data to estimate plausible values for the data that is missing. The outcome of interest (MUS presented to the GP) and all potential risk factors, were included in the MI model. In addition, variables that highly correlated with the potential risk factors and with MUS were selected, such as the sub-scales of the RAND-36,[26, 27] the sub-scales of the SCL-90,[19, 20] and the two sub-scales of the IES,[23, 24] since this increases the power of the multiple imputation model.[25] We did not dichotomize any of the continuous variables that were entered into the model and applied an adapted version of predictive mean matching using a SAS macro that makes partial use of the SAS (version 9.1) multiple imputation (MI) procedure. We generated five datasets and analyzed them separately. The results were combined using the 'MIANALYZE' procedure in SAS.

To study the crude risk factors for MUS, the course of MUS among different groups of survivors, that is the mean number of symptoms, was calculated for survivors with different demographic characteristics and disaster-related factors.

Figure 1: The course of MUS presented to the GP in the one year before and the four years after the disaster

Figure 1A: Male versus female survivors

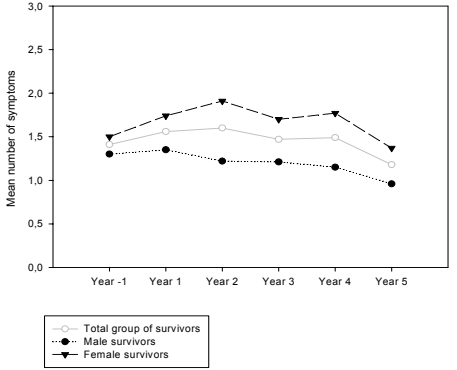


Figure 1B: High and low educational level

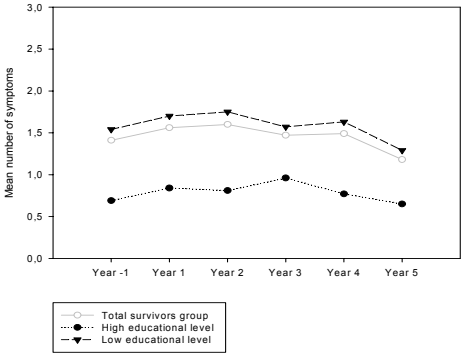


Figure 1C: Native Dutch versus immigrant survivors

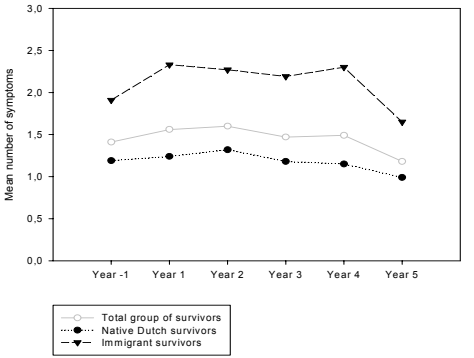


Figure 1D: Survivors with and without a paid job

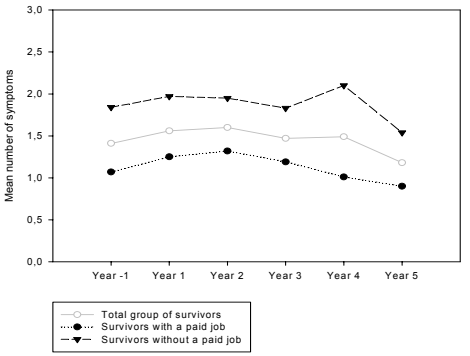


Figure 1E: Private and public health insurance

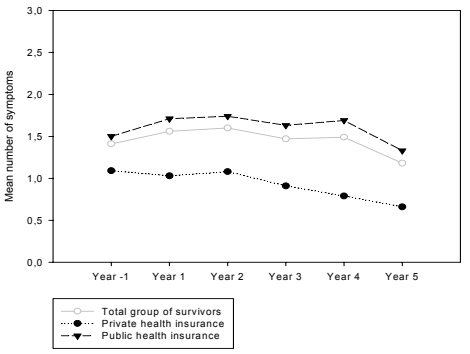


Figure 1F: Survivors with and without a destroyed house

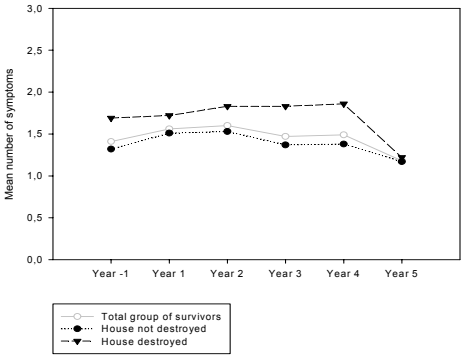


Figure 1G: Survivors who lost a loved one and who did not

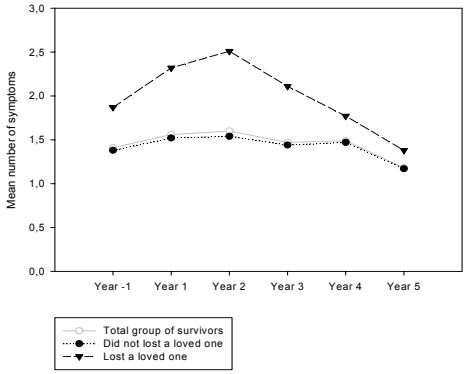


Figure 1H: Survivors with and survivors without injury

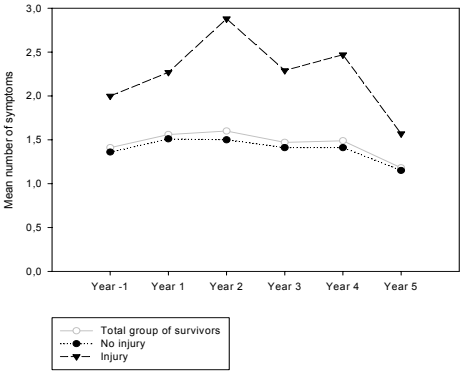


Figure 1I: High and low level of disaster exposure

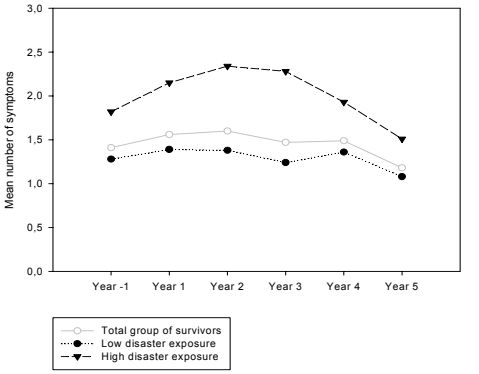
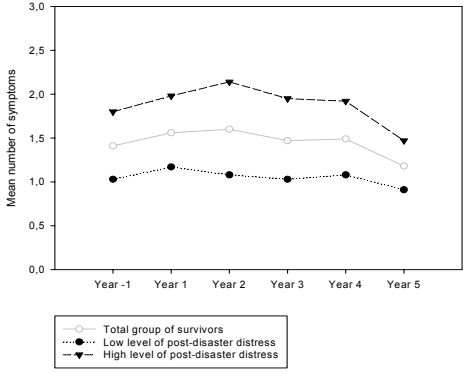


Figure 1J: High and low level of post-disaster distress



For the multivariate analysis of potential risk factors we dichotomized MUS into a high and a low level of symptoms, since the distribution of MUS presented to the GP was highly skewed. Also, risk factors for a high level of symptoms will be more useful for clinicians. Survivors who presented five or more MUS to the GP were considered as having a high level of MUS (90th percentile, based on the prevalence in year -1). We examined risk factors for MUS in the four years post-disaster (year 1 to year 4) using generalized estimating equations (GEE) models. In this study an unstructured correlation structure was used, which is the least restrictive structure.[28]

To examine the extent to which the risk factors in the final GEE model predicted a high level of MUS among survivors, we performed multiple logistic regression analyses for MUS presented to the GP in the four years post-disaster. We calculated the observed and predicted survivors with a high level of MUS, as well as the specificity, and the sensitivity.

Results

Course of MUS

In the five years that were examined in this study, 21.0% of all registrations in the EMRs of survivors were related to MUS. The most frequent presented symptoms were: back pain, coughing, fatigue, neck and shoulder symptoms and comprised respectively 10.3%, 5.0%, 5.0%, 4.6% and 4.2% of all MUS presented to the GP. Figure 1 shows the course of MUS in the five study years for several subgroups of survivors. In the year prior to the disaster (year -1), the survivors reported a mean number of 1.41 symptoms to the GP. Compared to year -1 the mean number of MUS was significantly higher in years 1 and 2 (M= 1.56 and M= 1.60, respectively) (table 1). The mean number of symptoms was increased in years 1 and 2 among several subgroups of survivors. For example, female survivors reported significantly more MUS to the GP in years 1 and 2, while males did not report a higher number of symptoms in the first two years post-disaster.

Risk factors for a high level of MUS in the five years post-disaster

For the multivariate analysis of potential risk factors we dichotomized MUS into a high and a low level of symptoms (≥ 5 symptoms). In the first year after the disaster, 9.1% of survivors had a high level of MUS, in years 2 to 4 this was, 9.7%, 8.2%, and 9.4% of survivors respectively. The results of the final GEE model shows that female gender (OR= 1.4;, 95% CI: 1.1, 1.8), immigrant status (OR= 1.9, 95% CI: 1.5, 2.5), and public health insurance (OR= 1.7, 95% CI: 1.2, 2.4) were risk factors for a high level of MUS (table 2). In addition, a high level of pre-disaster GP visits (OR= 1.8, 95% CI: 1.3, 2.3)

Table 1: The course of MUS presented to the GP in the one year before and four years post-disaster†

	Year -1	Year 1	Year 2	Year 3	Year 4
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Total group	1.41 (2.53)	1.56 (2.52) **	1.60 (2.78) *	1.47 (2.65)	1.49 (2.73)
Female survivors	1.50 (2.61)	1.74 (2.81)**	1.91 (3.11)**	1.70 (2.85)	1.77 (3.06) *
Male survivors	1.30 (2.43)	1.35 (2.13)	1.22 (2.28)	1.21 (2.35)	1.15 (2.22)
Low educational level	1.54 (2.70)	1.70 (2.67)*	1.75 (2.96)*	1.57 (2.77)	1.63 (2.89)
High educational level	0.69 (1.17)	0.84 (1.41)	0.81 (1.33)	0.96 (1.82)	0.77 (1.44)
Immigrant survivors	1.91 (2.97)	2.33 (3.16) **	2.27 (3.66)	2.19 (3.58)	2.30 (3.63)
Native Dutch survivors	1.19 (2.29)	1.24 (2.13)	1.32 (2.26)	1.18 (2.07)	1.15 (2.15)
No paid job	1.84 (3.14)	1.97 (2.93)	1.95 (3.14)	1.83 (3.03)	2.10 (3.35)
Paid job	1.07 (1.86)	1.25 (2.11)**	1.32 (2.43)**	1.19 (2.26)	1.01 (1.98)
Public health insurance	1.50 (2.68)	1.71 (2.68)**	1.74 (2.96)*	1.63 (2.78)	1.69 (2.89)
Private health insurance	1.09 (1.90)	1.03 (1.81)	1.08 (1.95)	0.91 (2.02)	0.79 (1.86)*
House destroyed	1.69 (3.07)	1.72 (2.80)	1.83 (3.29)	1.83 (3.26)	1.86 (3.11)
House not destroyed	1.32 (2.34)	1.51 (2.44)**	1.53 (2.60)*	1.37 (2.42)	1.38 (2.59)
Lost a loved one	1.87 (3.02)	2.32 (3.81)	2.51 (3.58)	2.11 (3.58)	1.77 (3.45)
Did not lost a loved one	1.38 (2.50)	1.52 (2.43)*	1.54 (2.72)*	1.44 (2.58)	1.47 (2.68)*
Injury	2.00 (3.51)	2.27 (3.24)	2.88 (5.02)	2.29 (4.09)	2.47 (3.87)
No injury	1.36 (2.44)	1.51 (2.46)**	1.50 (2.51)	1.41 (2.50)	1.41 (2.61)
High disaster exposure	1.82 (2.53)	2.15 (3.07)*	2.34 (3.72)*	2.28 (3.58)*	1.93 (3.40)
Low disaster exposure	1.28 (2.52)	1.39 (2.32)	1.38 (2.39)	1.24 (2.24)	1.36 (2.48)
High level of distress	1.80 (2.94)	1.98 (2.84)	2.14 (3.42)*	1.95 (3.13)	1.92 (3.19)
Low level of distress	1.03 (2.01)	1.17 (2.12)*	1.08 (1.86)	1.03 (2.00)	1.08 (2.12)

† T-tests were used to compare differences in the mean number of symptoms between year -1 and the years post-disaster;

* $p < .05$, ** $p < .01$.

as well as a high level of pre-disaster MUS (OR= 5.5, 95% CI: 4.1, 7.4) were related to a high level of MUS in the years after the disaster. In contrast, disaster-related factors, such as relocation and the loss of a loved one, were not related to a high level of

symptoms presented to the GP. Finally, concurrent psychological problems appeared to be a strong risk factor for a high level of MUS (OR= 3.9, 95% CI= 3.1-5.0).

Table 2: Association between a high level of MUS in the four years post-disaster and potential risk factors*

	Adjusted OR	95% CI
Female gender	1.4	1.1, 1.8
Age (per 10 years)	1.0	0.9, 1.1
Low educational level	1.4	0.9, 2.1
Immigrant status	1.9	1.5, 2.5
No paid job	1.2	0.9, 1.5
Public health insurance	1.7	1.2, 2.4
High no. of pre-disaster GP visits	1.8	1.3, 2.3
High no. of pre-disaster MUS	5.5	4.1, 7.4
Pre-disaster psychological problems	1.1	0.8, 1.4
Relocated	0.8	0.6, 1.1
Lost a loved one	1.3	0.8, 2.0
Injury self	1.5	1.0, 2.1
High disaster exposure	1.2	0.6, 1.6
High level of self-reported distress after disaster	1.2	0.9, 1.6
Psychological problems (concurrent)	3.9	3.1, 5.0

* A high level of MUS is defined as >= 5 symptoms presented to the GP in one year

Classification of observed and predicted survivors with a high level of MUS

Table 3 shows the observed and predicted MUS cases in years the four years post-disaster, based on the final multiple logistic regression models for MUS. In year 1, the model correctly predicted a high level of MUS in 35.5% of the observed cases. In years 2 to 4 the sensitivity of the model decreased (23.7%, 19.0%, 12.3% respectively). The specificity of the models was high, indicating that almost all survivors without a high level of MUS were predicted correctly.

Discussion

This longitudinal study examined the course of and risk factors for MUS presented to the GP by survivors of a disaster. Compared to the year prior to the disaster, survivors reported a higher mean number of MUS to the GP in the first two years after the disaster. Generalized estimated equations models showed that female gender, immigrant status, public health insurance, a high number of pre-disaster GP visits, and in particular, a high level of pre-disaster MUS and concurrent psychological problems

were risk factors for a high level of MUS post-disaster. The regression models for years 1 to 4 had a high specificity, but the sensitivity of the models was low, which indicates that the risk factors in the model were not sufficient to identify all survivors who reported a high level of MUS to the GP.

