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Program et al.

11 UNITED STATES DISTRICT COURT
 12 EASTERN DISTRICT OF CALIFORNIA,

13
 14 THE UNITED STATES OF AMERICA,
 15 Plaintiff,

16 V.

17 THE STATE OF CALIFORNIA;
 18 EDMUND GERALD BROWN JR.,
 Governor of California, in his Official
 Capacity; and XAVIER BECERRA,
 19 Attorney General of California, in his
 Official Capacity,
 20 Defendants.

Case No: 2:18-cv-00490-JAM-KJN

**ADDENDUM TO BRIEF OF *AMICI*
CURIAE NATIONAL HEALTH
 LAW PROGRAM *ET AL.* IN
 SUPPORT OF THE DEFENDANT'S
 OPPOSITION TO PLAINTIFF'S
 MOTION FOR A PRELIMINARY
 INJUNCTION**

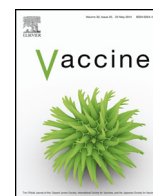
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2 Exhibit List

- 3
4 Exhibit A: Kimberly Gittings & Kelly L. Matson, *Establishing Herd Immunity Against Ebola Through Vaccination*, 34 Vaccine 2664 (2016).
- 5
6 Exhibit B: Jared M. Baeten, *Amplifying the Population Health Benefits of PrEP for HIV Prevention*, 217 J. of Infectious Diseases 1509 (2018).
- 7
8 Exhibit C: A. Elizabeth Iten et al., *Undocumented Immigration Status and Diabetes Care Among Mexican Immigrants in Two Immigration “Sanctuary” Areas*, 16 J. Immigr. Minority Health 229 (2014).
- 9
10 Exhibit D: Helen B. Marrow, *The Power Of Local Autonomy: Expanding Health Care To Unauthorized Immigrants In San Francisco*, 35 Ethnic & Racial Studies 72 (2012).
- 11
12 Exhibit E: Nicole L Novak et al., *Change in Birth Outcomes Among Infants Born to Latina Mothers After a Major Immigration Raid*, 17 Int’l J. Epidemiology 1 (2017)
- 13
14 Exhibit F: Ronald Glaser & Janice K. Kiecolt-Glaser, *Stress-Induced Immune Dysfunction: Implications for Health*, 5 IMMUNOLOGY 243 (2005)
- 15
16 Exhibit G: Lisseth Rojas-Flores et al, *Trauma and Psychological Distress in Latino Citizen Children Following Parental Detention and Deportation*, 9 Psych. Trauma 352 (2017).
- 17
18 Exhibit H: Kenneth E. Miller & Andrew Rasmussen, *War Exposure, Daily Stressors, and Mental Health in Conflict and Post-Conflict Settings*, 70 Soc. Sci. Med. 7 (2010).
- 19
20 Exhibit I: Allen S. Keller et al., *Mental Health of Detained Asylum Seekers*, 362 Lancet 1721 (2003).
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Exhibit A



Establishing herd immunity against Ebola through vaccination



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ABSTRACT

Objectives: In response to recent concern regarding Ebola outbreaks, this study aims to (1) determine the relationship between vaccination coverage and herd immunity, (2) determine the vaccination coverage necessary to establish herd immunity for previous Ebola viruses, and (3) recommend vaccination coverage thresholds for future Ebola viruses.

Methods: Herd immunity thresholds needed to block transmission of Ebola virus were determined using vaccine efficacy and number of secondary cases per infected case during an entire infectious period.

Results: In past Ebola outbreaks 42.2–63.0% of the population would need to be vaccinated in order to prevent transmission and outbreaks. Assuming 80% vaccine efficacy as reported by phase I clinical trials, 52.7–78.7% of the population would require vaccination coverage in order to establish herd immunity. In recent ring vaccination trials which considered the vaccine to be 100% effective after 10 days, 42.2–63.0% of the population would need to be vaccinated.

Conclusion: For future Ebola outbreaks, the spread of the virus can be prevented by vaccinating certain percentages of the population depending on vaccine efficacy and number of secondary cases per infected case.

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1. Introduction

In 2014 the largest Ebola epidemic in history spread through West Africa with additional cases reaching the United States [1]. The first case of Ebola was recognized in 1976 in the Democratic Republic of Congo as a rare and severe illness with fatal potential. The virus is transmitted from wild animals to people and spreads through the population from human-to-human transmission. Due to the dangerous nature of the virus, it is important to prevent its transmission through vaccination. Vaccination can reduce the risk of Ebola virus contraction and its related complications, physician visits, hospitalizations and death. By vaccinating a certain proportion of the population against the virus, transmission of Ebola in the community can be blocked through the establishment of herd immunity.

