

Review

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Recent Canadian efforts to develop population-level pregnancy intervention studies to mitigate effects of natural disasters and other tragedies

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Abstract

The preconception, pregnancy and immediate postpartum and newborn periods are times for mothers and their offspring when they are especially vulnerable to major stressors – those that are sudden and unexpected and those that are chronic. Their adverse effects can transcend generations. Stressors can include natural disasters or political stressors such as conflict and/or migration. Considerable evidence has accumulated demonstrating the adverse effects of natural disasters on pregnancy outcomes and developmental trajectories. However, beyond tracking outcomes, the time has arrived for gathering more information related to identifying mechanisms, predicting risk and developing stress-reducing and resilience-building interventions to improve outcomes. Further, we need to learn how to encapsulate both the quantitative and qualitative information available and share it with communities and authorities to mitigate the adverse developmental effects of future disasters, conflicts and migrations. This article briefly reviews prenatal maternal stress and identifies three contemporary situations (wildfire in Fort McMurray, Alberta, Canada; hurricane Harvey in Houston, USA and transgenerational and migrant stress in Pforzheim, Germany) where current studies are being established by Canadian investigators to test an intervention. The experiences from these efforts are related along with attempts to involve communities in the studies and share the new knowledge to plan for future disasters or tragedies.

Introduction

This paper addresses how teams of investigators in three different jurisdictions and types of vulnerabilities organized themselves and their studies of interventions to mitigate the effects of extreme stresses on pregnancy outcomes. The goal of this article is to inform other teams and communities about methodologies and approaches that may encourage and guide them to take action, especially immediately after natural disasters, to initiate projects that will provide valuable information that will inform public health officials and communities about best practices to improve pregnancy outcomes and to provide both quantitative and qualitative data that will reflect the experiences and context of the victims of these stressful situations.

The preconception, pregnancy and immediate postpartum and newborn periods are times for mothers and their offspring when they are especially vulnerable to major stressors – those that are sudden and unexpected and those that are chronic. Their adverse effects can last for years and transcend generations.^{1,2} Stressors can include natural disasters or political stressors such as conflict and/or migration, which, sadly, continue at extremely high rates. Between 1980 and 2015, the global number of 11,538 natural disasters were reported (including hurricane Katrina, the Haiti and Nepal earthquakes, the tsunami in Japan in 2011 and the Philippines typhoon).³ In the Americas alone, 2762 natural disasters occurred between 1980 and 2015,³ and six consecutive hurricanes formed in 2017.⁴ Global natural disasters reported in 2016 included 315 events and caused insured losses of USD \$54 billion.⁵ Climate change and increased incidences of pandemics are expected to threaten human populations even more

frequently over the next decades.⁶ The disaster risk has been predicted to increase if global trends continue.⁵ Over the past century, wars have decimated populations and infrastructure, and in recent years Mideast and Syrian conflicts have produced millions of refugees. Germany in 2015–2017 accepted over 1.5 million such refugees who became marginalized citizens who struggle to find their way in their new country.⁷ Damage, destruction and human suffering caused by natural disasters, conflicts and migration can be tremendous, and the capacity of local communities to respond to basic needs,^{8,9} let alone particular needs associated with pregnancy and childbirth, can be greatly compromised. As a result, natural disasters can leave pregnant women, their unborn children and future generations vulnerable to risks for metabolic syndrome and impaired neurodevelopment.^{10–15}

Studies have tracked outcomes with these victims for several years.¹⁰ Beyond tracking outcomes, the time has arrived for gathering more information related to identifying mechanisms, predicting risk and developing resilience-building and stress-reducing interventions to improve outcomes. Further, we need to learn how to encapsulate this information and share it with communities and authorities to mitigate the adverse developmental effects of future disasters, conflicts and migrations.

Establishing pregnancy intervention studies in affected populations is, unfortunately, difficult. The attractive study feature of a natural disaster is that it is a single stressful event in time whose effect is shared by a defined population. But the problem of studying a pregnancy intervention in such populations is that a 9-month clock starts ticking that defines all women who were pregnant at the moment of the disaster and therefore eligible for the intervention. A study needs to be hastily established in order to quickly recruit and intervene before the pregnancies are over. Similarly, it is difficult to establish studies where no major universities or clinical centres where researchers and appropriate resources can be found. Another barrier is that peer-reviewed funding schemes to support pregnancy intervention studies normally require a year or more before funds are available, and by then all the expectant mothers will have delivered after a natural disaster.