Most previous studies among survivors of disasters were cross-sectional and could not study the course of health problems over time.[13] Despite this, Lima et al. found in a longitudinal study a significant decrease in self-reported symptoms five years after an earthquake compared to seven months after the earthquake.[29] Another longitudinal study after an earthquake did, however, not find a decrease in symptoms between 3 months and nine months after the earthquake.[30] It can be speculated that the prevalence of symptoms did only decrease after a longer period since the disaster. Indeed, in a study among the survivors of the fireworks disaster that studied symptoms reported to the GP up to 2.5 years post-disaster, the number of symptoms was still elevated 2.5 years post-disaster.[31] In the present study was showed that the level of symptoms was similar to the baseline level in the third year post-disaster

In line with longitudinal studies in the general population, our study showed that baseline, or pre-disaster, MUS was a strong predictor of MUS at a later point in time.[32, 33] The other risk factors were also comparable with risk factors for MUS in the general population, such as female gender, and public health insurance (indicating low socio-economic status).[8, 10]

Although traumatic events, such as disasters, have been described in the literature as precipitating factors for MUS,[12] disaster-related factors were not related to a high level of MUS in our study. Psychological problems may mediate the relationship between traumatic exposure and MUS.[34] In a recent study we showed that self-reported psychological problems mediated the relationship between trauma exposure and self-reported physical health problems among the survivors of the fireworks disaster (B van den Berg, unpublished manuscript). Comorbid psychological problems, which are strongly related to MUS in the general population,[9] appeared to be the most important risk factors for MUS among the survivors of the disaster. Since it is more likely that survivors present physical symptoms to the GP than psychological problems, GPs should be alert for psychological problems among patients who present with symptoms such as headache, stomachache and back pain.

The risk factors that were identified in the present study are easy to recognize for GPs and can be used to identify individuals at risk for a high level of MUS. However, the risk factors are not very specific for MUS and are also risk factors for a high level of health care utilization and morbidity in general.[35, 36] Indeed, the identified risk factors were insufficient to identify all of survivors who reported a high level of MUS to the GP given the low sensitivity of the regression models.

Table 3: Classification of observed and predicted survivors with a high level of MUS in the four years post-disaster.*

	Predicted cases			
Observed cases	*Yes*	*No*	Sensitivity	Specificity
MUS year 1				
Yes	39	71	35.5%	98.2%
No	20	1086		
MUS year 2				
Yes	28	90	23.7%	98.6%
No	15	1083		
MUS year 3				
Yes	19	81	19%	99.1%
No	10	1106		
MUS year 4				
Yes	14	100	12.3%	91.6%
No	10	1092		

* There was no evidence of a lack of fit in any of the selected models according to Hosmer and Lemeshow test;

Sensitivity: the proportion of people with MUS who also have a positive result for the test (model);

Specificity: the proportion of people among those who do not have MUS who have a negative test (model).

This study has several strengths. Firstly, since disasters are unpredictable events, information on the health status of survivors before the disaster is rarely available. In the present study electronic medical records of survivors were used, which made information about the pre-disaster health available. Therefore, survivors could serve as their own controls by comparing the level of pre- and post-disaster symptoms. Secondly, this study examined the course of health problems up to five years post-disaster (medium term). Despite these advantages, possible selection bias is of concern in this study. An estimated 30% of all affected residents participated in the questionnaire health survey and participation was somewhat selective: women, those living with a partner, those aged 45-64 years and immigrants were more likely to participate.[17] In addition, the EMRs were not available for all survivors who participated in the health survey. Survivors for whom the EMR was available were somewhat younger, were less likely to have lost a loved one and were less likely to have a high level of disaster exposure (data not shown). Although further analyses indicated that the prevalence estimates of self-reported health problems were barely affected by this selective participation,[17] these factors might have affected the prevalence estimate of MUS reported to the GP. However, the course of symptoms will not be biased since

participants serve as their own control. In addition, it is not very likely that the association between risk factors and MUS will be different among those for whom the EMR was not available.

In conclusion, the mean number of MUS was elevated in the first two years after the disaster, and was back to the baseline level in the third and fourth year post-disaster. The identified risk factors for MUS presented to the GP among survivors were comparable to the risk factors for MUS in the general population. Although these symptoms were strongly related to a high level of MUS, they were not sufficient to identify all survivors with MUS. More specific risk factors for MUS should be identified such as selective attention and causal attributions.[37] Also, since effective treatments such as cognitive behavioral therapy for patients with MUS are available,[38] GPs should be trained to identify individuals with MUS at an early stage, before the symptoms become chronic and extensive medical investigations to detect a medical disorder are done.

Acknowledgments

We thank the participating general practitioners and their patients. And we thank Dr. H. Boshuizen (RIVM) for the use of her SAS macro for predictive mean matching.

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CHAPTER 7

Selective attrition and bias in a longitudinal health survey among survivors of a disaster

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Published in: BMC Medical Research Methodology (in press)

Abstract

Background: Little is known about the response mechanisms among survivors of disasters. We studied the selective attrition and possible bias in a longitudinal study among survivors of a fireworks disaster.

Methods: Survivors completed a questionnaire three weeks (wave 1), 18 months (wave 2) and four years post-disaster (wave 3). Demographic characteristics, disaster-related factors and health problems at wave 1 were compared between respondents and non-respondents at the follow-up surveys. Possible bias as a result of selective response was examined by comparing prevalence estimates resulting from multiple imputation and from complete case analysis. Analysis were stratified according to ethnic background (native Dutch and immigrant survivors).

Results: Among both native Dutch and immigrant survivors, female survivors and survivors in the age categories 25-44 and 45-64 years old were more likely to respond to the follow-up surveys. In general, disasters exposure did not differ between respondents and non-respondents at follow-up. Response at follow-up differed between native Dutch and non-western immigrant survivors. For example, native Dutch who responded only to wave 1 reported more depressive feelings at wave 1 (59.7%; 95% CI 51.2-68.2) than Dutch survivors who responded to all three waves (45.4%; 95% CI 41.6-49.2, $p < 0.05$). Immigrants who responded only to wave 1 had fewer health problems three weeks post-disaster such as depressive feelings (69.3%; 95% CI 60.9-77.6) and intrusions and avoidance reactions (82.7%; 95% CI 75.8-89.5) than immigrants who responded to all three waves (respectively 89.9%; 95% CI 83.4-96.9 and 96.3%; 95% CI 92.3-100, $p < .01$). Among Dutch survivors, the imputed prevalence estimates of wave 3 health problems tended to be higher than the complete case estimates. The imputed prevalence estimates of wave 3 health problems among immigrants were either unaffected or somewhat lower than the complete case estimates.

Conclusion: Our results indicate that despite selective response, the complete case prevalence estimates were only somewhat biased. Future studies, both among survivors of disasters and among the general population, should not only examine selective response, but should also investigate whether selective response has biased the complete case prevalence estimates of health problems by using statistical techniques such as multiple imputation.

Introduction

Epidemiologic studies after disasters have shown elevated levels of health problems among survivors such as post-traumatic stress disorder (PTSD), depression and physical symptoms.[1-3] The majority of the disaster studies have been cross-sectional, and although cross-sectional studies are useful for assessing the public health burden of the disaster, they do not give insight into the course of the health consequences and the health needs of survivors at different times post-disaster.

Since relatively little is known about the course of health problems among survivors of disasters, more longitudinal studies are needed.[1, 2, 4] However, attrition is a main methodological problem in longitudinal studies. A common approach for handling attrition is to delete observations with missing values, but this complete case analysis can result in a substantial loss of power. In addition, if respondents systematically differ from non-respondents, deleting incomplete observations might introduce bias in the prevalence estimates of the health problems.[5, 6] A good way to deal with missing data and to overcome possible selection bias in the prevalence estimates is to conduct multiple imputation.[6, 7] This technique fills in various values for each missing data point based on a statistical model. Because the missing values are drawn from a distribution, there will be a range of values imputed for each missing value, with variation appropriately reflecting the uncertainty about that value. Using this technique, it can be estimated what the prevalence of the outcomes of interest would have been if there had been no (systematic) attrition in the longitudinal study.

Evidence concerning selective response among survivors of disasters is conflicting. Some studies have shown that non-respondents are more likely to be male, single and to have a low socioeconomic status,[8-10] while other studies did not observe such an association.[11-15] Little is known about the association between the level of disaster exposure and non-response at follow-up. One may speculate that survivors who were highly affected by the disaster or who had high levels of post-disaster distress would be more motivated to participate at the follow-up of a health survey than survivors who were less affected. On the other hand, it can be hypothesized that highly exposed or distressed survivors would be less likely to respond because they do not want to be reminded of the stressful event. Several studies have found that depression, distress and symptoms of PTSD at baseline were associated with non-response at follow-up[8, 16, 17] while other studies found no association between baseline distress and non-response at follow-up.[12-15] In addition, the determinants of response at follow-up might also differ between groups of survivors. We recently observed that baseline health problems were associated with response among immigrant survivors and with non-response among native Dutch survivors at wave 2 of a study after a fireworks disaster in the Netherlands.[18] The information from these disaster studies is, however, not sufficient to understand the response mechanisms of survivors of disasters.

Furthermore, none of the previous studies after disasters have examined whether selective response biased the prevalence estimates of the health problems among survivors.

Since attrition will most likely occur in future longitudinal studies after disasters, more insight into the response mechanisms among survivors and possible bias resulting from selective response is desirable. In the present longitudinal study after a fireworks disaster in the Netherlands, we examine the selective response among survivors at the follow-up surveys. In addition, we study whether possible selective response had biased the prevalence estimates of health problems among survivors at wave 3 by comparing the estimates resulting from multiple imputation with estimates resulting from complete case analysis.

Material and methods

Background

On May 13 2000, a fireworks depot exploded in a residential area in the city of Enschede, the Netherlands. As a result of the explosion and subsequent fire, 23 persons were killed, more than 900 people were injured, and about 1,200 people were forced to relocate because their houses were destroyed or severely damaged. The Dutch government declared this a national disaster and started a longitudinal study into the health consequences of the disaster.

Study design

The first survey was performed 2.5 to 3.5 weeks post-disaster (wave 1). In total, 4,456 adult residents were living in the area that was designated by the municipality as the official disaster area. All residents of this area were invited to participate in the health survey by means of announcements in the local media and letters.

Approximately 18 months after the disaster, from November 2001 through January 2002, a second survey was conducted (wave 2). All participants at wave 1 who had given informed consent for future contact received an announcement letter. To stimulate participation, survivors were telephoned. If the survivor agreed to participate, a questionnaire in the preferred language (Dutch, English, German or Turkish) was sent, together with a gift voucher, to their home address. Survivors who did not return the questionnaire within three weeks were reminded by phone or by letter when the person could not be reached by phone.

In January through March 2004, nearly four years post-disaster, wave 3 of the longitudinal study was performed. All participants at wave 1 of the health survey who had given informed consent for future contact, and were not lost to follow-up, received an announcement letter. Participation was stimulated by means of telephone calls and

home visits. If the questionnaire was not returned within three weeks, the respondents were reminded by phone or by letter. Details of the study population and the health problems of survivors at the different waves of the study have been described elsewhere.[18-22]

Measures

We selected the following demographic variables to examine possible selective response: sex; age; educational level; employment status (having a paid job), and marital status (single).

To examine whether respondents and non-respondents at waves 2 and 3 had different disaster-related experiences, the following disaster-related factors were selected: injury (requiring medical treatment) sustained as a result of the disaster; the loss of loved ones (family, colleagues, friends); relocation due to severely damaged or destroyed house; whether survivors had experienced intense anxiety during the disaster and whether survivors had seen frightening things during the disaster.

We compared health problems at wave 1 between respondents and non-respondents at the follow-up surveys to study possible selective response. We used the Dutch versions of various validated instruments to measure health problems. Feelings of depression and anxiety were measured by the symptom check list (SCL-90).[23, 24] We dichotomized the scales into 'very high' and 'high' versus 'above average', 'average' and below 'average', according to established references for the healthy Dutch population.[24] The impact of event scale (IES)[25-27] was used to measure intrusions and avoidance reactions which serve as an indication for a clinical level of PTSD. Consistent with Carr et al., Basoglu et al. and others, survivors with an overall score above 25 were considered as having symptoms of PTSD.[28, 29] We used a questionnaire into subjective health complaints (VOEG) to measure 13 physical symptoms such headache and fatigue.[30] In this study, we used a cut-off of six or more symptoms which is one standard deviation above the reference mean. Sleeping difficulties were measured by the Groninger Sleep Quality Scale;[31] survivors with a score above 4 were defined as having severe sleeping difficulties. The RAND-36 was used to measure different aspects of functional status.[32] To examine selective response, four sub-scales were used; social functioning, physical role limitations, emotional role limitations and general health. Scores on the sub-scales were dichotomized using the cut-off scores resulting from a national study in the Netherlands; in this study cut-off scores were based on the mean score minus one standard deviation.[33] We used the scales described above as the outcomes of interest to examine whether possible selective response had biased the prevalence estimates of the health problems at wave 3.

Statistical analyses

Because the response mechanisms between waves 1 and 2 were found to be different for native Dutch survivors and non-western immigrant survivors,[18] we stratified the analysis according to ethnic background (native Dutch and immigrant status) in order to study selective response and possible biased prevalence estimates. We defined a non-western immigrant as either a respondent who was born in a non-western country of whom at least one parent was also born in a non-western country, or a respondent whose parents were both born in a non-western country. Most of the non-western immigrants were of Turkish origin (44.7%), followed by immigrants of Moroccan origin (14.0%).

We compared demographic characteristics, disaster-related experiences and wave 1 health problems for respondents and non-respondents at waves 2 and 3 in order to study possible selective response by performing Chi-square tests for categorical variables and ANOVA for continuous variables.

We used multiple imputation (MI) to study the effect of possible selective response on the prevalence estimates of the wave 3 health problems.[5] MI assumes that the missing data are "missing at random"; in other words, the missingness is not related to factors that were not measured in this study. Multiple imputations were performed with the Markov chain Monte Carlo (MCMC) simulation in SAS version 9.1 using the 'MI' procedure. The method imputes plausible values for the missing data using correlations between observed variables.[5] For that reason we included the health problems of interest (described above) from all three waves in the imputation model. In addition, other relevant predictor variables of these health problems were selected; sex; age; educational level; immigrant status; employment status; language; cigarette smoking; alcohol use; sustained injury due to the disaster; relocation; intense anxiety and having seen frightening things during the disaster. Since the power of the model increases when additional data other than the variables of interest are used,[6] other important health-related variables were selected: the somatization, hostility and interpersonal sensitivity sub-scales of the SCL-90,[23, 24] the use of sedatives and the presence of chronic diseases among survivors. These variables were measured at all three waves. Peritraumatic dissociation (measured only at wave 1),[34] and optimism,[35] the distrust sub-scale of the search for meaning scale,[36] and the pain, vitality and mental health sub-scales of the RAND-36[33] (all measured at waves 2 and 3) were also included in the imputation model. In addition, we included a variable for the approach of participants at wave 3 of the health survey (no contact, telephone contact or face to face).

We used one MI model for both the native Dutch and immigrant survivors because separate analysis results in a substantial loss of power and such an analysis assumes that there is a difference between native Dutch and immigrant for each

variable in the MI model. Because some determinants of response differed between native Dutch and immigrant survivors, interaction terms for immigrant status and gender, educational level, marital status, relocation, injury self, lost a loved one, intense anxiety, saw frightening things, feelings of depression, feelings of anxiety, physical symptoms, sleeping problems, social functioning, physical and emotional role limitations, and general health (measured at the three waves) were entered into the model. We did not dichotomize the variables entered in the model, instead linear effects were used in the MI model.

We generated five datasets that were analyzed separately. The results were combined using the 'MIANALYZE' procedure in SAS, in order to produce valid confidence intervals. Finally, we compared the imputed prevalence estimates of wave 3 health problems with the prevalence estimates resulting from complete case analysis for native Dutch and immigrant survivors separately.