Vaccines can affect more than just the individual who is vaccinated; vaccines can also protect people who have not been

immunized. The concept of “herd immunity” refers to an indirect protection of an entire community from disease by immunizing a critical proportion of the populace. Herd immunity breaks the chain of an infection’s transmission so that outbreak does not occur [2]. For example, transmission of measles can be blocked by vaccinating 92–95% of a given community [3]. The remaining 5–8% of the community who are unvaccinated and susceptible to measles receive “conferred immunity” from the vaccinated individuals. Given the proportion of vaccinated individuals, in terms of vaccination coverage, above a pre-determined herd immunity threshold, transmission of measles is blocked within the community.

The threshold for herd immunity needed to block transmission of Ebola virus in the population is currently unknown. Herd immunity is established when the prevalence of protected persons (I) is higher than the herd immunity threshold ($I > I_c$) [3,4]. When this occurs, Ebola virus transmission is blocked within the given population. However when prevalence is lower than the threshold, the number of infections is able to grow exponentially, thus spreading the virus within the population. Recent early phase trials of Ebola vaccinations report the efficacy of the vaccines, which can be used to determine the percentage of the population that requires vaccination in order to reduce community outbreaks and prevent transmission [5,6].

The objectives of this study are to determine the relationship between Ebola vaccination coverage and herd immunity,

Abbreviations: V_c , critical vaccination coverage; I_c , herd immunity threshold; R_0 , basic reproductive number; E , vaccine efficacy.

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Table 1

Average number of secondary cases per infected case (R_0) and prevalence of protected persons necessary to establish herd immunity (I_c) for studied Ebola virus outbreaks.

Ebola virus	R_0 , CI	I_c (%), CI
1995 Democratic Republic of the Congo epidemic [5]	2.7 (1.9–2.8)	63.0% (47.37–64.3%)
2000 Uganda epidemic [5]	2.7 (2.5–4.1)	63.0% (60.0–75.6%)
2014 Liberia epidemic [6]	1.73 (1.66–1.83)	42.2% (39.8–45.4%)

Where $I_c = [1 - (1/R_0)]$.

I_c = herd immunity threshold and R_0 = basic reproductive number.

determine the vaccination coverage necessary to establish herd immunity for previous Ebola viruses, and provide suggestions for vaccine coverage needed for future Ebola viruses.

2. Methods

This study mathematically determined the herd immunity threshold required to prevent transmission of Ebola. It was determined by accounting for the number of secondary cases per infected case (R_0) during the entire infectious period in a completely susceptible population, or basic reproductive number, in past outbreaks and the vaccine effectiveness. When $R_0 > 1$, outbreaks and resulting epidemics occur.

When vaccinations are administered within a specified population or community, the vaccine protects only a proportion (E) of the vaccinated individuals. The proportion of protected individuals who were vaccinated represents the effectiveness of the vaccine against infection transmission.

Using the mentioned variables, the critical proportion of protected individuals needed to establish herd immunity in a completely susceptible community can be determined from the equation $I_c = 1 - (1/R_0)$ [2–4]. The critical vaccination coverage (V_c) needed to establish herd immunity can next be determined by dividing the herd immunity threshold (I_c) by the level of vaccine effectiveness (E): $V_c = I_c/E = [1 - (1/R_0)]/E$ [2,4].

Citing R_0 values from past Ebola epidemics (Table 1), it is possible to mathematically derive the herd immunity threshold, and the number of protected persons required to establish herd immunity in a completely susceptible population.

After determining herd immunity thresholds for previous epidemics, data was pulled from phase I and III clinical trials in order to determine the critical vaccination coverage needed to establish herd immunity in past outbreaks given vaccine efficacy. Vaccine efficacy in early phase I clinical trials was measured by percentage of subjects with positive enzyme-linked immunosorbent assay results at week 12 after vaccination. Antibodies directed against specific antigens were measured throughout the trial and an end point titer with a background-corrected optical density reading of ≥ 30 was considered a positive result [7]. A more recent phase 3 trial of Ebola ring vaccination determined efficacy of ring vaccination based on zero cases of Ebola virus disease at 10 days or more post-randomization and vaccination [8].

Table 2

Vaccine coverage (V_c) required to establish herd immunity against past Ebola viruses for varying levels of vaccine effectiveness.

Vaccine effectiveness (E)	1995 Democratic Republic of the Congo epidemic	2000 Uganda epidemic	2014 Liberia epidemic
40%	100%	100%	100%
60%	100%	100%	70.3%
80%	78.7%	78.7%	52.7%
90%	70.0%	70.0%	46.9%
100%	63.0%	63.0%	42.2%

Where $V_c = I_c/E$.

V_c = vaccine coverage and I_c = herd immunity threshold.