In this article, we will identify three contemporary situations where current studies of pregnant women and their offspring are being established by Canadian investigators after natural disasters or historical/political crises. An expressive writing intervention that may be effective, inexpensive and readily administered to large populations to reduce stress in pregnant women will be described. This intervention also provides both quantitative and qualitative data to better appreciate the context being experienced by these natural disaster victims. And, last, the experiences of interacting with the communities involved will be related.

Methods

Three contemporary stressful situations

Fort McMurray – Wood Buffalo, Alberta, Canada wildfire

On 1 May 2016, a wildfire started south of the northern Albertan city of Fort McMurray – Wood Buffalo (FMWB). Within 3 days, the fire had massively multiplied in size and approached the town and nearby municipalities, forcing a mass evacuation of some 88,000 people. Only a few days after the evacuation order, 10,000 people were stranded in work camps in the oilfields to the north of the city, while the remaining 78,000 were

successfully evacuated to southern cities. Large shelters in stadiums and exposition arenas were established to temporarily house evacuees until they moved in with friends and families or temporarily rented housing in Alberta and across Canada.¹⁶ This natural disaster became Canada's worst in every respect with an estimated cost of \$9 billion. In this disaster, 2400 buildings (10% of total), mostly family houses, were destroyed. Many structures left intact experienced smoke damage or ash contamination. During the height of the fire, the air pollution index rose to 38 (on a 10-point scale).¹⁷ The city's water supply was contaminated, and the large amount of residual ash and soil contained 19 different toxic metals and compounds reaching levels 20 times above recommended limits.¹⁸ Residents were not allowed to return to the city until June 1, and then only limited numbers were permitted access. Over the next 2 months, about half of the evacuees returned, but even 20 months after the fire, some 10–20% of residents did not return. Compounding their problems, many FMWB families were experiencing economic difficulties before the wildfire due to layoffs or decreased working hours brought on by lower oil demand and prices. Psychologists and other experts predicted correctly that after families returned to their homes the cases of domestic abuse and interpersonal violence would increase due to the stresses and uncertainties brought on by this natural disaster.¹⁹ Cumulatively, the stresses due to the natural disaster and consequent uncertainty and disruption of lives, toxic chemical ingestion and proinflammatory stimulus of air-borne pollutants had the potential to accumulate to the point where individual resilience was overcome and people lost the ability to cope. In this situation, pregnant women and their unborn children were particularly vulnerable to this kind of accumulated stress. Owing to a young population, it was estimated that approximately 1250 (range 1100–1400) of the 88,000 people evacuated were pregnant women and another 600 were pre-conception (i.e. within 6 months of becoming pregnant).

Houston, Texas, USA, hurricane Harvey

The flood of late August 2017 caused by hurricane Harvey presented an opportunity to conduct a natural experiment within, arguably, one of the most vulnerable communities in the United States: Harris County in Houston, Texas, which includes approximately 4.5 million people. The scope of the damage is estimated at \$125 billion USD; 32,000 families were displaced during the storm.²⁰ There are 72,000 babies born each year in Harris County, which has high rates of teen pregnancy (8.9%) and preterm birth (11.9%).²¹ Based on data described by the Texas Department of State Health Services, an estimated 54,000 women were pregnant at the time of hurricane Harvey and another 36,000 would have conceived within the 6 months following hurricane Harvey.²¹ Hence, the magnitude of the disaster is ideal for determining the effects of prenatal maternal stress (PNMS) because hurricane Harvey provided a sizeable sample of pregnant women with a relatively sudden onset (unlike many life events). This permits careful assessment of any potential moderating effects of the timing of the hurricane in pre-conception or pregnancy.