Results

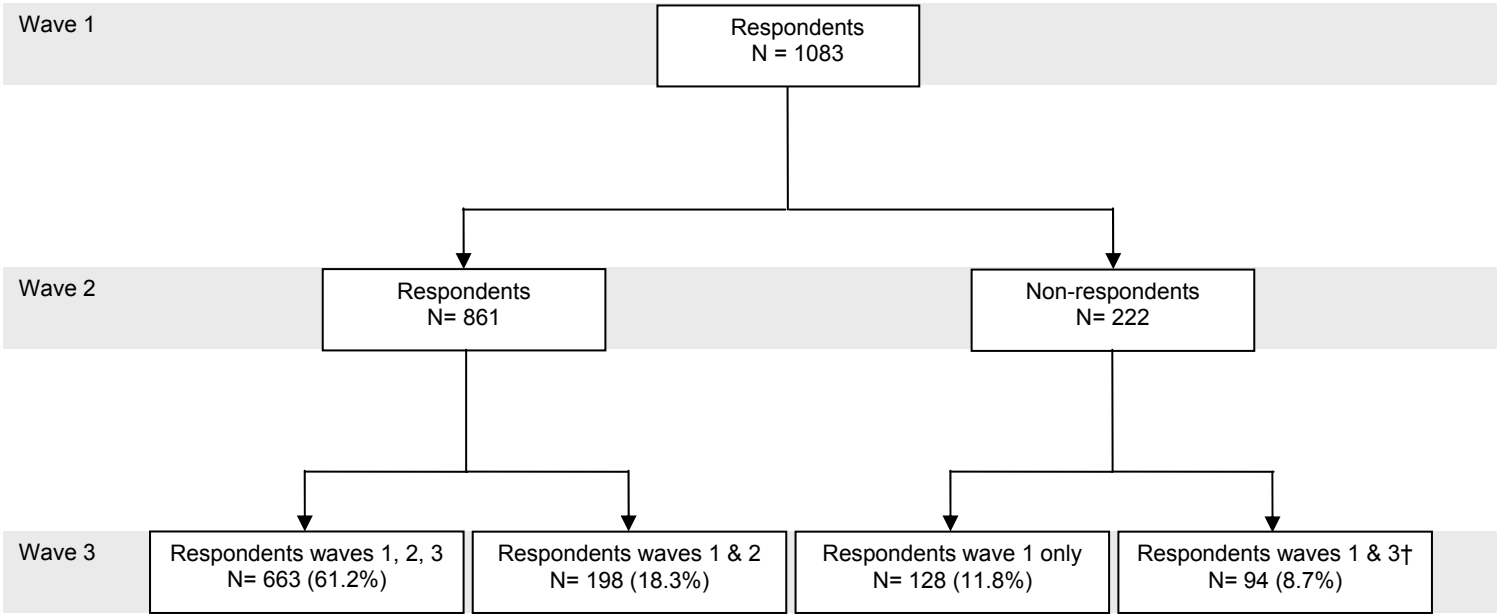
Selective response at waves 2 and 3 among native Dutch survivors

In total, 1,083 native Dutch survivors completed the questionnaire at wave 1 (figure 1). Of these survivors, 663 (61.2%) participated at all three waves of the longitudinal study. Three other response groups can be distinguished: 128 survivors (11.8%) who responded to wave 1 only; 198 survivors who responded to waves 1 and 2 (18.3%); and 94 survivors who responded to waves 1 and 3 (8.7%).

Demographic characteristics of native Dutch respondents and non-respondents at the three waves are shown in table 1. There were some demographic differences between respondents and non-respondents at the follow-up surveys; men were more likely to respond to wave 1 only, while native Dutch women were more likely to respond to all three waves of the study. Those survivors who responded to waves 1 and 3 but not to wave 2 were younger than the other response groups. Native Dutch survivors who responded only to wave 1 or to waves 1 and 2 had a somewhat lower educational level than survivors who responded to wave 3, however this difference was not statistically significant. Finally, respondents who responded to all three waves were less likely to live alone than those who responded to waves 1 and 2.

Table 2 shows the associations between response and disaster-related experiences and wave 1 health problems for the different native Dutch response groups. There were no clear differences in disaster exposure among the different groups, except for a lower percentage of injured survivors among those who responded to waves 1 and 2 but not to wave 3 compared to survivors who responded to all three waves.

Figure 1: Flow chart response native Dutch survivors



* Non-respondents also include those survivors who were lost to follow-up due to death or emigration

† All participants who had given informed consent at wave 1 were invited to participate at wave 3 of the health survey

Table 1: Demographic characteristics of native Dutch respondents and non-respondents at the three waves of the longitudinal study*

	Respondents at Wave 1 only (N= 128)	Respondents at Waves 1 & 2 (N= 198)	Respondents at Waves 1 & 3 (N= 94)	Respondents at Waves 1, 2, 3 (N= 663)	*p* value
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	
Male	59.8 (51.2-68.3)	49.0 (42.0-56.0)	48.9 (38.7-59.0)	42.8 (39.0-46.6)	0.004
Age					
18 – 24	16.4 (9.9-22.8)	9.6 (5.5-13.7)	19.2 (11.1-27.2)	10.4 (8.1-12.7)	0.004
25 – 44	43.0 (34.3-51.6)	43.9 (37.0-50.8)	53.2 (43.0-63.3)	43.9 (40.1-47.7)	
45 – 64	26.6 (18.9-34.3)	30.3 (23.9-36.7)	22.3 (13.8-30.7)	35.0 (31.4-38.6)	
65+	14.1 (8.0-20.1)	16.2 (11.1-21.3)	5.3 (0.7-9.8)	10.7 (8.4-13.1)	
Age, Mean	42.0 (39.4-44.9)	45.1 (42.7-47.4)	37.3 (34.4-40.2)	43.5 (42.4-44.7)	0.0005
Education					
Primary school	14.9 (8.7-21.1)	14.5 (9.6-19.4)	8.0 (2.4-13.5)	10.4 (8.1-12.7)	0.4
Junior high	37.2 (28.7-45.6)	32.3 (25.8-38.8)	8.0 (2.4-13.5)	10.4 (8.1-12.7)	
Senior high/professional	34.7 (26.4-43.0)	33.9 (27.3-40.5)	30.7 (21.3-40.0)	33.7 (30.1-37.3)	
High professional /university	13.2 (7.3-19.1)	19.4 (13.9-24.9)	25.0 (16.1-33.8)	21.6 (18.5-24.7)	
Paid job	62.0 (53.5-70.4)	57.4 (50.5-64.3)	75.3 (66.5-84.0)	64.0 (60.4-67.7)	0.03
Single	24.4 (16.9-31.8)	26.5 (20.4-32.6)	20.0 (11.8-28.1)	17.8 (14.9-20.7)	0.04

* Groups of respondents are exclusive; Anova was used for continuous variables and X^2-tests for categorical variables

Table 2: Disaster exposure and health problems three weeks post-disaster among native Dutch respondents and non-respondents at the three waves of the longitudinal study*

	Respondents at wave 1 only (N= 128)	Respondents at waves 1 & 2 (N= 198)	Respondents at waves 1 & 3 (N= 94)	Respondents at waves 1, 2, 3 (N= 663)	*p* value
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	
Disaster exposure					
Relocated	25.4 (17.9-32.9)	16.2 (11.1-21.3)	20.4 (12.2-28.6)	20.1 (17.1-23.2)	0.3
Injury self	6.3 (2.1-10.5)	1.5 (0.0-3.2)	5.3 (0.7-9.8)	8.3 (6.2-10.4)	.009
Lost a loved one	6.3 (2.1-10.5)	4.6 (1.7-7.5)	4.3 (0.2-8.4)	6.1 (4.3-7.9)	0.8
Intense anxiety	59.6 (51.1-68.1)	53.0 (46.1-60.0)	47.9 (37.7-58.0)	60.5 (56.8-64.2)	0.05
Saw frightening things	24.2 (16.8-31.6)	19.7 (14.2-25.2)	28.7 (19.4-37.8)	24.7 (21.4-28.0)	0.3
Health problems at wave 1					
Depressive feelings (high)	59.7 (51.2-68.2)	44.8 (37.9-51.7)	50.0 (39.8-60.0)	45.4 (41.6-49.2)	0.04
Feelings of anxiety (high)	50.0 (41.3-58.7)	38.9 (32.1-45.7)	46.7 (36.5-56.8)	41.9 (38.1-45.7)	0.2
Intrusion and avoidance (high)	70.1 (62.2-78.0)	67.9 (61.4-74.4)	68.5 (59.0-77.9)	70.7 (67.2-74.2)	0.9
Physical symptoms (high)	48.8 (40.1-57.5)	42.2 (35.5-49.1)	43.6 (33.5-53.6)	46.7 (42.9-50.5)	0.6
Sleeping problems (high)	41.6 (33.1-50.1)	38.5 (31.7-45.3)	41.8 (31.7-51.8)	44.6 (40.8-48.4)	0.5
Poor social functioning	52.4 (43.8-61.1)	37.1 (30.4-43.8)	41.9 (31.8-51.9)	42.6 (38.8-46.4)	0.06
Physical role limitations	56.1 (47.5-64.7)	47.7 (40.7-54.7)	53.2 (43.0-63.3)	59.1 (55.4-62.8)	0.2
Emotional role limitations	72.2 (64.4-80.0)	61.4 (54.6-68.2)	69.7 (60.3-79.0)	78.8 (75.7-81.9)	0.0001
Poor general health	20.2 (13.3-27.2)	17.9 (12.6-23.2)	16.5 (8.9-24.0)	17.7 (14.8-20.6)	0.9

* Groups of respondents are exclusive

Native Dutch survivors who participated only at wave 1 were more likely to report a high level of feelings of depression (59.7%; 95% CI 51.2-68.2) compared to those who responded in all three waves (45.4%; 95% CI 41.6-49.2). Also, wave 1 only respondents tended to have somewhat more problems with social functioning at wave 1 compared to the other response groups, though this difference was not statistically significant. Overall, survivors who responded to waves 1 and 2 but not to wave 3 seemed to have lower levels of health problems three weeks post-disaster compared to the other response groups. Finally, the wave 1 health problems among respondents at waves 1 and 3 tended to be similar to all-wave respondents.

Selective response at waves 2 and 3 among survivors of non-western origin

At wave 1 of the health survey, 352 survivors of non-western origin participated (figure 2). Of this group, only 86 (24.4%) responded to all three waves; 118 immigrant survivors (33.5%) responded to wave 1 only , 75 immigrants (21.3%) responded to waves 1 and 2, and 73 immigrants (20.8%) responded to waves 1 and 3.

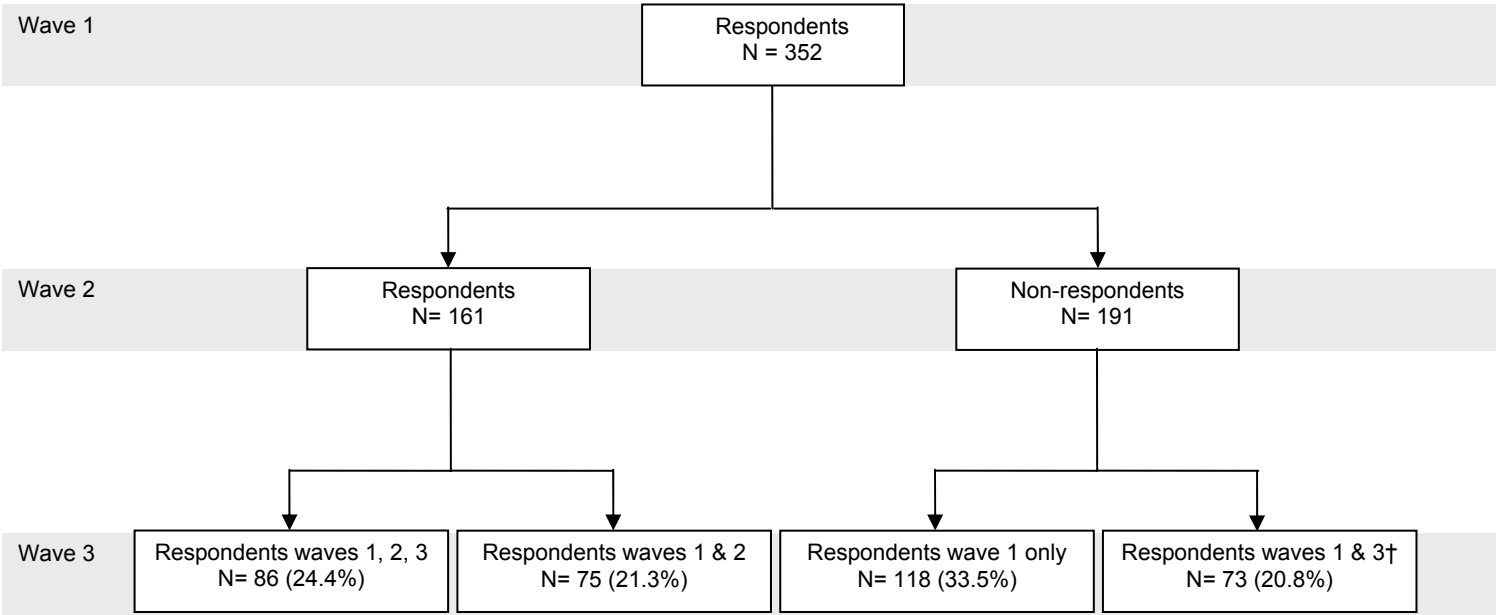
Male survivors of non-western origin tended to respond to wave 1 only, while female immigrant survivors were somewhat more likely to respond also to wave 3, but this difference was not statistically significant. In addition, immigrants who responded to waves 1 and 2 were somewhat older than respondents at wave 1 only and respondents at waves 1 and 3 (table 3).

Non-western immigrants who did not respond to all three waves tended to have a somewhat lower level of exposure to the disaster than survivors who responded to all three waves of the health survey, although this was not true for personal injury (table 4). In addition, immigrant survivors who responded to wave 1 only as well as those who responded to waves 1 and 3 had a lower level of health problems three weeks post-disaster compared to survivors who responded to all three waves. For example, those who responded to wave 1 only and those who responded to waves 1 and 3 had a lower level of intrusions and avoidance reactions, physical symptoms, and sleeping problems.

Comparison between imputed and complete case prevalence estimates of wave 3 health problems among native Dutch survivors

Figure 3 shows the imputed and complete case prevalence estimates of wave 3 health problems among native Dutch survivors. The imputed prevalence estimates were systematically higher than the prevalence estimates resulting from the complete case analyses. The most notable difference between the imputed and complete case estimates was found for feelings of anxiety (prevalence 25.3%; 95% CI, 22.4-28.5 and prevalence 20.1%; 95% CI, 17.2-23.0 respectively).

Figure 2: Flow chart response survivors of non-western origin



* Non-respondents also include those survivors who were lost to follow-up due to death or emigration;

† All participants who had given informed consent at wave 1 were invited to participate at wave 3 of the health survey.