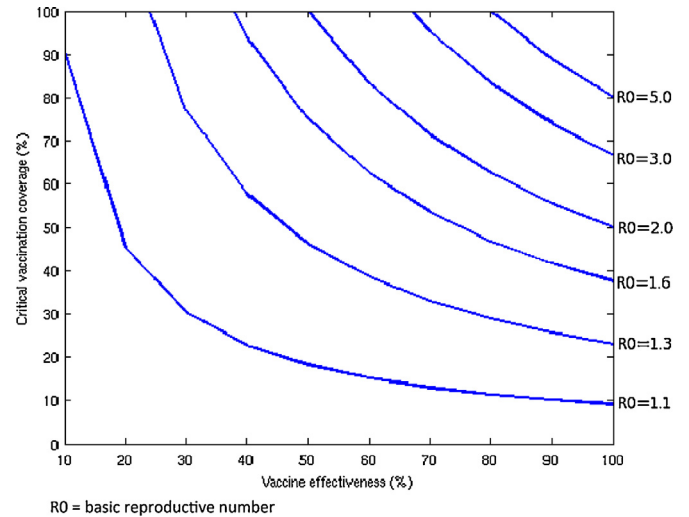


Fig. 1. Critical vaccination coverage (%) needed to provide herd immunity against varying Ebola viruses and variable vaccine efficacy. R_0 = basic reproductive number.

3. Results

In past Ebola virus epidemics, the prevalence of protected persons needed to establish herd immunity ranged from 42.2% in the most recent epidemic to 63.0% in earlier epidemics (Table 1).

The required vaccination coverage to establish herd immunity for past Ebola epidemics varied depending on vaccine efficacy. The required vaccination coverage to establish herd immunity for these past Ebola epidemics ranges from 52.7% to 78.7% assuming the vaccine is 80% effective as reported by a phase I clinical trial [7]. A 2015 phase-3 ring vaccination cluster-randomized trial reports the efficacy of the vaccine in different scenarios. In individuals who randomly received the ring vaccination, the vaccine was considered to be 100% efficacious after 10 days [8] which requires 42.2–63.0% of the population to be vaccinated in order to provide herd immunity. The 2015 study reports an estimated 75.1% and 76.3% overall vaccine efficacy in all eligible participants, which equates to a critical vaccination coverage of 56.2–83.9% and 55.2–82.6% respectively.

To account for real-world human error and varying degrees of efficacy, Table 2 reports the vaccination coverage that would have been required to establish herd immunity against past epidemic Ebola viruses for different levels of vaccine effectiveness.

The vaccination coverage required to establish herd immunity against future Ebola viruses for varying levels of vaccine effectiveness and differing R_0 values is demonstrated in Fig. 1. For example, when the number of secondary cases per infected cases, R_0 , is equal to 1.1 and the vaccine is approximately 90% effective, only about 10% of the given population will have to be vaccinated in order to provide herd immunity against the virus.

4. Discussion

This study explored the relationship between Ebola vaccination coverage and herd immunity while assessing the vaccination coverage necessary to establish herd immunity for previous Ebola epidemics. The results suggest that higher levels of vaccination coverage would have been needed in order to provide herd immunity against previous Ebola epidemics. Given that the recent 2014 Ebola epidemic had a lower R_0 value, it may suggest that less vaccine coverage than previous epidemics would be needed in order to prevent transmission.

Additionally, results of this study suggest that future Ebola virus transmission can be blocked by vaccinating susceptible populations. Fig. 1 demonstrates vaccination coverage needed in order to prevent future Ebola outbreaks in a 100% susceptible population given varying R_0 values and vaccine effectiveness. As seen in Fig. 1, it is easiest to prevent an outbreak when a virus has a low R_0 value and high vaccine efficacy. This study suggests that for Ebola viruses with $R_0 \geq 3$ and vaccine effectiveness of 70%, nearly all of the population would need to be vaccinated in order to establish herd immunity. With a lower R_0 value and a vaccine efficacy of 70%, a smaller percentage of the population would need to receive the vaccine in order to prevent outbreak.

It is important to note that there are several limitations to this study. The study utilizes a simple threshold theorem which makes several assumptions: (1) random vaccination within the population, (2) homogenous mixing of persons within the population, (3) homogeneous distribution of vaccine-induced protected and infected persons within the population, and (4) fully susceptible population [2]. It can be speculated that because this model assumes a fully susceptible population, vaccination coverage needed to establish herd immunity in a population with individuals already protected due to natural infections would be less than the proposed thresholds within this study. Additionally, this study assumes that vaccine efficacy is equal to the percentage of patients from previous trials with positive enzyme-linked immunosorbent assays when this value may not truly correlate to the vaccine efficacy and immunity.