Pforzheim, Germany, historical trauma and migration

Another grave concern is the effect from traumatic events upon subsequent generations. In order to study the mechanisms of transgenerational programming by stress and trauma in humans,

a group of concerned practicing health care professionals initiated a population-based study of personal and transgenerational stress in the city of Pforzheim and the surrounding county of Enzkreis, Germany. Pforzheim, which is located in the state of Baden-Württemberg in southwest Germany, is uniquely suited for this investigation based on two population characteristics. It was attacked by the Allies on February 23, 1945 which destroyed almost 85% of the city's infrastructure and killed nearly a third of its population. This death toll was the largest in relation to the population size compared to other German cities at the time. Today, Pforzheim is a city of about 120,000 inhabitants and more than 50% of its population is estimated to have a migration background (among the highest percentage of all cities in Germany). Some 75% of children under 3 years of age have a migration background.

This unique historical background and demographic reality render Pforzheim particularly suitable for a population-based intervention study. On the one hand, assuming that historical war trauma has transgenerational sequelae, the stressful experiences from World War II bombings may potentially be detectable in the local F2 and F3 generations. On the other hand, political crises bringing on migration stress, contemporary war trauma and low socioeconomic status may determine health outcomes in the F0 and F1 generations of the migrant population. Thus, the likelihood of discovery of biomarkers and causal mechanisms leading to stress-associated adverse health life trajectory outcomes in a multi-year, prospective community-based study is high as is the opportunity to test interventions designed to build resilience and reduce stress.

Approaches and assessments

Fort McMurray and Houston

Mothers who participated in the FMWB and Houston studies were administered a combination of standardized questionnaires to assess stress levels related to the natural disasters and an expressive writing intervention. Phase 1 of the studies included both questionnaires and the expressive writing intervention which was aimed at decreasing stress and supporting maternal resilience. For both studies, PNMS, depression, perceived stress and peritraumatic dissociation as well as the degree of objective hardship of each disaster according to four categories of trauma exposure: threat, scope, loss and change were assessed. This survey was adapted to reflect the specific events in Fort McMurray and Houston. In phase 2 of the studies, we proposed face-to-face infant assessments at 18 months of age based on the Bayley scales of infant development, third edition²² to determine the effects on a maternal intervention on child development. These assessments have already commenced in Fort McMurray and will soon start in Houston. Phase 3 (in FMWB only) will attempt to determine which 'omics and other biomarkers of allostatic load predict preterm delivery, whether biomarkers indicate the responsiveness to the expressive writing intervention and confirm the inverse relationship of biomarkers to resilience.

Pforzheim

Therapeutic interventions such as psychotherapy, mindfulness meditation or expressive writing will be administered. In a three-phase project, a primarily prospective cohort study will be combined with retrospective assessments based on extensive questionnaires delivered to women and their families (including those exposed to transgenerational trauma) through a

customized smartphone app. Phase 1 will include the assessment and analysis of pregnant women and their children using standardized questionnaires to determine lifestyle and transgenerational stress as risk factors for preterm birth and protective/moderating factors. During Phase 2 of the study, outcomes and biomarkers affected by risk factors will be assessed for mother and child through medical recorders and tissue collection and analysis. Phase 3 will implement resilience building and coping skills and interventions as a means of capacity building to promote mental well-being and prevent negative pregnancy outcomes. The maternity pass (a maternal health record kept during pregnancy) plus a similar child health card and the school entry exams administered at ages 4–5 are additional resources that will be used to transfer data directly for analysis. This study will suggest tools to increase resilience, reduce stress and support maternal and fetal health.

Intervention – expressive writing

An intervention we selected for all three sites was informed by previous work that suggests that increased stresses caused by a natural disaster or accumulated stresses over time and generations increase an individual's allostatic load.²³ Consequently, interventions that reduce allostatic load should decrease stress and increase resilience.