Table 3: Demographic characteristics of respondents and non-respondents of non-western origin at the three waves of the longitudinal study*

	Respondents at wave 1 only (N= 118)	Respondents at waves 1 & 2 (N= 75)	Respondents at waves 1 & 3 (N= 73)	Respondents at waves 1, 2, 3 (N= 86)	*p* value
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	
Male	53.4 (44.3-62.4)	48.0 (36.5-59.3)	45.2 (33.6-56.6)	45.4 (34.7-55.9)	0.6
Age					
18 – 24	20.5 (13.1-27.8)	12.2 (4.7-19.6)	17.8 (8.9-26.6)	8.1 (2.2-13.9)	0.03
25 – 44	55.6 (46.5-64.6)	43.2 (31.8-54.4)	57.5 (46.0-68.8)	60.5 (50.0-70.8)	
45 – 64	22.2 (14.6-29.7)	40.5 (29.2-51.6)	21.9 (12.3-31.4)	31.4 (21.4-41.2)	
65+	1.7 (0.0-4.0)	4.1 (0.0-8.6)	2.7 (0.0-6.4)	0.0	
Age, Mean	35.9 (33.5-38.4)	41.1 (37.9-44.2)	36.4 (33.4-39.4)	38.5 (36.1-40.8)	0.04
Education					
Primary school	39.8 (30.9-48.6)	52.1 (40.6-63.4)	43.1 (31.6-54.5)	38.3 (27.9-48.6)	0.8
Junior high	23.9 (16.1-31.6)	21.1 (11.7-30.3)	23.5 (13.6-33.2)	22.2 (13.3-31.0)	
Senior high/professional	29.2 (20.9-37.4)	22.5 (12.9-32.0)	23.6 (13.7-33.3)	29.6 (19.8-39.3)	
High professional /university	7.1 (2.4-11.7)	4.2 (0.0-8.7)	9.7 (2.8-16.5)	9.9 (3.5-16.2)	
Paid job	41.4 (32.4-50.3)	40.6 (29.3-51.7)	46.0 (34.4-57.4)	39.2 (28.7-49.5)	0.9
Single	23.3 (15.6-30.9)	15.3 (7.0-23.5)	17.1 (8.3-25.7)	12.9 (5.7-20.0)	0.3

* Groups of respondents are exclusive; Anova was used for continuous variables and X^2-tests for categorical variables

Table 4: Disaster exposure and health problems three weeks post-disaster among respondents and non-respondents of non-western origin at the three waves of the longitudinal study*

	Respondents at wave 1 only (N= 118)	Respondents at waves 1 & 2 (N= 75)	Respondents at waves 1 & 3 (N= 73)	Respondents at waves 1, 2, 3 (N= 86)	*p* value
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	
Disaster exposure					
Relocated	21.1 (13.7-28.5)	34.8 (23.9-45.6)	32.8 (21.9-43.6)	38.6 (28.2-48.9)	0.05
Injury self	8.2 (3.2-13.2)	8.2 (1.9-14.4)	13.0 (5.2-20.7)	7.0 (1.5-12.4)	0.6
Lost a loved one	10.9 (5.2-16.5)	4.1 (0.0-8.6)	8.7 (2.1-15.2)	9.3 (3.1-15.4)	0.4
Intense anxiety	76.3 (68.6-84.0)	72.0 (61.7-82.2)	71.2 (60.7-81.6)	80.2 (71.6-88.6)	0.5
Saw frightening things	58.5 (49.5-67.4)	64.0 (53.0-74.9)	56.2 (44.6-67.6)	68.6 (58.6-78.4)	0.3
Health at wave 1					
Depressive feelings (high)	69.3 (60.9-77.6)	84.6 (76.3-92.8)	74.6 (64.5-84.6)	89.9 (83.4-96.3)	0.004
Feelings of anxiety (high)	66.7 (58.1-75.2)	80.3 (71.2-89.3)	74.6 (64.5-84.6)	81.5 (73.2-89.7)	0.09
Intrusion and avoidance (high)	82.7 (75.8-89.5)	93.9 (88.4-99.3)	82.4 (73.5-91.1)	96.3 (92.3-100.0)	0.006
Physical symptoms (high)	58.7 (49.7-67.6)	70.3 (59.8-80.6)	52.9 (41.0-64.1)	76.5 (67.4-85.5)	0.007
Sleeping problems (high)	61.8 (52.9-70.6)	83.6 (75.1-92.0)	59.4 (48.0-70.7)	85.9 (78.4-93.3)	0.008
Poor social functioning	69.0 (60.6-77.3)	71.8 (61.5-82.0)	72.5 (62.1-82.7)	76.7 (67.6-85.6)	0.7
Physical role limitations	71.9 (63.7-80.0)	73.2 (63.0-83.2)	67.4 (56.5-78.2)	81.2 (72.8-89.5)	0.4
Emotional role limitations	73.6 (65.6-81.6)	87.5 (79.9-95.0)	83.7 (75.1-92.2)	84.1 (76.3-91.8)	0.2
Poor general health	48.0 (38.9-57.0)	66.7 (55.9-77.4)	60.3 (48.9-71.5)	75.6 (66.4-84.7)	0.002

* Groups of respondents are exclusive

Figure 3: Imputed and complete case prevalence estimates of health problems at wave 3 among native Dutch survivors

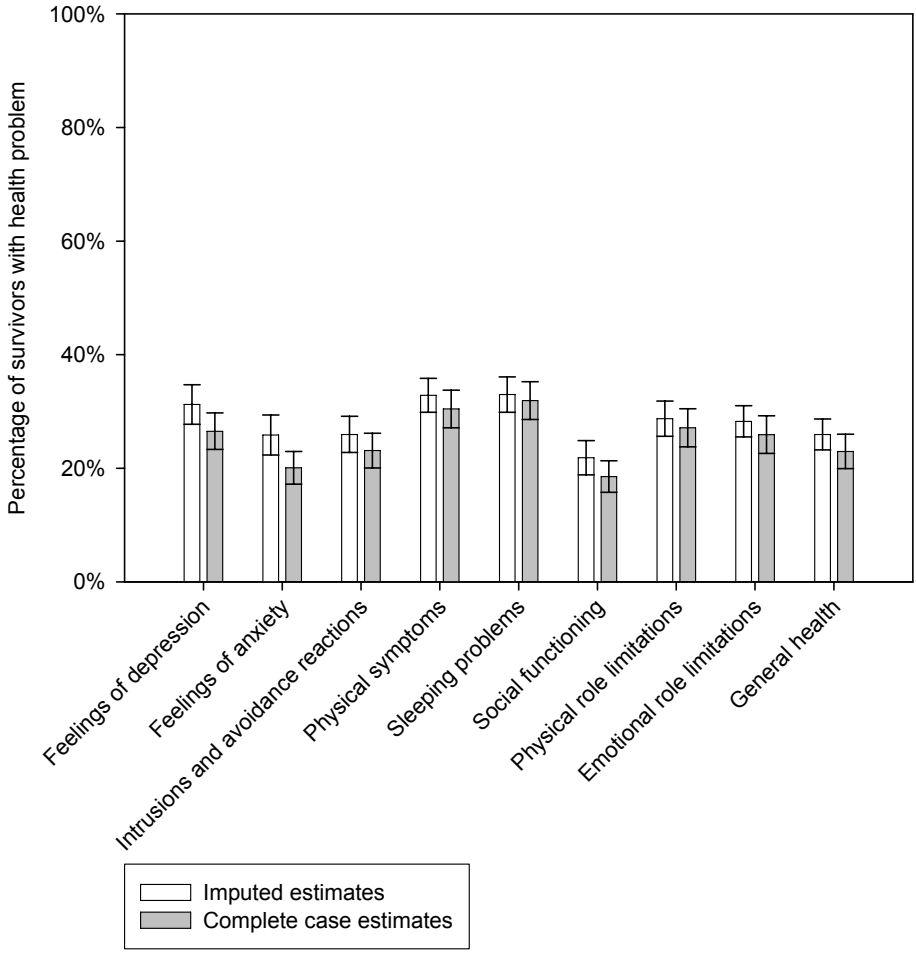
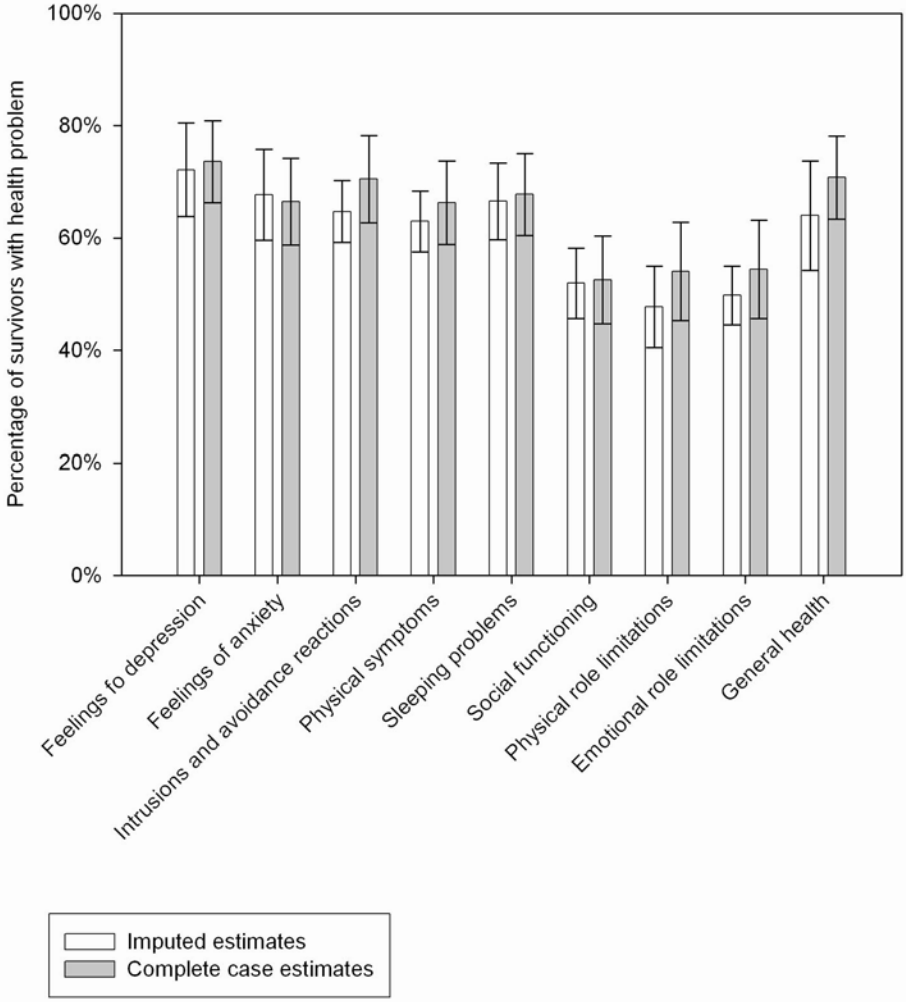


Figure 4: Imputed and complete case prevalence estimates of health problems at wave 3 among survivors of non-western origin



Comparison between imputed and complete case prevalence estimates of wave 3 health problems among survivors of non-western origin

The prevalence estimates of the health problems at wave 3 among non-western survivors resulting from multiple imputation and complete case analysis are shown in figure 4. The imputed estimates for depressive feelings, feelings of anxiety, sleeping problems and social functioning hardly differed from the estimates resulting from complete case analysis. The imputed prevalence estimates of intrusions and avoidance reactions, physical symptoms, physical and emotional role limitations and general health tended to be lower than the complete case estimates.

Discussion

In this study among survivors of a fireworks disaster, selective response occurred at the two follow-up surveys. We examined whether selective response had biased the prevalence estimates of the wave 3 health problems by comparing prevalence estimates resulting from complete case analysis and estimates resulting from multiple imputation. The complete case prevalence estimates of the wave 3 health problems were only somewhat biased, and the direction differed between the native Dutch survivors and immigrant survivors.

Similar to other studies after disasters, non-respondents at follow-up were more likely to be male.[8-10] In agreement with two longitudinal studies after disasters, we did not find an association between damaged or destroyed house or property loss and non-response at follow-up.[10, 14] In addition, we did not find clear associations between response at follow-up and other disaster-related experiences, such as the loss of a loved one and intense anxiety. In this study, we found an association between health problems at wave 1 and response at waves 2 and 3. Some previous studies also showed an association between health problems at baseline and non-response at follow-up.[8, 16, 17] However, the response mechanisms in this study differed between native Dutch survivors and survivors of non-western origin. Among native Dutch survivors, health problems at wave 1 tended to be associated with non-response at follow-up (waves 2 and 3). In contrast, among immigrant survivors, health problems at wave 1 were associated with response at follow-up. These different response mechanisms between native Dutch and immigrant survivors were also found in a recent study among the survivors of the fireworks disaster in which determinants for response at wave 2 of the health survey were examined.[18] It can be speculated that immigrant survivors of the fireworks disaster were not accustomed to participation in a health survey and believed that completion of the questionnaire was not meaningful in the absence of health problems. Although the underlying reasons remain unclear, different response mechanisms among ethnic groups have also been found in a longitudinal

general population study by Psaty et al.[37] In their study among whites and non-whites in the USA, poor health status was associated with non-response among whites and with response at follow-up among non-whites.

In this study we allowed survivors who participated at wave 1 but not at wave 2 to re-enter the study at wave 3. At wave 3, all eligible survivors were strongly motivated to participate; all survivors were stimulated to participate by means of telephone calls. In addition, eligible survivors for whom the telephone number was unknown and all immigrant survivors were visited at home. Survivors who re-entered the study at wave 3 differed from survivors who did not (wave 1 only). For example, among both native Dutch and immigrant survivors, those who re-entered the study at wave 3 were somewhat less likely to be male, were somewhat more likely to have a paid job and were somewhat less likely to be single. This group of respondents indirectly provides insight into non-response at wave 2 as well as additional information that is useful when performing MI.

The different response mechanisms among native Dutch and immigrant survivors were also confirmed after multiple imputation of the missing values. Among native Dutch, the imputed estimates of the wave 3 health problems tended to be higher than the complete case estimates. In contrast, the imputed prevalence estimates among immigrant survivors tended to be somewhat lower than the estimates of health problems at wave 3 resulting from complete case analysis. Additional analyses showed that the differences between imputed and complete case estimates of wave 2 health problems were similar to the differences between the complete case and imputed prevalence estimates of wave 3 health problems (data not shown). This confirms the robustness of our findings, since both native Dutch and immigrant survivors have similar response mechanisms from wave 1 to wave 2 and from wave 2 to 3.

We could not demonstrate very large differences between the imputed and complete case estimates of the health problems at wave 3. This result was unexpected since the selective response at the follow-up surveys would suggest prevalence estimates that were more strongly biased. While these results are reassuring, we can not exclude that some of the prevalence estimates were more biased than our results indicate. First, the lack of biased prevalence estimates at wave 3 might be due to weak associations between the predictor and outcome variables in the imputation model. Second, it is possible that other variables, not included in the model, were more important predictors of response and that missing data were not missing at random. However, we included all variables in the imputation model that were likely to be related to response in a health survey. Despite this, it is possible that the mechanism for missing data was non-ignorable; in other words, the missing data depended on variables not measured in this study or on the health status of non-respondents at follow-up. We believe that the method of multiple imputation was adequate given the

strong correlations between the variables that were used in the multiple imputation model. In addition, a necessary condition for this method was fulfilled;[5] the existing correlations between all factors used in the imputation model were systematically in the same direction. In this study, multiple imputation gives insight into the magnitude of selection bias on the prevalence estimates. Multiple imputation has some additional advantages above other methods to handle missing data; with multiple imputation all available information is used, therefore avoiding the loss of power associated with complete case analysis.[5, 6] Furthermore, the fact that standard errors and confidence intervals resulting from multiple imputations are more appropriate than those resulting from other techniques such as single imputation is another important advantage of multiple imputation.[5-7]

Besides non-response at follow-up, selective participation occurred at wave 1 of the longitudinal study in which 35.2% of all affected residents participated. Affected residents who participated at wave 1 were more likely to be women, to be between 25-44 or 45-64 years of age, to live with a partner, to be a single parent and to be of immigrant background. Analyses of multiple imputations showed that the selective participation did not affect the prevalence estimates of health problems at wave 1.[38] In the present study we were, however, primarily interested in bias resulting from selective attrition at the follow-up surveys. Despite selective response, the prevalence estimates of health problems at wave 3 were not completely different when we corrected for the selective response by means of multiple imputation. This is important information, emphasizing the fact that selective response is only problematic when it biases the prevalence estimates of health problems.