This study relies heavily on the accuracy of the basic reproductive value (R_0) reported for past Ebola outbreaks that are included in Table 1 and used to calculate the results in Table 2. As seen in Table 1 of this study, the R_0 value of the 1995 DRC and 2000 Uganda epidemics are 2.7 whereas the most recent 2014 Liberia epidemic's value was significantly lower at 1.73. Although the strains for the outbreaks were the same, the varying R_0 values can vary due to several factors because it is a property that combines the process of contagion within a population and the patterns of contact within the population. Some variables that affect R_0 may include the number of susceptible people in the population that the affected patients are in contact with, containment and control measures for the virus, and stages of outbreak [9]. In 2014, the World Health Organization (WHO) redesigned frame work and created intensive public health containing measures to be implemented from both local and international levels [10]. The R_0 value for the 2014 epidemic was calculated from data collected during July and September 2014, after said measures were initiated. It is possible that containment measures were improved in the most recent outbreak thus resulting in a decreased R_0 value.

Currently, there are known contraindications to Ebola vaccination for specific age ranges. Of note, the phase 1 trial by Sarwar, which this study utilized for vaccine efficacy data, was limited to adults aged 18–60 years [7]. Applying the data from our study we can speculate that if 52.7–78.7% of a mixed age population of individuals was vaccinated this would provide community protection to the young and the older adults who were ineligible to receive the phase I trial vaccine in that population. Due to the restrictions in

age, a larger percentage of the adult population needs to be vaccinated in order to protect those who cannot be vaccinated. If children and older adults were also eligible to be vaccinated, it would be easier to reach the herd immunity threshold by being able to vaccinate more individuals.

The most recent phase 3 trial of Ebola vaccination in Guinea involved ring vaccination in a cluster-randomized style. Ring vaccination involves administering vaccination only to a cluster of high risk individuals who are in close contact with a confirmed isolated infected person [8,11]. Although different from traditional methods of vaccination this method demonstrates notable efficacy. Eligible individuals in the clusters were given either immediate or delayed Ebola vaccination. Of the immediately vaccinated individuals the vaccine was 100% effective as determined by no symptoms of Ebola virus disease 10 days after vaccination. Of all eligible individuals who received immediate or delayed vaccination (21 days after randomization) the vaccine was 75.1% effective and 76.3% effective depending on cluster [8]. Because this was a cluster trial of individuals in close contact with isolated infected person(s) the R_0 value of the virus is likely higher than in populations where individuals are not in close proximity. Therefore, it is possible that critical vaccination coverage values may be lower in other communities. Importantly, the basic reproductive value of the outbreak in Guinea was not reported so it is difficult to conclude exactly how the critical vaccination coverage would be affected.

In future outbreaks with a 100% efficacious vaccine, as reported by the Guinea ring vaccination trial, 42–63% of the population would have to be vaccinated to prevent transmission. There are several stressors that could affect the ability to vaccinate individuals against Ebola in the future. When outbreak occurs, access to adequate supply of vaccine to vaccinate sufficient number of individuals is not always possible within desired time range to control transmission. Thus, it is important that future Ebola outbreak protocols include intensive measures for containment to prevent transmission. If supply is a potential issue it would be wise to distribute vaccine supply in levels of priority. Similar to vaccination protocols within hospitals an important target population to vaccinate would be healthcare workers [12]. The Guinea trial demonstrates the value of ring vaccination in Ebola and the importance of vaccinating individuals who have been or will be in close contact with the virus. This can include contacts of sick individuals such as family and friends, caregivers, and contacts of contacts.

5. Conclusions

The novel data within this study can have future impacts in preventing outbreaks and transmission of the rare but dangerous Ebola virus. As clinical trials are still underway for development of Ebola vaccines, the information from this study can be utilized in the future with novel vaccine efficacy data to determine vaccine coverage needed to prevent outbreaks.

Conflict of interest: None declared.

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Exhibit B

Amplifying the Population Health Benefits of PrEP for HIV Prevention

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(See the Major Article by Volz et al, on pages 1522–9.)

Pre-exposure prophylaxis (PrEP) prevents HIV infection. Robust evidence—first from pivotal clinical trials [1, 2], then rigorous studies testing best-practice models of implementation [3–6], and most recently real-world case studies of clinical delivery [7]—demonstrate that PrEP is highly effective, indeed incredibly so, at providing individual protection against HIV acquisition for men and women from diverse populations worldwide. Regulatory review and normative guidance from the US Food and Drug Administration in 2012 and from the US Centers for Disease Control and Prevention (CDC) in 2014 have been followed by World Health Organization recommendations in 2015, and thereafter by endorsements by more than two dozen countries (www.prepwatch.org). PrEP is thus a central part of global, evidence-based, gold-standard HIV prevention for at-risk individuals.

Nevertheless, for PrEP to have an important impact on the HIV epidemic, it needs to have not just benefits for individuals but at the population level, synergizing with other prevention and treatment interventions to achieve substantive reductions in new infections and resultant morbidity and mortality from

HIV. By 2020, the US National HIV/AIDS Strategy calls for a 25% reduction in new diagnoses [8] and UNAIDS has set a global goal of <500 000 new infections, a 75% reduction compared to 2010 [9]. These are ambitious targets, for any setting, and achieving them will require the best strategy and science to guide interventions and measure impact.