Since the 1980s, James W Pennebaker has developed, tested and refined a simple intervention to help people deal with stressors utilizing expressive writing.^{24,25} He has demonstrated that short bursts of expressive writing (i.e. 15–20 min) are sufficient to allow for emotional disclosure (the active ingredient in the intervention),^{24–28} and to improve biochemical markers of physical and immune functioning.^{29–34} As a self-reflective learning activity, expressive writing allows for review and cognitive processing of innermost thoughts and feelings. Worries are off-loaded from working memory and, as a result, anxiety is relieved. Expressive writing provides an avenue for disclosing traumatic events, thereby improving the likelihood of long-term health. As well, expressive writing has been found to cultivate both resilience and optimism. People with the greatest resilience tend to make the most meaning from their experiences and those who are optimistic tend to view difficult times as temporary and consider them realistically, rather than worse than they are. Upon long-term follow-up of expressive writing interventions, many studies have found evidence of health benefits including improved mood/affect and feelings of greater psychological well-being. Smyth's 13 study meta-analysis of expressive writing found a significant overall benefit ($d=0.47$, $P<0.0001$) in objective or self-reported health areas such as physical health, psychological well-being, physiological functioning and general functioning.³⁵ Hence our team chose expressive writing as a simple, cheap and relatively inexpensive intervention to test in the FMWB region and in Houston.

We recruited women between the ages of 15 and 45 who were pregnant at the time of the fire or hurricane or who became pregnant within 6 months after the disaster. Social media (Facebook, Twitter, Kijiji), conventional media (TV, radio, newspaper) or ads posted in the health care clinics were used to recruit participants. Facebook ads were purchased that informed eligible women about the study and then directed them to a secure site where they were informed about the study, able to register in the study and they could provide consent. In FMWB, participants were recruited between 1 November 2016 and 1 June

2017. In Houston, participants were recruited between 10 January 2018 and 31 July 2018. Inclusion criteria were English speaking pregnant women who were ordered evacuated in May 2016 or experienced the hurricane in August 2018 and women who conceived post-fire or post-hurricane, but were pregnant at the time of joining the study.

Once accepted into the study, participants completed a battery of questionnaires and a demographic survey. Each participant was randomly assigned into one of three intervention groups developed in consultation with J. Pennebaker: (1) no writing, (2) a writing group that addressed non-emotional issues of healthy lifestyle (control group), and (3) a group that wrote about their innermost feelings (active group). Participants gained access to an automated online portal that allowed 15-minute writing sessions with prompts for writing topics that were developed in consultation with Dr Pennebaker. The instructions for writing were provided upon entrance into the portal, 'In narrative form, please write constantly without stopping for 15 minutes about the topic indicated. Provide as much factual detail and description as possible.' Each of the 4 days of writing had a different guiding question.

Establishing studies

In late May and early June 2016, the idea took shape at the University of Alberta that while it would be of large interest to follow the birth outcomes of the pregnant mothers who were evacuated from FMWB, it would be of greater value to include an intervention to mitigate the expected adverse outcomes. Enthusiasm for the idea was evident; however, the logistics of establishing the elements of the study and then funding it while women were still pregnant were daunting. Fortunately, the Alberta community pulled together in a tremendous display of collaboration by providing cash, small grants and in-kind donations equalling \$58,000 – enough to initiate the study.

These funds were used, in part, for the social media and traditional media ads to recruit the subjects. Two excellent graduate students served as study assistants and prepared the data collection protocols on REDCap, ethics information and applications, and intervention materials. A summer student prepared the background information for the study and subsequent grant applications. A meeting with local leaders and our patient navigators in FMWB provided the community support necessary for initiating the project.

A company that specializes in social media use – especially Facebook – coordinated all of the team's Facebook recruitment ads focussing them on the pregnant and postpartum women of FMWB particularly the Fort McMurray Mommy Network on Facebook. Posters advertising the study were placed in the 26 Wood Buffalo primary care clinics where pregnant women would view them during prenatal visits until 30 weeks. One of the pregnant women in the area became the team's patient navigator and provided considerable valuable assistance for connecting with other women. The Facebook ads and posters directed potential subjects to the study website at Mommybabyfmm.com.

The REDCap team at the University of Alberta provided support to develop the written protocols for all of the components of the study and tested the system's functionality and usability. REDCap hastened the progress of the study, recruiting, consenting and initiating women into the study, provided background questionnaires and delivered the intervention to subjects via their smart phones, tablets or laptops. Equally expert was the

Research Ethics and Management Online (REMO) team at the University of Alberta who worked expeditiously to approve the many protocols and amendments to the project while ensuring the rigor and oversight of their accountability mandate (REB approval obtained from University of Alberta). On 7 November 2016, 6 months after the fire, the study went live. Facebook ads were initiated and the project director appeared on a popular radio show announcing the study which resulted in several follow-up TV and newspaper articles that helped with recruitment. It was also helpful to offer financial incentives; we awarded \$50 online gift certificates after completion of the intervention.