Conclusion

To date, most studies that have examined response in longitudinal studies have focused on whether respondents were systematically different from non-respondents. Our results indicate that considerable attrition and selective response only somewhat biased that prevalence estimates of health problems among survivors. Therefore, future studies, both among survivors of disasters and among the general population, should not only examine selective response, but should also investigate whether selective response has biased the prevalence estimates of health problems by using statistical techniques such as multiple imputation. Although the present study focused on potential bias in the prevalence estimates of health problems, investigations into risk factors for health problems should also take into account possible bias due to selective response. This is especially important in longitudinal studies after disasters since these studies examine the health needs of survivors and provide information on which post-disaster health interventions are based.

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CHAPTER 8

General discussion

In this thesis symptoms were studied that are frequently unexplained among survivors disasters in general and after the Enschede fireworks disaster in particular. The objectives of this thesis were:

1. To examine the prevalence rate of symptoms among survivors;
2. To examine potential risk factors for symptoms among survivors;
3. To evaluate similarities between the self-reported symptoms and MUS presented to the general practitioner (GP).

To answer the research questions, a systematic review was performed and two data collection methods were used: a three-wave longitudinal health survey among survivors of the Enschede fireworks disaster using self-administered questionnaires; and an ongoing surveillance program in which health problems were registered by GPs in the electronic medical records (EMRs) of survivors. At wave 1 of the health survey, three weeks post-disaster, symptoms were measured in a 13-item symptom-scale. At waves 2 and 3 (18 months and nearly four years post-disaster) this scale was expanded with 8 symptoms. The health problems presented to the GP were registered according to the International Classification of Primary Care (ICPC) which documents the patient's symptoms, examination findings, diagnosis and interventions.[1] To answer the research questions, a cluster was constructed of symptoms that were likely to remain medically unexplained, such as fatigue, abdominal pain, headache, nausea, back pain, and coughing.

Discussion of the main findings

Prevalence of symptoms among survivors of disasters

The results of this thesis indicate that physical symptoms are common among survivors of disasters and can be persistent. A systematic review of the literature published between 1983 and 2003 demonstrated that the prevalence rate of self-reported symptoms was elevated among survivors of natural (e.g. earthquakes and floods) and man-made disasters (e.g. the Chernobyl accident and airplane crashes) both immediately after the event and in the years that followed. Among the survivors of the fireworks disaster, the level of self-reported symptoms was higher compared to controls up to four years after the disaster. Although still elevated compared to controls, the level of symptoms had decreased at wave 3 when compared to wave 2.

These self-reported symptoms appeared to be related to a high level of functional impairment, illness behaviour and psychological problems. Despite this, the majority of self-reported symptoms were not presented to the GP. Indeed, the prevalence of symptoms presented to the GP was much lower than the prevalence rate of self-reported symptoms. Nevertheless, the mean number of symptoms presented to

the GP was higher in the two years after the disaster compared to the year prior to the disaster.

There is no evidence that the elevated level of symptoms among survivors of the fireworks disaster was the result of exposure to toxic substances. No elevated body burden of heavy metals, which are important elements of firework, was detected in the blood and urine samples of survivors.[2] Further, although symptoms were more common among survivors, the most prevalent symptoms were similar among survivors and controls, and no unique pattern of symptoms could be identified for survivors of this specific disaster (see appendix). As a result, the elevated prevalence rates of symptoms among survivors of the disaster support the hypothesis that disasters are related to physical symptoms that are frequently medically unexplained.

To date, most studies that focused on MUS in the aftermath of collective traumatic events were performed only once individuals had started to report symptoms, and conspiracy theories about exposure to toxic substances had developed, such as happened in the aftermath of an airplane crash in Amsterdam,[3-5] and after the first Gulf War.[6] After the airplane crash in Amsterdam on October 4, 1992, there were suspicions about the plane's cargo and the potentially harmful effects this might have had on the survivors. In the years after the disaster, conspiracy theories developed about possible exposure to depleted uranium and chemical components of the nerve gas Sarin.[3] Survivors reported physical symptoms such as headache, skin problems, respiratory symptoms and fatigue, which they attributed to exposure to these substances but which could not be explained by a medical disorder.[4, 5] In the aftermath of the Enschede fireworks disaster, no such theories developed, despite the fact that the exact cause of the disaster has never been recovered and the question of guilt is still unresolved. This indicates that physical symptoms may also develop in the absence of conspiracy theories; the symptoms might have developed as a result of distress or existing symptoms may have been aggravated by the disaster. The fact that the symptoms have been reported after different kinds of disasters suggests that such symptoms are part of the normal distress reaction to traumatic exposure.

It can be hypothesized that the reassuring results of the blood and urine samples that were obtained three weeks after the disaster, in which no elevated body burden was detected, have contributed to the absence of conspiracy theories. In addition, the surveillance program and the epidemiological studies might have served as a signal of acknowledgment of the problems of the survivors. In addition, financial compensation relatively shortly after the disaster, emphasis on contact between fellow survivors, and the establishment of a mental health care centre specifically for the survivors might also have contributed to the prevention of conspiracy theories. The aftermath of an accident in Drachten, the Netherlands, supports this hypothesis. After a fire in a waste disposal company that occurred almost simultaneously with the fireworks

disaster, no study into the health effects was performed. Some years after the fire, affected employees and residents started to attribute their physical symptoms to the fire, resulting in a study into the health effects 4.5 years after the fire.[7]

Survivors of the fireworks disaster only sought medical care for a minority (< 29%) of their symptoms. Apparently, most symptoms were not considered a reason to seek medical care. This is consistent with findings in the general population in which symptoms are very common, but most are only mild and thus not presented to the GP.[8-10] It is possible that, in the absence of conspiracy theories about exposure to toxic substances, survivors had fewer health worries and causal attributions about their symptoms and might have attributed their symptoms to psychological distress. Indeed, it was shown by Rief et al. that causal attributions about organic causes for the symptoms and cognitions about vulnerability to disease were highly correlated with illness behaviour such as health care utilization, while psychological causal attributions did not show any association with health care utilization.[11] In addition, Sensky demonstrated that somatic attributions of symptoms were associated with the frequency of general practice visits.[12]

Although the results of this thesis indicate that self-reported symptoms were more common among survivors and that the number of symptoms presented to the GP was elevated in the years after the disaster, it was not possible to examine how GPs treat survivors with MUS. From previous studies, it is known that the majority of GPs find patients with persisting MUS difficult to manage.[13, 14] This is an important problem given the fact that one in six patients in general practice present with MUS.[15, 16] Although several strategies for the management of MUS have been proposed, such as reassuring, counselling, education and explanation, evidence on adequate treatment options in general practice is limited.[17, 18] The most promising treatment for more severe cases with MUS is cognitive behavioural therapy (CBT), which is often performed in mental health care settings.[19] CBT attempts to change aspects of the patients' thoughts and behaviour to help them cope with their symptoms rather than focusing on the cause of the symptoms. Since CBT is a specialist treatment, this therapy would be an option for only a minority of all patients who present with MUS in general practice.[20] In addition, studies suggest that CBT is less effective when provided in general practice.[16] More insight is needed into effective management strategies of GPs for patients with MUS.[18, 20]

Risk factors for symptoms

We examined risk factors to identify survivors who are likely to develop symptoms, and to better understand the relationship between traumatic exposure and physical symptoms. The risk factors were divided into predisposing factors, precipitating factors, and perpetuating factors (3-P model).[21] This 3-P model is useful for grouping the many

biological, psychological and social factors that can affect symptoms and divide the factors according to their role in the development and maintenance of the symptoms.

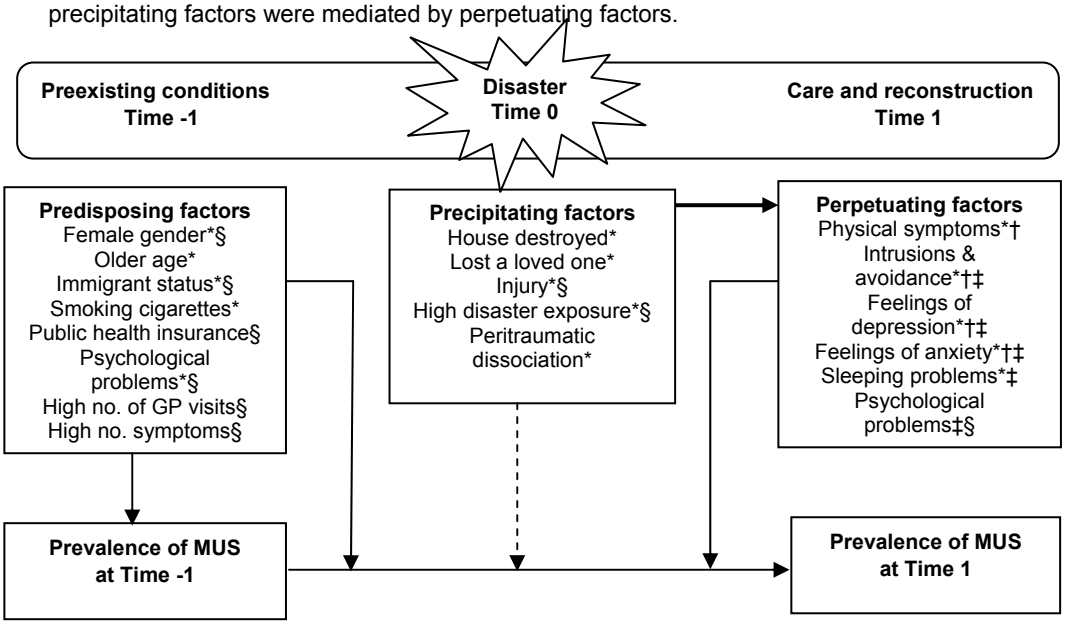
We identified several predisposing factors for self-reported symptoms and for symptoms reported to the GP, such as female gender and immigrant status (see figure 1). These predisposing factors were similar with factors for symptoms in previous disaster studies and MUS as observed in clinical practice.[21-24]

Consistent with previous disaster studies, precipitating factors such as having ones house destroyed and having a high level of disaster exposure were related to a higher mean number of self-reported symptoms when we did not adjust for perpetuating factors.[25-28] However, the relationship between disaster-related factors and physical symptoms was mediated by psychological distress reactions such as post-traumatic stress disorder (PTSD) and depression (perpetuating factors) (figure 1). In addition, symptoms presented to the GP were not directly associated with disaster-related factors. Instead, post-disaster psychological problems, which are related to disaster-related factors, were important risk factors for these symptoms. These results are consistent with the findings of a study among peacekeepers, in which was shown that physical symptoms were not directly related to mission-related factors, but were better predicted by symptoms of PTSD.[29] The finding that psychological problems mediate the relationship between disaster-related factors and symptoms supports the hypothesis of Schnurr and Green that a distress reaction following traumatic exposure is essential for precipitating changes in physical health status.[30] Although they proposed PTSD as the primary pathway through which trauma leads to poor health, we observed that other distress reactions such as feelings of depression and anxiety were also important mediators in this relationship.

Despite this strong relationship between psychological problems and physical symptoms, the psychological problems cannot explain all symptoms reported by survivors. Firstly, not all survivors with a high level of symptoms also reported a high level of psychological distress (see table 4 chapter 3). This indicates that physical symptoms can also develop in the absence of psychological distress. Secondly, not all survivors reported physical symptoms while almost all survivors experienced distress as a result of the disaster to some degree. Thirdly, it is important to note that, in addition to psychological distress, the interpretation of symptoms and causal illness attributions play an important role in the development and aggravation of the symptoms.[11, 31] For these reasons, we believe that a distress reaction following trauma is important but is not an essential condition for development of physical health problems.

The identified risk factors for symptoms presented to the GP are easy for GPs and policy makers to recognize and therefore useful identifying individuals and groups of survivors at risk for developing symptoms. Although the risk factors were strongly

Figure: Predisposing, precipitating and perpetuating factors for self-reported symptoms and symptoms presented to the GP among survivors of the Enschede fireworks disaster; precipitating factors were mediated by perpetuating factors.



* Risk factors for self-reported symptoms among survivors of the fireworks disaster (Chapter 5)

†Measured at an earlier point in time

‡ Measured simultaneously

§ Risk factors for symptoms presented to the GP among survivors of the fireworks disaster (Chapter 6).

related to a high level of symptoms, these factors were insufficient to identify all survivors with a high level of symptoms, given the low sensitivity of the regression model. Several important risk factors for symptoms, such as other adverse life events,[32, 33] adverse childhood experiences,[24, 34] illness beliefs,[11, 31] social support factors,[37] and personality traits such as neuroticism and negative affectivity[32] were not measured in the present study, which could account for the low sensitivity. Because the health survey after the fireworks disaster was focused on measuring the health status of survivors to inform policy makers and health care workers, adverse childhood experiences, illness beliefs and personality traits were not measured. Other adverse life events and social support factors were measured at waves 2 and 3 but were not included in the multiple regression models for technical reasons. Univariate analysis showed that other adverse life events and lack of social support were associated with higher level of symptoms among survivors (data not shown).

In conclusion, some important risk factors for symptoms among survivors of disasters identified in this thesis were female gender, immigrant status, public health insurance (which indicates a low socio-economic status) and psychological problems such as symptoms of PTSD, depression and anxiety. The risk factors for symptoms among survivors were comparable with the risk factors for MUS in the general population.[22-24, 32, 33] This finding suggests that other risk factors that were not measured in this study, but have been found in studies among the general population, may also predict symptoms among survivors of disasters. Disaster-related factors were not very useful in predicting survivors at risk for symptoms. Instead, our results indicate that it is more useful to identify those with a high level of distress as a result of the disaster.

Similarities between self-reported physical symptoms and MUS

A third aim of this thesis was to examine similarities between self-reported symptoms and MUS presented to the GP. Some authors have argued that MUS cannot be detected by means of questionnaires, since questionnaires lack the ability to distinguish MUS from medically explained symptoms.[36] Instead, only examination by a physician can exclude medical disorders.

In this thesis, the self-reported physical symptoms were found to share common risk factors with MUS presented to the GP by survivors of the disaster and among the general population. The results also showed several other similarities between the self-reported symptoms and MUS; the physical symptoms reported by survivors and controls were strongly associated with functional impairment and illness behavior such as health care utilization and sick leave, which are also features of those suffering from MUS. In addition, self-reported symptoms were associated with a high level of self-reported psychological problems (feelings of depression and anxiety) which are also common among individuals with MUS. Furthermore, when presented to the GP, 56% (shortness of breath and pain in chest and the region of the heart) to 91% (fatigue) of symptoms remained medically unexplained after medical examination, indicating that the majority of self-reported symptoms are likely to remain unexplained. The percentages of symptoms that remained medically unexplained were comparable with the percentages of symptoms that remained unexplained after the airplane crash in Amsterdam.[4]

Notwithstanding these similarities with MUS, medical disorders cannot be ruled out by means of questionnaires. Physical examination by a GP is necessary when one wishes to know whether or not the symptoms among respondents are medically unexplained. However, it may be less relevant to know whether or not the symptoms are medically unexplained than to identify features that make the symptoms disabling and predict their clinical course, such as the number and severity of symptoms, disabling cognitions, and associated functional impairment and illness behavior.[37] Also,

the idea that physical symptoms can be divided into those that reflect disease and those that are psychogenic is theoretically questionable.[37, 38] Many symptoms that are related to a disease can be explained only partly by that disease.[38] Therefore, questionnaires can be used to detect symptoms that are frequently unexplained and that show similarities with medically unexplained symptoms that are presented in general practice.