In this issue of the *Journal of Infectious Diseases* [in press], Volz and colleagues present an innovative set of analyses, using molecular sequence data from HIV infections among men who have sex with men (MSM) in the United Kingdom, combined with mathematical modeling, which together provide one potential strategy to maximize population health benefits of PrEP. Specifically, the authors analyzed publicly collected HIV sequence data from nearly 7000 MSM (linked to basic demographic data), used phylogenetic and phylodynamic methods to characterize transmission-associated subgroups with greater risk for HIV acquisition and onward virus spread, and then estimated the population-level benefits that would occur from different scenarios under which a limited amount of PrEP (enough for 15 000 individuals) would be available. Their principal finding (ie, that young MSM, aged < 25 years, had greater HIV risk) seems on first pass to be not particularly surprising, as adolescent and young adult men and women in countries around the world have been repeatedly called out as a high-risk population. However, the Volz and colleagues' results go further than simply documenting younger age as a risk factor for HIV,

demonstrating that young MSM are also more likely to transmit to other young MSM if they do acquire the virus (75% of infections in this group attributed to other young MSM), multiplying the HIV risk within this age group. As a result, prioritized introduction of PrEP to younger MSM would have multiplied benefits, blocking both first-generation infections as well as large numbers of onward transmissions in this group. Thus, high levels of transmission, combined with high connectivity among similarly aged men, in the words of the authors “amplifies incidence ... and PrEP effectiveness” in young MSM.

Amplified effectiveness is what is needed at this time for PrEP and for the total toolbox of effective HIV prevention strategies. The findings of Volz and colleagues remind us that HIV prevention is about a best prevention plan for an individual, but must also be about prevention for his or her current and future partners and, ultimately, about the population more generally. HIV, like other infectious diseases, can benefit from interventions that limit transmission cascades, as seen most dramatically in the last few years in the public health response to the outbreak in Scott County, Indiana linked to injection drug use [10]. As done by Volz and colleagues and by others [11, 12], phylodynamic analyses of viral sequences from that outbreak have been used to characterize opportunities for strategic prevention efforts [13]. This innovative use of molecular epidemiology and mathematical modeling offers exciting new opportunities to use complex science

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to guide public health decision making in real time. The approach is arguably a continued evolution of the “know your epidemic, know your response” rallying cry from UNAIDS a decade ago, backed up by cutting-edge data analytics.

For PrEP, population health benefits can only occur with enough coverage of the population accessing it to result in those key infections prevented to avert subsequent generations of transmissions. We are not there yet. In the United States, PrEP uptake has skyrocketed, with >120 000 individuals estimated to have initiated PrEP since 2012 [14]; still, CDC estimates that 1.2 million persons, including MSM, people who inject drugs, and heterosexual adults, have indications for considering PrEP use [15]. Some geographies are beginning to see PrEP use at levels that should result in population benefits—for example, Seattle and King County, Washington recently reported that one-third of high-risk MSM there are estimated to be on PrEP currently and there are now more people on PrEP in that locality than are taking antiretroviral treatment (and that is in the context of that locality also achieving the UNAIDS goal of 90% of individuals diagnosed, linked to care, and on suppressive antiretroviral therapy) [16]. New initiatives related to access to PrEP (as well as treatment and other prevention interventions) in Florida and elsewhere in the southern United States offer encouragement that population benefits may be on the horizon for a part of this country that faces substantial disparity in new HIV infections [17]. The United States accounts for most PrEP use in the world at this time, although the vast majority of new infections occur in low and middle income countries; UNAIDS has called for 3 million persons to be on PrEP by 2020 [9]. Ambitious programs like the DREAMS initiative (<https://www.pepfar.gov/partnerships/ppp/dreams/>), supported by the US President’s Emergency Plan for AIDS Relief (PEPFAR), is prioritizing prevention for adolescent girls and young women in 10 African countries

with a multifaceted prevention program, which includes PrEP. In Kenya, a national roll-out program for PrEP is prioritizing delivery to highest-burden counties, bringing services to populations most at risk, and using messaging that is simultaneously entertaining, appealing, and informative [18]; this is a new way to do public health.