Processes

Mothers who clicked on the study website first read through the purpose and other information describing the study and then provided consent. A battery of questionnaires taking 25 min to complete provided background and baseline levels of stress, anxiety and depression. Then mothers were randomly assigned to one of the three arms. Mothers were encouraged to remain in the study regardless of the arm to which they were assigned since the team intended to perform follow-up assessments of their children and they would all receive benefit from the 'placebo' effect of being in a study.

In the fall of 2016 the Canadian Institutes of Health Research offered a granting scheme to support wildfire studies and, by 11 months after the fire, the team received a grant. It allowed the team to coalesce around five important concepts. These were prenatal maternal stress and its effect on pregnancy and health outcomes, resilience, the development of an allostatic load index based upon biomarkers and other predictors, the assessment of a population-level intervention to promote resilience, decrease stress and improve outcomes, and the means to collaborate with stakeholders and end-users in the assessment and administration of the intervention to vulnerable populations.

The establishment of the FMWB study enabled the team to share its protocols with others experiencing natural disasters. When hurricane Harvey hit Houston on 25 August 2017, team member Dr S. King identified a colleague at the University of Houston willing to collaborate in a similar study. The team shared its questionnaires, ethics protocols, intervention and recruiting methodologies with her. By mid-January 2018, just over 4 months after the hurricane, women were being recruited into the Houston study (see <http://harveymomstudy.com/>), and by 31 July 2018, when recruitment stopped, 1108 women were recruited and more than 800 had completed the intervention and immediate follow-up (REB approval obtained from University of Houston and University of Alberta). Preliminary results demonstrate that the expressive writing intervention was effective in reducing depression in groups of very vulnerable women (manuscript in preparation).

Like some cities experiencing a natural disaster, Pforzheim does not have a major health university close to it, hence in this case a group of concerned area health professionals started their own study without any grants or funding from major funders. They are all members of the existing and intensely collaborative *Netzwerk Frühe Hilfen* (Network of Early Intervention), which provides an exceptionally supportive framework for a population-based study in maternal and child health.

The study team plans to recruit 200–300 mother–child dyads through a variety of media outlets (REB approval obtained from

University of Lethbridge). Recruitment will continue for those who will become pregnant over the course of the study. Women from the city of Pforzheim and the Enzkreis District with and without influencing factors and comparable sociodemographic and somatic factors will be matched, compared with each other and studied from their first presentation to the gynaecologist/obstetrician.

Connecting to communities

From the conceptualization of these projects, we recognized that their success would be assessed not only by how well they developed the means to predict and mitigate risk for adverse pregnancy outcomes in at-risk populations, but also by how effectively they translated their knowledge to connect to their own and similar communities in addressing ongoing or future natural disasters. We employed a participatory action research approach to engage participant and knowledge users to define research activities and next steps for knowledge sharing and translation.³⁶ We recognized the importance of forming a Community Advisory Committee early on in the project which included community leaders, decision makers, knowledge users and engaged participants. This committee has been invaluable in shaping our knowledge translation activities which have included a 'townhall' meeting held in the community in the fall of 2017 in which we met with many of our participants and their babies to share preliminary results, as well as a recent meeting in Spring 2018 with key decision makers in our geographical area that are charged with creating and implementing policy related to pregnancy, mental health care and disaster relief. A good foundation has been established for sharing and translating results when the data are analysed and then for implementing appropriate health procedures.

Discussion

Prenatal maternal stress

Excellent Canadian data now support the link between natural disaster-caused PNMS and poor pregnancy and child developmental outcomes.³⁷ Dr S. King and her team from McGill University have been studying the effects of prenatal exposure to the Quebec Ice Storm of January 1998 (*Project Ice Storm*). They recruited nearly 200 women who were pregnant during the ice storm or who became pregnant within 3 months after the storm. At recruitment 5 months after the disaster, the women completed questionnaires on their objective degree of exposure (or 'hardship'), their subjective distress (i.e. their symptoms of post-traumatic stress disorder), and their cognitive appraisal of the disaster (as an overall negative, neutral or positive experience). Results showed that exposure to the storm in the first or second trimester resulted in, on average, a 1- to 2-week shorter gestation compared to the pre-conception and third trimester-exposed groups.³⁸ A subjective distress-by-timing interaction showed that high maternal distress predicted lower birth weights (by ~500 g) when the ice storm occurred in mid-gestation. As well, the higher the mothers' levels of subjective distress from the ice storm, the greater the 'head-sparing' effect in boys, that is, the larger the head relative to body length at birth.