Methodological considerations

Study design

Epidemiological studies that include pre-disaster health data and comparison populations that are not exposed to the (suspected toxic) stressor are very useful in assessing the estimated burden of distress and disease that are attributable to the disaster exposure.[39] Compared to most previous disaster studies, the design of the present study had several advantages. Firstly, the majority of studies after disasters has been cross-sectional and therefore the course of health problems among survivors in the short, medium and long-term was largely unexplored.[40, 41] The present study was performed three weeks, 18 months and nearly four years post-disaster, allowing conclusions about the course of health problems among survivors in the short- and medium term after the disaster.[2] Secondly, information about disaster exposure was obtained three weeks post-disaster, which minimized recall bias.[42] Thirdly, a stratified control group was included at waves 2 and 3.[2] Finally, since disasters are unexpected events, pre-disaster questionnaire data are seldom available. In the present study, the health problems of survivors could be extracted from the electronic medical records (EMRs) of GPs starting one year prior to the disaster, which provided insight into the health status of a large group of survivors in the one year prior to, and the first four years after, the disaster. In this dataset, survivors could serve as their own controls by comparing the level of pre- and post-disaster symptoms.[43]

Selective response and possible bias

Of concern in this study were selective response and possibly biased prevalence estimates of the health problems of survivors. Demographic characteristics such as gender, marital status, and socio-economic status have often been related to response in several general population and disaster studies.[44-49] After disasters, disaster-related distress and experiences might also contribute to selective participation.[44, 50] For example, several studies have found that depression, distress and symptoms of PTSD at baseline were associated with non-response at follow-up.[26, 45, 50] An additional problem in the aftermath of a disaster is often the difficulty in correctly estimating the total affected population.

After the fireworks disaster, survivors registered at the Information and Advice Centre (IAC) that was established to supply information to survivors and to coordinate response to their needs. The database of the IAC was supplemented with information from the municipal registry office and included demographic information of the affected population. On the basis of this database, it was estimated that about 30% of all affected residents participated in wave 1 of the health survey. To study selective response at this first wave, the database of the IAC was combined with the database of the health survey and with the database of the GPs. Compared to non-participants, participants at wave 1 were more likely to be women, to be between 25-44 or 45-64 years of age, to live with a partner, to be a single parent and to have an immigrant background. In addition, the participants had consulted their GP more often and had more health problems than those who did not participate.[51]

At wave 2, 1116 of the 1567 wave 1 participants completed the questionnaire (response= 72%). Response was again selective; fewer men, fewer immigrants and fewer survivors with a paid job participated at wave 2. In addition, response was related to disaster-related factors and health problems reported at wave 1, with different response mechanisms for native Dutch and immigrant survivors.[52]

At wave 3, 995 survivors (response= 65%) participated and response was once more selective: females and survivors in the age categories 25-44 and 45-64 were more likely to respond. Among native Dutch survivors, health problems at wave 1 tended to be associated with non-response at follow-up (waves 2 and 3). In contrast, among immigrant survivors, health problems at wave 1 were associated with increased response at follow-up. It can be speculated that immigrant survivors of the fireworks disaster were not accustomed to participation in a health survey and believed that completion of the questionnaire was not meaningful in the absence of health problems (chapter 7, this thesis).

In addition to selective response, skipped items in the questionnaire (item non-response) was also responsible for missing data. For example, in chapter 6, 13.6% of the study population had one or more missing values in the questionnaire completed at wave 1. Survivors with missing values had a lower educational level, were more often immigrants, were more often unemployed, were more likely to have a public health insurance, were more likely to have a high level of pre-disaster GP visits and a high level pre-disaster mental health problems.

Selective participation was of less concern in the surveillance program; in total, 74% of all GPs in the city of Enschede participated in this program, having 89% of survivors on their list. The most common reasons for GPs not to participate were that they had only a few or no survivors on their list (N= 9), that they did not register the medical information electronically (N= 3), and that they did not want to spend extra time to register all the information (N= 4). Given these reasons, it is not very likely that the

patients on the list of the non-participating GPs differed from patients on the list of participating GPs.

To study the magnitude of the selection bias in the health surveys and to correct for selective response and item non-response, analyses of multiple imputations were used. Multiple imputation (MI) is a statistical technique for analyzing incomplete data sets.[53, 54] With MI, various plausible imputation values are calculated for every missing value by using the intercorrelations of variables from the non-missing data. For example, in chapter 7 of this thesis five different imputation values were calculated for the health problems of survivors who did not participate at the follow-up waves. MI takes into account two sources of uncertainty in the imputed value for a missing datum: uncertainty in the form of sampling variability and uncertainty regarding correctness of the imputed value. The combined variance is greater than the variance obtained from single imputation, which is a major advantage of MI.[53, 54]

Although there was selective participation at the three waves of the health survey, multiple imputation barely affected the prevalence estimates indicating that the estimates were only somewhat biased (chapter 7, this thesis).[51, 55] These results indicate that selective response and attrition at follow-up may not necessarily have had an important impact on the prevalence estimates of health problems.

Outcome measures

In the health surveys, physical symptoms were measured by means of the Questionnaire into Subjective Health Complaints, the VOEG.[56] This questionnaire was originally developed to measure stress among blue-collar workers and asks whether respondents regularly have symptoms such as headache, back pain and stomachache. In this thesis a shortened version of 13 items was used,[57] which was extended with 8 symptoms at waves 2 and 3. Although the reliability and the construct validity of the 13-item VOEG are satisfactory,[58] the cause, duration and severity of the symptoms reported in this questionnaire are not determined. As a result this scale does not provide insight into the clinical relevance of symptoms. Several other scales are available that do measure the severity of symptoms or associated impairment such as the physical symptoms questionnaire (Dutch: Lichamelijke Klachten Vragenlijst, LKV),[59] the Screening for Somatoform Symptoms (SOMS) scale, [60, 61] and the Subjective Health Complaints Inventory.[62, 63] However, these scales have several limitations. Firstly, they have not been validated for the Dutch situation. Secondly, it is not known whether the scales are also applicable in studies after disasters. For example, the SOMS was developed to detect the presence somatoform disorders and the LKV was developed to measure the severity and course of somatoform disorders. Finally, these scales have a large number of items (LKV: 51 items; SOMS: 53 items or 29 items).

A difficulty with the use of questionnaires in general is that self-reports might be an overestimation of symptoms that are clinically relevant, since the reported symptoms might be transient and self-limited. Nevertheless, the self-reported symptoms among the survivors of the fireworks disaster were related to a high level of functional impairment, illness behavior and psychological problems (chapter 3).

Contrary to questionnaire data, symptoms registered in the EMRs of survivors might be an underestimation of the symptoms that are experienced. For example, studies have indicated that more than 80% of the general population experiences at least one symptom every two to four weeks.[9] Of these symptoms only a minority causes impairment and is presented to the GP.[9, 10] This phenomenon has been called the iceberg of morbidity.[8] The results of chapter 4 indicated that only a minority (< 29%) of self-reported symptoms were presented to the GP. In addition, GPs might not register all symptoms that are presented. Engel and Katon describe MUS as a four-part process.[64] An individual must first experience the symptoms. Cognition, related to how individuals think about the symptoms, follows. This step includes beliefs about the cause of symptoms and assignment of medical importance. In the third step, an individual seeks medical care for the symptoms, an act that is mediated by the belief in the symptom's significance. The judgment of the clinician concerning whether the symptom can be explained by a medical disorder comprises the fourth step. It can be argued that self-reported symptoms represent the symptoms in step one and that the symptoms presented to the GP are those from step four. Relatively little is known about the cognitions of individuals that mediate the behavioral step to seek medical care (steps 2 and 3), and the present study did not provide insight into this behavioral step.

Another disadvantage of using existing registration systems is that disaster-related exposure and other risk factors for health problems cannot be assessed. Despite these disadvantages, the health problems in the EMRs of survivors can easily be compared with the health problems registered in the EMRs of unaffected populations, which is an important advantage of the use of EMRs. Furthermore, EMR data do not depend on the willingness of individuals to complete a questionnaire, and therefore selective response and attrition is of less importance. In conclusion, the use of existing registration systems overcome important disadvantages of the use of questionnaires such as selective response, the large variety in questionnaires and measurement times which makes comparisons between studies difficult, and the absence of an appropriate control population.

Conclusions and recommendations for future studies

The level of symptoms that are frequently unexplained was elevated among the survivors of the fireworks disaster, despite the lack of elevated levels of heavy metals in the blood and urine of survivors due to the disaster and despite the absence of 'conspiracy' theories about possible exposure to toxic substances. In addition, the literature review showed that the level of self-reported physical symptoms was higher among survivors than among controls after different kinds of natural and man-made disasters. These findings indicate that elevation of physical symptoms are part of the distress reaction following traumatic exposure. For that reason, it is too limited to solely focus on mental health problems among survivors of disasters. Because higher levels of symptoms can be expected in the aftermath of disasters, measuring these symptoms should be part of the health impact assessment after disasters.

In the aftermath of the Enschede fireworks disaster, no conspiracy theories about possible exposure to toxic substances developed. It can be hypothesized that the reassuring results of the blood and urine samples that were obtained three weeks after the disaster, in which no elevated body burden was detected, have contributed to the absence of such a theory. To prevent the development of conspiracy theories, taking blood and urine samples shortly after a new disaster to detect possible elevated body burden and performing an epidemiological study can be recommended, especially if there is suspicion about exposure to toxic substances.

Existing registration systems are very useful for gaining insight into the health status of a large group of survivors before the disaster and in the years after the disaster. However, existing registration systems do not disclose all health problems that are experienced by survivors, and disaster-related exposure and other risk factors for health problems cannot be assessed. Therefore, the use of registration systems might be best supplemented with data from questionnaires that measure the experiences of survivors during the disaster and the health problems of survivors after the disaster. Measurement of physical and psychological disaster exposure and pre-disaster risk factors is recommended shortly after the disaster, since otherwise this information will be lost. Health problems shortly after the disaster can be seen as a normal reaction to an abnormal event; therefore, mental health problems of survivors and other possible risk factors for health problems such as social support factors and illness beliefs might best be measured some time after the disaster, when the health problems have become persistent. Health problems in the longer term could be examined using the EMRs of GPs.

Performing an epidemiological study after disasters is not only recommended to prevent the development of conspiracy theories. Such a study also provides insight into health problems of survivors, which is important information for both policy makers and health professionals. However, selective participation and biased prevalence

estimates of health problems are of concern when health surveys using questionnaires are performed. Selective response occurred in all three waves of the longitudinal health survey after the fireworks disaster and the response mechanism was different for native Dutch than immigrant survivors. This indicates that different strategies should be used to encourage participation of native Dutch and immigrant survivors.

Despite selective response, multiple imputation hardly affected the prevalence estimates of the health problems of survivors. Therefore, future studies should not only examine selective response, but should also investigate whether selective response biases the complete case prevalence estimates of health problems by using statistical techniques such as multiple imputation. This is especially important in the aftermath of disasters, when epidemiological studies also have policy-directed goals, and the outcomes of the study will be used for interventions.

Self-reported symptoms had associated features that are similar to MUS presented to the GP, such as a high level of functional impairment and psychological distress. Therefore, questionnaires can be used to measure symptoms that show similarities with MUS, either as a supplement to the EMRs or when EMRs are not available. However, currently there are no validated scales for the Dutch population. Therefore, a new scale should be developed or an existing scale should be validated and adjusted for the Dutch situation. Such a scale should meet several criteria. For example, it should be a short questionnaire that measures symptoms that are likely to remain medically unexplained when presented to the GP. In addition, it should measure the severity of the symptoms and associated functional impairment.

Disaster-related factors were not independent risk factors for symptoms; the relationship between disaster exposure and physical symptoms was mediated by psychological problems such as symptoms of PTSD, depression and anxiety. This finding suggests that GPs and health care workers should not focus on what survivors have experienced during the disaster; rather they should identify those individuals who have a high level of distress after the disaster.

The examined risk factors were not sufficient to identify all survivors at risk for developing symptoms and additional risk factors such as childhood experiences and illness beliefs will most likely be relevant for survivors of disaster as well. For that reason, future studies after disasters should measure these factors. Also, more insight is needed into risk factors that are specific for MUS, such as cognitions and causal attribution that increase worries about the symptoms and that aggravate symptoms and precipitate health care utilization for symptoms. These factors will provide more insight into the relationship between traumatic exposure and physical symptoms and may help policy makers and clinicians with the identification of those at risk and the management of individuals with MUS.

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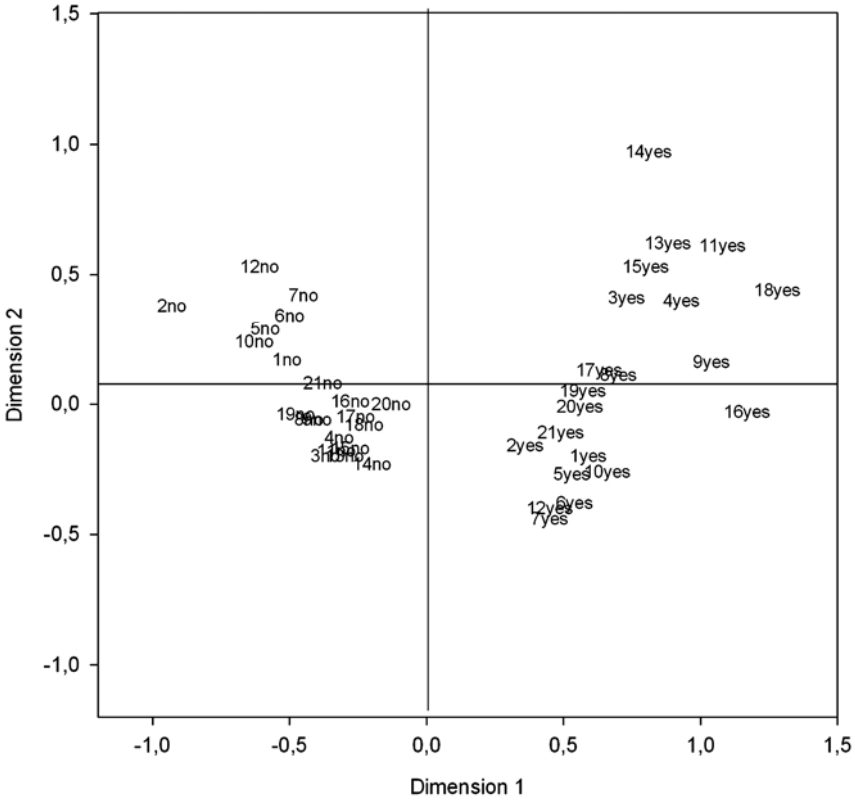
Appendix

Pattern of symptoms among survivors and controls

To identify symptom clusters among survivors and controls, we applied multiple correspondence analysis (MCA) to the 21 binary items. MCA is a statistical technique that is useful for exploring relationships between categorical variables and summarizing them into a small number of clusters or dimensions.[21] The primary outcome of MCA is the percentage of the principal inertia explained by a certain dimension, which is similar to explained variance by a factor in factor analysis.

For both the survivors and the controls, the first dimension of the (MCA) distinguished between the presence of symptoms (yes) and the absence of symptoms (no). The first dimension accounted for 27.0% of the inertia in the survivor group and for 25.3% in the control group. Figure 1 shows a graphic representation of the 21 symptoms reported by the survivors at wave 2 according to the first two dimensions emerging from the MCA. The second and following dimensions differed between survivors and controls but accounted for less of the inertia (≤ 7%) than the first dimension. In addition, the clustering of symptoms was not comparable with one of the functional somatic syndromes. For example, in the survivor group tight feeling in the chest, ringing in the ears, deafness, poor vision and lump in throat clustered together and headaches, pain in back and pain in neck and shoulders clustered together on the second dimension. Exclusion of the survivors and controls with a chronic disease did not change the results of the MCA (data not shown).