The results from Volz and colleagues touch on an important, but potentially sensitive, topic for prioritizing prevention interventions. The idea of “targeting” prevention, to an individual or to a group, may be off-putting, both to those targeted (who wants to have a target applied to them?) and to others (who may have the impression that PrEP is otherwise denied to them). The best available evidence to date suggests that open access to PrEP results in high uptake and likely diminished stigma and discouragement. Moreover, individuals seeking PrEP appear to be commonly self-selecting for being at risk, with high prevalence and ongoing incidence of curable sexually transmitted infections (harbingers of HIV exposure) and corresponding behavioral risks [3]. Conversely, new HIV infections in PrEP-accessing persons have sometimes been concurrent with loss of PrEP access (eg, because of loss of insurance coverage) [7]. Public health agencies and others working on PrEP outreach may be able to address these areas of challenge by prioritizing access to PrEP for all who want it, with directed messaging and marketing to those for whom PrEP needs and potential for benefit are greatest. Indeed, in the United Kingdom, the setting for the work by Volz and colleagues, privately-sourced PrEP, guided by websites providing instructions on how to access the medication prior to its incorporation into the National Health Service but without public health targeting at all, has been reported to have resulted in a 40% decline in new HIV infections in the last year in London [19].

PrEP is an intervention for an individual, but with enough individuals taking PrEP, particularly if infections among

those most likely to acquire and pass on the virus are blocked, population-level benefits will follow. Bringing together robust public health, cutting-edge molecular science, quality clinical care and behavioral science, innovative community engagement and messaging, and strong political will amplify the prevention benefits of PrEP.

Notes

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Potential conflict of interest. The author has led studies of pre-exposure prophylaxis in which study medication was donated by Gilead Sciences and has served on an advisory committee for Gilead Sciences. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Exhibit C

Undocumented Immigration Status and Diabetes Care Among Mexican Immigrants In Two Immigration “Sanctuary” Areas

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Abstract The objective of this study is to investigate the relationship between immigration status and the patient experience of health care, diabetes self-management, and clinical outcomes among Mexican immigrants with diabetes receiving health care in two immigration sanctuary cities. We used data from the Immigration, Culture and Health Care study, a cross-sectional survey and medical record study of low-income patients with diabetes recruited from public hospitals and community clinics in the San Francisco Bay Area and Chicago. Undocumented Mexican, documented Mexican immigrants, and US-born Mexican-Americans’ health care experiences, diabetes self-management, and clinical outcomes were compared using multivariate linear and logistic regressions. We found no significant differences in reports of physician

communication, or in measures of diabetes management between undocumented and documented immigrants. All three groups had similar clinical outcomes in glycemic, systolic blood pressure, and lipid control. These results indicate that, at least in some settings, undocumented Mexican immigrants with diabetes can achieve similar clinical outcomes and report similar health care experiences as documented immigrants and US-born Mexican-Americans.

Keywords Immigrants · Diabetes · Hispanic/Latino · Mexican-American · Sanctuary · Disparities · Undocumented immigrants

We recognize that some Mexican immigrants, regardless of immigration status, consider themselves Mexican-American and others do not. For sake of clarity we will use the terms documented and undocumented immigrants to refer to this heterogeneous group [1].

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Introduction

Nearly 60 % of the of the estimated 10.3 million undocumented immigrants living in the United States are Mexican [2, 3] and nearly half of the Mexican population living in the United States is undocumented [4–6]. Undocumented immigrants are less likely to have health insurance [7, 8], to access and use health care services [9–13], and to report having a primary care provider [14] or a regular source of care [15]. Studies have found that those with concerns about deportation are at heightened risk of emotional health problems and report poorer health status [14, 16]. While disparities in access to health care and multiple social stressors may translate into poorer clinical outcomes for undocumented immigrants, few studies have examined how immigration status relates to clinical health outcomes or to patient experiences of health care.

An examination of the impact of immigration status on outcomes is important to population health. Despite having lower prevalence of many medical conditions compared to

the general population in the United States, Mexican Americans are more likely to be at greater risk for morbidity and mortality related to chronic illness, particularly diabetes [17, 18]. Mexican Hispanics in the US are 1.7 times as likely to have diabetes as non-Hispanic whites [19] and an estimated 9.5 % of Latino adults suffer from diabetes [20]. Diabetes is increasingly common among foreign-born Latinos as well, likely reflecting changes in obesity in source countries, such as Mexico [21]. Prior research indicates that lack of documentation—and the fear associated with it—are powerful deterrents to seeking health care [22], however it is not clear how immigration status impacts the care or the outcomes of diabetes.

We set out to address this research gap by analyzing data from a survey and medical record abstraction study that included US-born Mexican Americans and Mexican immigrants with diabetes receiving care in two sanctuary areas in the US. Sanctuary areas are cities, counties, or states that have policies and statutes limiting routine reporting of the documentation status of people seeking police or health services [23]. Advocates have argued that sanctuary policies at an institutional level allow for hospital administrators and health care providers to create trust in the local immigrant community [24]. It is plausible that a ‘safe’ environment created by these policies may decrease some of the barriers to health care access and foster trust with clinicians, thereby potentially resulting in better adherence to diabetes self-care practices and medications, and positive clinical outcomes. It is also plausible that the social burdens associated with undocumented status, which include stigma and barriers to employment and financing, might render diabetes self-care very difficult, or spill over into patient doctor interactions and thus negatively impact clinical outcomes. We specifically set out to evaluate whether undocumented immigration status in two sanctuary areas is associated with: (1) poorer perceived doctor-patient interactions; (2) poorer diabetes self-management (which include measures of diabetes self-care, self-care barriers/supports, diabetes self-efficacy, and medication adherence); and (3) poorer control of clinical outcomes: blood glucose, blood pressure, and cholesterol when compared to documented Mexican immigrants and US-born Mexican Americans.