Project Ice Storm has followed the children's cognitive development throughout childhood and adolescence. They found that the mothers' objective degree of exposure to the storm (e.g. more

days without power) explained 12% of the variance in their infants' Bayley IQ scores (a 0.75 s.d. difference between low and high objective stress), and explained 17% of variance in receptive language abilities at age 2 years, after controlling for birth outcomes;³⁹ these effects were especially significant when exposure occurred in early pregnancy. The impacts on cognitive and language development continued through age 5 years¹⁰ and throughout childhood.¹¹

Project Ice Storm has also demonstrated the programming power of objective PNMS on body mass index and obesity at age 5 [odds ratio (OR) = 1.37];¹² this association steadily increases in magnitude between age 5 ($r=0.23$) and 15 ($r=0.34$).¹³ Greater objective PNMS also predicts greater insulin secretion ($r=0.62$)¹⁴ and proinflammatory cytokines ($r=0.42-0.46$)¹⁵ in adolescence. The team has also shown powerful associations between the children's DNA methylation in adolescence and both objective PNMS⁴⁰ and maternal cognitive appraisal.⁴¹ This association with epigenetic markers of PNMS significantly mediates the effects of PNMS on child outcomes such as body mass index⁴² and cytokines.⁴³ Subjective and objective PNMS also predict outcomes such as autistic-like symptoms at age 6 ($r=0.43$ and 0.45),⁴⁴ and internalizing and externalizing problems throughout childhood with correlations in the range of 0.40–0.50.¹¹ King's group is following two other prenatal disaster-exposed cohorts that are replicating results from Project Ice Storm. The Iowa Flood Study (2007) is finding similar effects of PNMS on child cognitive development, with PNMS in early pregnancy predicting adiposity at ages 2 and 4.⁴⁵ The Queensland Flood Study (QF2011)⁴⁶ in Australia reported that third trimester exposure is a vulnerable period for motor development⁴⁷ as was also found in Project Ice Storm.⁴⁸ The studies described herein are logical extensions by including interventions to mitigate these adverse outcomes. The results should be informative about whether interventions improve outcomes, which ones, and the best ways to implement them in a population.

Lessons learned and shared

One purpose for this article was to share our experience in setting up pregnancy intervention studies in a hurry following a natural disaster or at a more comfortable pace in a population with potentially interesting information based on historical and political realities. Our lessons learned that we share here can pertain to both situations. Should you wish to start a study under similar circumstances, we encourage you to get started. We found the following to be keys to our success. Begin with local support, both cash and non-cash in-kind, from as many sources as possible. We are willing to share our methods so that recruitment can start as quickly as possible. Involve several local health care professionals, stakeholders, subjects and end-users from the affected population in the organization of the study to build a diverse team. Facebook ads, local media and posters are all helpful in recruitment. It is also helpful to connect with the local clinics where pregnant women attend for their prenatal visits so that a study coordinator can call and invite them to join the study. Once participants register and consent, keep the background questionnaires as short as possible. Completing them in 15 min is optimal. Some subjects will still require encouragement by a study coordinator along with on-line or phone prompts to complete the intervention and follow-up questionnaires. If your study protocol includes the collection of biological samples and/or developmental follow-up, then begin as early as possible to find a suitable space to collect

these. If there is media hype around the stressful event, then build off of it as much as possible. Get your study listed among the positive community responses to the weather or environmental event. As your project develops, encourage the formation of an inter-disciplinary team with various skill sets that enrich and extend the quality of your study. Finally, be adventurous. This is not a traditional process that is well planned and well-funded before you begin. Just start and trust the process and believe in your own abilities to achieve a success.

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