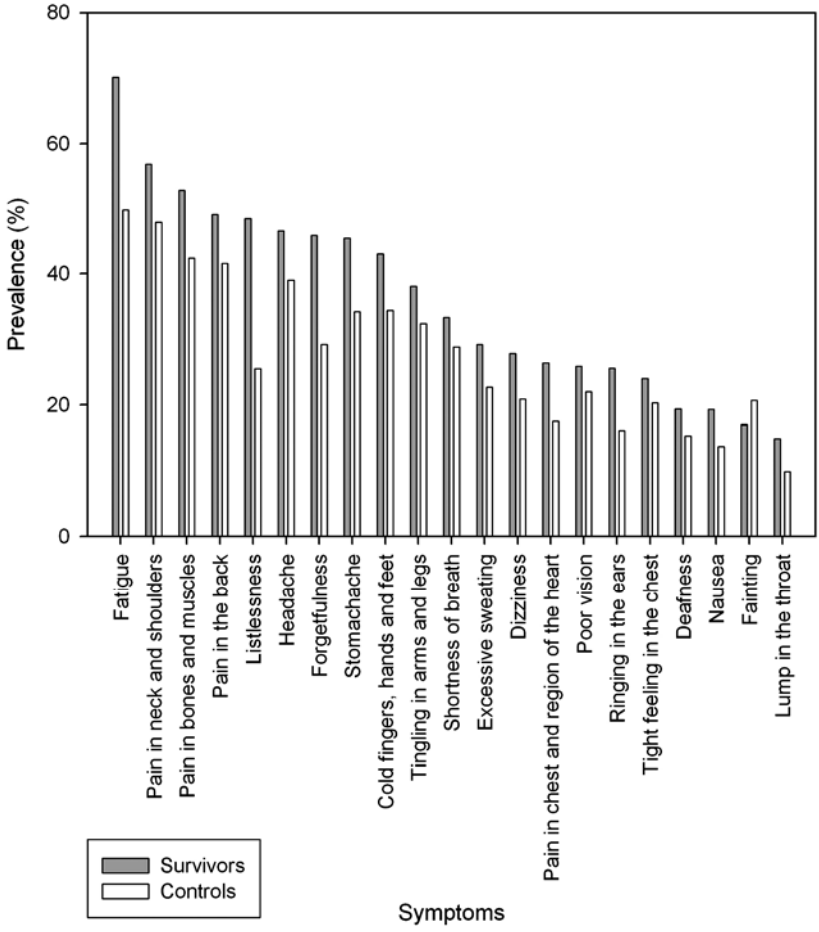
Figure 1: Multiple correspondence analysis: two-dimensional representation of 21 symptoms reported by survivors at wave 2*



* Dimension 1 on the X-axis distinguished between symptoms that were present (yes) and symptoms that were not present. Dimension 2 (Y-axis) accounted for a small proportion of the inertia (< 7%), the clustering of dimension 2 was not comparable with on of the functional somatic syndromes. 1= stomachace; 2= fatigue; 3= shortness of breath; 4= pain in chest and the region of the heart; 5= pain in bones and muscles; 6= headache; 7= pain in back; 8= tingling in arms and legs; 9= dizziness; 10= l

Figure 2 shows the prevalence of the 21 symptoms at wave 2 among survivors and controls. A unique pattern of symptoms among survivors of the fireworks disaster was not likely since the most prevalent symptoms were similar between survivors and controls, with higher prevalence rates among survivors.

Figure 2: Prevalence of symptoms among survivors and controls at wave 2 of the longitudinal health survey



Summary

Most studies after disasters have focused on mental health problems such as post-traumatic stress disorder (PTSD), depression and anxiety among survivors of disasters. Besides mental health problems, survivors may develop physical health problems as a result of the traumatic event. Partly due to the health effects of the Gulf War and the aircraft disaster in the Bijlmermeer in Amsterdam, there is a growing recognition that traumatic events such as disasters can be related to physical symptoms that often remain medically unexplained. Despite this, symptoms that are frequently unexplained such as headache, fatigue and stomachache are have not often been studied after disasters.

The studies described in this thesis examine symptoms that are frequently medically unexplained among residents affected by the Enschede fireworks disaster that occurred on May 13, 2000. As a result of the explosion of a fireworks depot in a residential area in Enschede, the Netherlands, 23 persons were killed, more than 900 people were injured and about 1200 people were forced to relocate because their houses were destroyed or severely damaged. After this disaster, a longitudinal study of the health consequences of the disaster was started. The study consisted of a 3-wave longitudinal health survey that was performed three weeks (wave 1), 18 months (wave 2) and almost 4 years (wave 3) after the disaster. In addition to this longitudinal health survey, the electronic medical records (EMRs) of GPs were used to study changes in health problems among survivors.

The main objectives of this thesis were 1) to examine the prevalence of symptoms among survivors of disasters, 2) to explore risk factors for these symptoms among survivors and 3) to investigate whether self-reported symptoms show similarities with medically unexplained symptoms (MUS) that are presented to the general practitioner (GP).

In chapter 2, the literature published between 1983 and 2003 is reviewed to examine the prevalence rate of and risk factors for symptoms among survivors of disasters. In total, 57 studies were selected that examined physical symptoms among survivors of different kinds of natural and man-made disasters. Survivors reported a higher level of symptoms than controls both immediately and in the years after the disasters. However, there was a large variation in the prevalence rates of symptoms depending on the type of disaster and the measurement time. Risk factors for symptoms have not often been studied among disaster survivors. Despite this, a few risk factors for symptoms have been consistently found in previous disaster studies such as female gender, high physical damage and symptoms of PTSD.

Chapter 3, addresses the course and prevalence of physical symptoms among survivors of the fireworks disaster. In addition, it examines whether the self-reported symptoms show features similar to those of MUS such as associated functional impairment and psychological problems. At wave 2, 15 of 21 symptoms in the questionnaire were significantly more prevalent among survivors compared to controls. The most prevalent symptoms were similar among survivors and controls, with higher prevalence rates among survivors such as for fatigue (70.1% vs. 49.9%), pain in neck and shoulders (56.9% vs. 48.0%) and pain in bones and muscles (52.9% vs. 42.4%). At wave 3, almost four years post-disaster, 12 of the 21 symptoms were significantly more prevalent among survivors than among controls. The self-reported symptoms showed several similarities with MUS; self-reported symptoms were associated with functional impairment and with a higher level of illness behavior such as sick leave and painkiller use which are also features of those suffering from MUS. Also, a higher level self-reported symptoms were associated with a high level of feelings of depression and anxiety which is also common among individuals with MUS.

In Chapter 4, it is assessed whether survivors presented their self-reported symptoms to the GP and whether survivors who presented their symptoms to the GP had a high level of functional impairment and distress. Also, to examine whether self-reported symptoms are similar to MUS, the proportion of symptoms that are medically unexplained after clinical judgment is described. The majority of self-reported symptoms was not presented to the GP and survivors were most likely to report persistent symptoms to the GP. For example, survivors with self-reported stomachache at waves 1 and 2 were more likely to report stomachache to their GP (28%), than survivors with stomachache either at wave 1 (6%) or at wave 2 (13%). Presenting symptoms to the GP was not consistently associated with a high level of functional impairment and distress. After clinical examination, 56% (shortness of breath and pain in chest and the region of the heart) to 91% (fatigue) was not associated with a medical disorder and remained medically unexplained. These results suggest that self-reported physical symptoms are likely to be similar to MUS.

In chapter 5, predisposing, precipitating and perpetuating factors for self-reported symptoms at waves 2 and 3 are studied. In addition, it is examined whether risk factors for physical symptoms differ between survivors and controls. Random coefficient analysis showed that female gender (B= 1.0, 95% CI: 0.6, 1.4), immigrant status (B= 1.0, 95% CI: 0.6, 1.4), cigarette smoking (B= 0.5, 95% CI: 0.1, 0.8) and pre-disaster psychological problems (B= 0.8, 95% CI: 0.1, 1.4) were predisposing factors for symptoms reported at waves 2 and 3. Although disaster-related factors were associated with symptoms, the magnitude of this association was reduced when perpetuating factors were added to the model; intrusions and avoidance, depression, anxiety and sleeping problems were important risk factors for physical symptoms and

mediated the relation between traumatic exposure and physical symptoms. The risk factors for symptoms were similar between survivors and controls.

In chapter 6, we evaluated the prevalence and course of unexplained symptoms presented to the GP from one year before the disaster until four years after the disaster. We also examined risk factors for a high level of symptoms (≥ 5 symptoms, 90th percentile) and examined the extend to which the identified risk factors predicted a high level of symptoms among survivors. Compared to the year prior to the disaster, the mean number of MUS was increased in the first two years after the disaster. Several risk factors for MUS were identified by using generalized estimating equations: female gender (OR= 1.5, 95% CI: 1.2, 1.8), immigrant status (OR= 1.9, 95% CI: 1.5, 2.4), a high level of pre-disaster MUS (OR= 7.4, 95% CI: 5.3, 10.4) and concurrent psychological problems (OR= 3.8, 95% CI: 3.1, 4.7). Disaster-related factors, such as relocation and having a high level of disaster exposure, were not directly related to MUS. The regression model could not explain most of the variation in MUS that occurred in the years post-disaster and the identified risk factors were insufficient to identify all survivors who will report a high level of MUS to the GP.

In chapter 7, the selective response at waves 2 and 3 of the longitudinal health survey is examined. In addition, we studied whether selective response had biased the prevalence estimates of health problems among survivors by comparing prevalence estimates resulting from multiple imputation and from complete case analysis. Multiple imputation fills in plausible values for the missing data using correlations between observed variables. Analyses were stratified according to ethnic background in this chapter. Among both native Dutch and immigrant survivors, females and survivors in the age categories 25-44 and 45-64 years old were more likely to respond to the follow-up surveys. Among native Dutch, those who responded only to wave 1 reported somewhat more health problems at wave 1, three weeks post-disaster, than those who responded to all three waves. In contrast, immigrants who responded only to wave 1 had fewer health problems at wave 1 such as depressive feelings and physical symptoms than those immigrants who responded to all three waves. Among native Dutch survivors, the imputed prevalence estimates of wave 3 health problems tended to be higher than the complete case estimates. The imputed prevalence estimates of wave 3 health problems among immigrants were either unaffected or somewhat lower than the complete case estimates. These results indicate that despite selective response at the follow-up waves, the complete case prevalence estimates of the health problems of the survivors of the fireworks disaster were only somewhat biased.

In chapter 8, the main findings of the studies in this thesis are discussed. The review of the literature showed that the prevalence rate of self-reported symptoms was elevated among survivors of different kinds of disasters. Among the survivors of the fireworks disaster, the level of self-reported symptoms was higher compared to controls

up to four years after the disaster. Besides this, the mean number of symptoms presented to the GP was higher in the two years after the disaster compared to the year prior to the disaster. We identified several important risk factors for symptoms among survivors such as female gender, immigrant status and psychological problems. The risk factors for symptoms among survivors were comparable with the risk factors for MUS in the general population. This finding indicates that other risk factors that were not measured in this study but that have been found in studies among the general population might also predict symptoms among survivors of disasters. In addition, the results showed several similarities between the self-reported symptoms and MUS.

In addition, several methodological issues are discussed in chapter 8. The design of the study that was performed after the fireworks disaster in Enschede has several advantages. The longitudinal health survey allowed conclusions about the course of health problems of survivors in the short, medium term after the disaster. Besides this, the electronic medical records (EMRs) of GPs provided insight into the health status of a large group of survivors starting in the year prior to the disaster up to five years post-disaster. Although there was selective participation at the three waves of the health survey, multiple imputation barely affected the prevalence estimates indicating that the estimates were only somewhat biased. The advantages and disadvantages of the use of questionnaires and EMRs in epidemiological studies after disasters are discussed in addition to the design of the study and selective response.

Finally, conclusions are drawn and recommendations are given. The findings indicate that elevation of physical symptoms are part of the distress reaction following traumatic exposure. For that reason, it is recommended to measure these symptoms in studies after disasters. It can be hypothesized that the reassuring results of the blood and urine samples that were obtained three weeks after the disaster have contributed to the absence of such a theory. To prevent the development of conspiracy theories, taking blood and urine samples shortly after a disaster to detect possible elevated body burden and performing an epidemiological study can be recommended, especially if there is suspicion about exposure to toxic substances. Electronic medical records can be supplemented with data from questionnaires to get insight into the health effects of the disaster. Since the self-reported symptoms showed several similarities with MUS, questionnaires can be used to measure physical symptoms that are frequently unexplained. However, a new scale should be developed or an existing scale should be validated and adjusted for the Dutch situation, since no validated scales are available yet. Finally, despite the fact that some important risk factors were identified in this study, more studies into risk factors that are specific for MUS are needed.

Samenvatting

De meeste studies na rampen richten zich op de psychische problemen van getroffenen zoals post-traumatische stress stoornis (PTSS), depressie en angst. Naast deze gezondheidsgevolgen van psychische aard kunnen getroffenen ook lichamelijke klachten ontwikkelen als gevolg van traumatische ervaringen. Mede door de gezondheidseffecten van de eerste Golfoorlog en van de vliegramp Bijlmermeer is er meer erkenning gekomen voor het feit dat traumatische gebeurtenissen gerelateerd kunnen zijn aan lichamelijke klachten die vaak niet verklaard kunnen worden door een medische ziekte. Desondanks zijn klachten die vaak niet verklaard kunnen worden door een medische oorzaak, zoals hoofdpijn, vermoeidheid en buikpijn maar zelden onderzocht in studies na rampen.

In dit proefschrift worden deze lichamelijke klachten onderzocht bij bewoners die getroffen zijn door de vuurwerkramp in Enschede welke plaats vond op 13 mei 2000. Als gevolg van de ontploffing van een vuurwerkopslagplaats in een woonwijk in Enschede vonden 23 mensen de dood, raakten meer dan 900 mensen gewond en werden ongeveer 1200 mensen gedwongen te verhuizen omdat hun huis verwoest of ernstig beschadigd was. Na deze ramp werd een longitudinaal onderzoek naar de gevolgen van de ramp gestart. Het onderzoek bestond uit een vragenlijstonderzoek met drie metingen die 3 weken, 18 maanden en ongeveer 4 jaar na de ramp werden uitgevoerd. Tijdens meting 2 en 3 werd een vergelijkbare vragenlijst afgenomen bij een controle groep in Tilburg. Bovendien werden de elektronische dossiers van de huisartsen gebruikt om zo het beloop van de gezondheidsproblemen van de getroffenen te kunnen bestuderen.

De hoofddoelen van dit proefschrift waren 1) het onderzoeken van de prevalentie van klachten bij getroffenen van rampen in het algemeen en bij de getroffenen van de vuurwerkramp in het bijzonder, 2) het bestuderen van risico factoren voor deze klachten bij getroffenen en 3) onderzoeken in hoeverre zelfgerapporteerde klachten overeenkomsten vertonen met lichamelijk onverklaarde klachten (LOK) zoals die gepresenteerd worden aan de huisarts.

In hoofdstuk 2 is de literatuur die is verschenen tussen 1983 en 2003 bestudeerd om inzicht te krijgen in de prevalentie van en risico factoren voor klachten onder getroffenen van rampen. In totaal zijn 57 artikelen geselecteerd waarin lichamelijke klachten zijn onderzocht bij getroffenen van natuurrampen en van rampen die door de mens zijn veroorzaakt. De resultaten laten zien dat getroffenen van rampen zowel direct na als in de jaren na de ramp meer klachten rapporteren dan controle personen. De prevalentie schattingen van de klachten varieerden echter sterk, afhankelijk van het type ramp en het tijdstip van afname van de vragenlijst.

Risicofactoren voor fysieke klachten zijn niet vaak bestudeerd onder getroffenen van rampen. Desondanks zijn een paar risicofactoren in verschillende studies na rampen gevonden, zoals het vrouwelijk geslacht, een hoge mate van fysieke schade en symptomen van post-traumatische stress stoornis (PTSS).