Methods

Participants and Data Collection

We analyzed data from the Immigration, Culture and Health Care (ICHC) Study, a cross-sectional study of a convenience sample of African American, Spanish- and English-speaking Mexican/Mexican American, and non-Hispanic white adults with diabetes who received care in

nine free-standing or hospital-based safety-net clinics in the San Francisco Bay Area and Chicago in 2008–2009. The main purpose of the ICHC was to explore factors that impact diabetes self-management and health outcomes in minority populations. To be included in the study, patients had to have type 2 diabetes, be 18 years of age or older, and speak English or Spanish. Patients who exhibited cognitive impairment, active substance abuse, and/or psychosis were excluded. Recruitment was stratified by race/ethnicity and patient language in order to ensure a diverse sample. The participation rate among eligible patients was 91 %.

After providing written informed consent in English or Spanish, participants completed an in-person survey with a trained bilingual research assistant. Clinical data was abstracted from participants’ electronic health record. The values for glycosylated hemoglobin (A1C), low-density lipid (LDL) cholesterol and systolic blood pressure recorded within 1 year prior and closest to the date of the interview were abstracted. For this specific study, we analyzed data for the 401 patients of the ICHC study sample population who self-identified as Mexican or Mexican American. All analyses measuring patient perception of culturally competent care were performed with the additional inclusion criterion of having reported a consistent primary care provider during the last 12 months ($N = 317$). This study was approved by the Committee for Protection of Human Subjects at the University of California, San Francisco; Cook County Health and Hospital System; UC Berkeley; and by participating institutions in Chicago and the San Francisco Bay Area.

Measures

Immigration Status

Immigration status was measured using responses to questions about country of birth and US citizenship and permanent residency with a green card for foreign-born participants. Participants who reported the United States as their country of birth were considered US-born Mexican Americans. Immigrants who reported having US citizenship or legal permanent residency were considered to be documented. Participants who reported neither status were categorized as undocumented immigrants by exclusion.

CAHPS-Cultural Competency

We used the trust and positive communication subdomains from the Consumer Assessments of Healthcare Providers and Systems’ Cultural Competency Item Set (CAHPS-CC) to assess patient experiences of care. CAHPS-CC is a 26-item set of Likert-response questions designed to

measure patients' overall experience of their physician's interpersonal and cultural competence as well as their experience of their physician's office. CAHPS-CC has been validated for use in ethnically diverse low-income populations in English and Spanish [25]. Self-reports were heavily skewed towards positive responses. Therefore, responses were dichotomized into two categories [26]: the upper 25 % ("optimal") and the lower 75 % ("suboptimal"). Further details about this tool are provided in the [Appendix](#).

Diabetes Self-Management Measures

Diabetes demands daily self-management, and people with this chronic disease generally need to make lifestyle modifications to achieve successful glycemic control. We used several instruments to capture different facets of patient self-management that we believed may be associated with life as an undocumented immigrant: (1) *Diabetes self-care* was measured through a brief adapted version of the Summary of Diabetes Self-Care Activities (SDSCA) scale [27]. This instrument represents a multidimensional process that calls for daily engagement in a complex set of behaviors relating to diet, exercise, foot care, and glucose monitoring recommendations. Many of these life-style modifications may be impacted by competing demands associated with immigrant employment and lifestyle [28]. (2) *Diabetes self-care barriers/supports* were measured using a diabetes-related health belief instrument translated for use with Spanish-speaking Mexican Americans [29]. These questions focus on barriers to implementing lifestyle changes, beliefs in the benefits of effective self-management, perceptions that one can control the effects of diabetes, beliefs regarding the impact of one's job on diabetes therapy, and perceptions of support for their diabetes provided by family and friends. Of these different beliefs, the perceptions of control over one's diabetes and perception of social support are potentially the most critical factors. Close familial and social relationships create social support that can improve glucose control [30]. However, immigration status may have an impact on these through changes in social and family configurations common to undocumented life [31]. (3) *Diabetes self-efficacy* was measured through an 8-item scale originally developed and tested in Spanish for the Diabetes Self-Management study [32]. Self-efficacy, or the ability to perform self-care tasks, has been shown to have a positive effect on glycemic control, quality of life, and adherence to diet, exercise, and blood glucose testing [33]. (4) *Medication adherence* was measured using the Morisky scale [34]. These two last factors are influenced by trust in one's physician [35], which in turn may be affected by immigration status. Details about these scales are provided in the [Appendix](#).