Hoofdstuk 3 richt zich op het beloop en de prevalentie van lichamelijke klachten bij de getroffenen van de vuurwerkramp. Bovendien is bestudeerd in hoeverre de zelfgerapporteerde klachten dezelfde kenmerken hebben als LOK in de algemene populatie zoals geassocieerde functionele beperkingen en psychische problemen. Tijdens meting 2 werden 15 van de 21 klachten op de vragenlijst significant vaker gerapporteerd door getroffenen dan door controle personen. Ondanks de hogere prevalentie van klachten bij getroffenen waren de meest voorkomende klachten hetzelfde voor getroffenen en controles, zoals voor vermoeidheid (70.1% versus 49.9%), pijn in nek en schouders (56.9% versus 48.0%) en pijn in botten en spieren (52.9% versus 42.2%). Tijdens meting 3, bijna vier jaar na de ramp, werden 12 van de 21 klachten vaker gerapporteerd door getroffenen dan door controles. De zelfgerapporteerde klachten vertoonden verscheidene overeenkomsten met LOK; de klachten waren geassocieerd met functionele beperkingen en met meer ziektegedrag zoals het gebruik van de ziektewet en het gebruik van pijnstillers. Bovendien waren klachten geassocieerd met een hoge mate van depressie en angst.

In hoofdstuk 4 is onderzocht in hoeverre getroffenen hun zelfgerapporteerde klachten bij de huisarts hebben gemeld. Daarnaast is gekeken of degenen die met hun klachten naar de huisarts gingen meer functionele beperkingen en psychische problemen hadden. Bovendien is onderzocht welk deel van de klachten na een medisch oordeel van de huisarts lichamelijk onverklaard bleken te zijn. De meerderheid van de zelfgerapporteerde klachten was niet gemeld bij de huisarts en getroffenen waren het meest geneigd om met aanhoudende klachten naar de huisarts te gaan. Bijvoorbeeld, getroffenen met zelfgerapporteerde buikpijn op meting 1 en 2 rapporteerden vaker buikpijn aan de huisarts (28%) dan getroffenen die alleen buikpijn hadden op meting 1 (6%) of meting 2 (13%). Het melden van klachten aan de huisarts hing niet consistent samen een hoge mate van functionele beperkingen en psychische problemen. Na een klinisch onderzoek was 56% (benauwdheid en pijn in borst- en hartstreek) tot 91% (vermoeidheid) van de klachten niet gerelateerd aan een medische ziekte en bleef dus onverklaard.

In hoofdstuk 5 zijn predisponerende, rampgerelateerde en instandhoudende factoren voor zelfgerapporteerde klachten onderzocht. Daarnaast is onderzocht of de risico factoren voor lichamelijke klachten hetzelfde zijn voor getroffenen en controles. Random coëfficiënten analyse liet zien dat vrouwelijk geslacht (B= 1.0, 95% BI: 0.6, 1.4), allochtone status, (B= 1.0, 95% BI: 0.6, 1.4), sigaretten roken (B= 0.5, 95% BI: 0.1, 0,8) en psychologische problemen voor de ramp (B= 0.8, 95% BI: 0.1, 1.4)

predisponerende factoren waren voor klachten op meting 2 en 3. Hoewel rampgerelateerde factoren zoals een verwoest huis en het verliezen van een dierbare, samenhingen met klachten, werd deze relatie zwakker als de instandhoudende factoren werden toegevoegd aan het model. Herbeleving en vermijdingsreacties, depressie, angst en slaapproblemen waren belangrijke instandhoudende factoren voor klachten en medieerden de relatie tussen blootstelling aan trauma en lichamelijke klachten. De risico factoren waren hetzelfde voor getroffenen en controles.

In hoofdstuk 6 is de prevalentie en het beloop van onverklaarde klachten bij de huisarts bestudeerd vanaf een jaar voor de ramp tot vier jaar na de ramp. Bovendien hebben we risico factoren voor een hoog niveau van klachten (≥ 5 klachten, 90^{e} percentiel) onderzocht en hebben we gekeken in hoeverre de geïdentificeerde risico factoren een hoog niveau van klachten bij getroffenen konden voorspellen. Vergeleken met het jaar voor de ramp was het gemiddelde aantal klachten verhoogd in de eerste twee jaren na de ramp. Verschillende risico factoren voor LOK werden gevonden: vrouwelijk geslacht (OR= 1.5, 95% BI: 1.2, 1.8), allochtone status (OR= 1.9, 95% BI: 1.5, 2.4), een hoog niveau van LOK voor de ramp (OR= 7.4, 95% BI: 5.3, 10.4) en psychologische problemen voorkomend in het hetzelfde jaar als LOK (OR= 3.8, 95% BI: 3.1, 4.7). Rampgerelateerde factoren zoals verhuizing als gevolg van de ramp en een hoge mate van blootstelling aan de ramp hingen niet direct samen met LOK. De factoren die waren op genomen in het regressie model waren niet voldoende om alle getroffenen met een hoog aantal klachten te identificeren.

In hoofdstuk 7 is de selectieve respons op de vervolgmetingen 2 en 3 van het longitudinale onderzoek bestudeerd. Daarnaast is onderzocht in hoeverre selectieve respons de prevalentie schattingen van de gezondheidsproblemen van de getroffenen heeft beïnvloed. Hiervoor zijn de prevalentie schattingen gebaseerd op multiple imputatie vergeleken met schattingen gebaseerd op ‘complete case analyse’. Multiple imputatie vult aannemelijke waarden in voor de missende waarde en maakt daarbij gebruik van correlaties tussen de geobserveerde variabelen. De analyses in dit hoofdstuk zijn gestratificeerd naar etnische achtergrond. Voor zowel de autochtone als de allochtone getroffenen werd gevonden dat vrouwen en getroffenen in de leeftijdscategorieën 25 tot 44 en 45 tot 64 jaar minder vaak deelnamen aan de vervolgmetingen. Bij autochtone getroffenen waren gezondheidsproblemen op meting 1 geassocieerd met non-respons op meting 2 en 3, terwijl bij allochtone getroffenen gezondheidsproblemen op meting 1 geassocieerd waren met respons op meting 2 en 3. De geimputeerde prevalentie schattingen van de gezondheidsproblemen op meting 3 bleken wat hoger te zijn voor de autochtone getroffenen dan de schattingen op basis van complete case analyse, terwijl de geimputeerde prevalentie schattingen voor gezondheidproblemen op meting 3 onder de allochtone getroffenen wat lager waren of niet verschilden van de complete case schattingen. Deze resultaten geven aan dat

ondanks de selectieve respons, de prevalentie schattingen van de gezondheidsproblemen van de getroffenen op basis van complete case analyse nauwelijks gebiased waren.

In hoofdstuk 8 worden de belangrijkste bevindingen van de studies in dit proefschrift bediscussieerd. Lichamelijke klachten blijken vaak voor te komen bij slachtoffers van rampen. De literatuur review toonde aan dat het aantal zelfgerapporteerde klachten verhoogd was bij slachtoffers van verschillende soorten rampen. De getroffenen van de vuurwerkramp rapporteerden een hoger aantal klachten vergeleken met de controle groep, tot vier jaar na de ramp. Daarnaast melden zij de eerste twee jaar na de ramp meer klachten bij de huisarts dan in het jaar voor de ramp. De resultaten toonden een aantal belangrijke risico factoren voor klachten bij getroffenen zoals het vrouwelijk geslacht, een allochtone status en psychische problemen. Deze risico factoren bleken overeen te komen met de risico factoren voor LOK in de algemene populatie. Dit wijst erop dat andere risicofactoren die niet in deze studie werden onderzocht ook risicofactoren voor klachten bij getroffenen van rampen zullen zijn. De zelfgerapporteerde klachten vertoonden veel overeenkomsten met LOK zoals gepresenteerd aan de huisarts.

Ook worden in hoofdstuk 8 een aantal methodologische punten besproken. Het design van het onderzoek dat is uitgevoerd na de vuurwerkramp in Enschede heeft verschillende voordelen. Door het longitudinale design van het vragenlijstonderzoek konden uitspraken worden gedaan over het beloop van gezondheidsproblemen van getroffenen op de korte en middellange termijn. Bovendien heeft het monitoren van de elektronische dossiers van getroffenen inzicht verschaft in de gezondheidsstatus van een grote groep getroffenen vanaf het jaar voor de ramp tot vijf jaar na de ramp. Ondanks selectieve respons werden de prevalentie schattingen van de gezondheidsproblemen nauwelijks beïnvloed door multiple imputatie. Daarom kan worden aangenomen dat de schattingen slecht een in geringe mate gebiased waren. Naast selectieve respons, zijn de voor- en nadelen van het gebruik van vragenlijsten en het gebruik van elektronische dossiers in gezondheidsonderzoek na rampen bediscussieerd.

Tot slot zijn worden conclusies getrokken en aanbevelingen gegeven. De bevindingen in dit proefschrift wijzen erop dat lichamelijke klachten onderdeel zijn van de reactie op traumatische stress. Daarom wordt het aanbevolen om lichamelijke klachten te meten in studies na rampen. Daarnaast, lijkt erop dat het onderzoeken van bloed en urine van getroffenen en het uitvoeren van een epidemiologisch onderzoek onder getroffenen de ontwikkeling van complot theorieën heeft voorkomen. Daarom worden ter voorkoming van complot theorieën, bloed en urine onderzoek en een epidemiologisch onderzoek aanbevolen, te meer als er sprake is van mogelijke blootstelling aan schadelijke stoffen. Voor het meten van gezondheidseffecten bij

getroffenen kunnen elektronische dossiers worden aangevuld met informatie uit vragenlijstonderzoek. Omdat de zelfgerapporteerde klachten veel overeenkomsten vertoonden met LOK, kunnen vragenlijsten worden gebruikt voor het meten van lichamelijke klachten die vaak niet verklaard kunnen worden door een medische oorzaak. Echter, omdat een goed gevalideerde vragenlijst voor het meten van dit soort klachten ontbreekt, wordt het ontwikkelen en valideren van een vragenlijst aanbevolen. Tot slot, ondanks het feit dat een aantal belangrijke risico factoren voor klachten zijn gevonden, is meer onderzoek naar risico factoren die specifiek zijn voor fysieke klachten wenselijk.

Dankwoord

Uiteraard wil ik iedereen die mij geholpen heeft bij het schrijven van dit proefschrift heel hartelijk danken.

Ten eerste, Linda, mijn dagelijks begeleidster en co-promotor. Ik heb ontzettend veel van je geleerd over epidemiologisch onderzoek en het schrijven van artikelen. Daarnaast heb ik veel geleerd van jou als persoon en je kijk op de wereld. De afgelopen vier jaar heb ik erg prettig met je samengewerkt en onze gezamenlijke hardloopuurtjes en congresbezoeken waren, én blijven, gezellig!
Rebecca, ook met jou heb ik erg fijn samengewerkt en ook van jou heb ik erg veel geleerd. Je hebt me gemaakt tot een geoefend data-analyste en je was in staat de onbegrijpelijke dingen van de statistiek voor mij begrijpelijk te maken. Ik vond het jammer dat je wegging bij het RIVM maar ik weet zeker dat je als docent op de universiteit helemaal op je plek zit. Ik vind het fijn dat je vandaag mijn paranimf wilt zijn.
Joris, bedankt dat je mijn co-promotor wilde zijn. Ik heb veel aan je adviezen gehad en heb met veel plezier met je samengewerkt. Ook als sociaal wetenschapper was je voor mij zeer welkom in het wereldje tussen de epidemiologen.
Anja, met jou heb ik veel leuke gesprekken gehad over werk, het schrijven van artikelen maar ook over persoonlijke dingen. Ik ben je dank verschuldigd omdat je altijd dingen voor me wilde opzoeken en tijd voor me vrijmaakte. Het congres in Toronto zou niet zo leuk zijn geweest als jij en Dirk-Jan er niet waren geweest!
Pauline, bedankt voor onze discussies over (M)UPS, onze samenwerking bij het organiseren van BRON en leuke gesprekken tijdens symposia en onverwachte treinreisjes.
Peter, de psycholoog waarmee is samenwerkte. Bedankt voor je vaak kritische blik op mijn manuscripten.
Erik, jouw commentaar dwong mij vaak nog eens kritisch naar mijn artikel te kijken. Ik vond onze discussies altijd erg interessant en nuttig.
Bert, van jou heb ik vooral begeleiding op afstand gekregen, hiervoor wil ik je graag bedanken.
Ook wil ik mijn collega's van MGO graag bedanken voor jullie gezelschap, nuttige tips, interesse in mijn proefschrift en de kritische vragen tijdens het inhoudelijk overleg.

Het Gezondheidsonderzoek Getroffenen Vuurwerkramp Enschede (GGVE) en daarmee dit proefschrift zou zonder de medewerking van de getroffenen van de vuurwerkramp en de betrokken huisartsen niet mogelijk zijn geweest. Daarom wil ik hen hierbij van harte bedanken.

Ik wil ook graag een aantal mensen buiten het werk bedanken.
Lieve papa en mama, jullie waren altijd geïnteresseerd in mijn werk, heel erg bedankt voor jullie steun.
Daphne en Cleome, met jullie kan ik altijd alle belangrijke en onbelangrijke dingen die ik meemaak bespreken. Ik ben heel erg blij dat jullie mijn zusjes zijn!
Lieve oma, ook jou wil ik bedanken voor je interesse in mijn proefschrift. Ik heb nu veel geleerd, maar van jou kan ik nog veel meer leren.
Lilian met jou is het altijd zo gezellig en kan ik nachten lang kletsen. De laatste tijd moest ik af en toe verstandig zijn en op tijd naar huis, maar dat is nu voorbij! Ik ben blij dat je vandaag mijn paranimf wil zijn!
Myriam, fijn om een vriendin te hebben die ook AiO is, ik kon altijd mijn ervaringen delen en advies aan je vragen. Succes nog even met jouw boekje!
Sanneke, bedankt voor onze gezellige culti-avondjes waardoor mijn gedachten weer even ergens anders waren dan bij het proefschrift.
Rianne, bedankt voor je leuke ideeën, onze doe-dingen en voor je levensinstelling die me er altijd weer aan herinnert dat er nog zó veel andere leuke dingen zijn in het leven behalve werken.
Paulien, jij bedankt voor je heerlijke en gezellige etentjes bij jou in Utrecht!
Ook al mijn andere vrienden waarmee het altijd super gezellig is en die me de nodige ontspanning hebben gegeven wil ik graag bedanken. Jullie waren altijd weer geïnteresseerd in de vorderingen van mijn proefschrift. Altijd als ik jullie zag was ik nog stéédś bezig met dat proefschrift. Maar, nu is het af dus tijd voor een mooi feestje!

Ja, en tot slot wil ik jou, Aris, bedanken. Maar als ik alle dingen zou beschrijven waarvoor ik jou dank voor verschuldigd ben dan moet ik nog een hoofdstuk aan dit proefschrift toevoegen. Om een lang verhaal kort te maken: je bent mijn Held!

Bellis

About the Author

Bellis van den Berg was born on 18th December 1977, in Willeskop, the Netherlands. She completed secondary school in 1995 at the Minkema College in Woerden and started her study Psychology at the Free University in Amsterdam. She graduated with a major in Social Psychology in 2002. From September 2002 until November 2006 she was appointed as a PhD-fellow at the Institute of Risk Assessment Sciences at Utrecht University and worked on this thesis and some other research projects related to the Enschede fireworks disaster at the National Institute for Public Health and the Environment (RIVM) in Bilthoven, the Netherlands. Currently she is working as a researcher at the Centre for Health Impact Assessments of Disasters (CGOR) at the RIVM.