Health Outcomes

Measurements of hemoglobin A1C (A1C), systolic blood pressure (SBP), low-density lipoprotein (LDL) and weight were obtained by clinical chart review, selecting the last measurement prior to the survey interview. Categorical health outcomes were determined by clinical recommendations [36] for people with diabetes and established as follows: poor A1C control $\geq 8\%$, high SBP ≥ 130 mmHg, and high LDL ≥ 100 mg/dL.

Covariates

We included the following variables in our adjusted model: age, gender, highest level of education achieved, employment status, marital status, diabetes duration, BMI, and number of comorbidities (past myocardial infarction, transient ischemic attack/stroke/cerebrovascular accident, cancer, hypertension, arthritis, and hypercholesterolemia). Regressions comparing documented and undocumented Mexican immigrants additionally included English proficiency and number of years in the US. Food insecurity, which is defined as the risk of going hungry because of an inability to afford food [37], and is common in this low-income population [38], was measured using the well-validated six-item Food Security Survey Module [39]. Food security is associated with both hypo and hyperglycemia [40].

Analysis

Chi-square tests (for differences of proportions) and *t* tests (for differences in means) were used to examine the association between immigration status and socio-demographic characteristics, perceived doctor-patient interactions, diabetes-related behaviors, and clinical outcomes after testing that the normality assumption was met. Clinical outcomes (A1C, systolic BP, and LDL) were analyzed both as binary variables determined by clinical cut-off recommendations and as continuous variables.

Multivariable linear and logistic regression analyses were conducted to calculate beta coefficients or adjusted odds ratios, and 95 % confidence intervals for health care experiences, diabetes self-management, and the three clinical outcomes. Each model included age, gender, highest level of education achieved, employment status, marital status, diabetes duration, BMI, and number of comorbidities. The adjusted model for the comparison between undocumented and documented Mexican immigrants additionally included limited English proficiency and number of years in the US in the regression. If there was no evidence of association between immigration status and the outcomes, power calculations were carried out to

determine if group sizes were large enough to detect clinically important differences across the three groups.

Results

Of the 401 subjects in the study, 124 (31 %) were US-born Mexican Americans, 166 (41.4 %) documented Mexican immigrants, and 111 (27.7 %) undocumented Mexican immigrants. Socio-demographic and clinical characteristics are shown in Table 1. Gender, annual income, type of residence, and report of food insecurity did not vary across the three groups. While similar with respect to education, marital status, and acculturation, undocumented Mexican immigrants were more likely than documented immigrants to be younger (50 vs. 56 years, $p < 0.05$), employed (39 % vs. 24 %, $p < 0.05$), have lived in the US for fewer number of years (15 vs. 32, $p < 0.05$) and have limited English proficiency (77 % vs. 63 %, $p < 0.05$). Compared to US-born Mexican Americans, undocumented Mexican immigrants were more likely to be employed (39 % vs. 26 %, $p < 0.05$) and married/living together (56 % vs. 29 %, $p < 0.05$), less likely to have a high school education (12 % vs. 38 %, $p < 0.05$) and much less likely to be Anglo-oriented on the Acculturation Rating Scale for Mexican Americans-II [41] (4 % vs. 80 %, $p < 0.05$). Patients in all three groups reported a mean diabetes duration of about 10 years. Undocumented immigrants reported somewhat fewer comorbidities than both documented immigrants and US-born Mexican Americans (1.8 vs. 2.1 vs. 2.3, $p < 0.05$).

Table 2 examines participant report of patient perception of culturally competent care and diabetes-related behaviors across the three groups. There were no statistically significant differences between the three groups on either physician trust or reports of positive physician communication. Diabetes self-care behaviors (healthy diet, exercise, blood glucose testing, and foot care) did not differ between the two immigrant groups or between the undocumented and US-born. These results need to be interpreted cautiously as power calculations indicate less than 80 % power to detect statistical differences with this sample size and data driven standard deviations.

When compared to US-born Mexican Americans, undocumented immigrants were more likely to, on a 1–5 scale, perceive barriers to following a diabetic diet and taking medications (3.2 vs. 2.7, $p < 0.001$) and report impact of their job on their therapy (2.8 vs. 2.4, $p = 0.013$). Power calculations indicate at least 80 % power to detect the differences in these two diabetes self-care barriers.

Results from separate multivariable logistic and linear regression analyses of patient perception of culturally

competent care and diabetes-related behaviors also showed no statistically significant differences among the three groups, with the exception of perceived barriers to following a diabetic diet and taking medications. Documented and undocumented immigrants are 1.2 and 1.3 times more likely than US-born Mexican Americans to perceive higher level of these barriers to diet and medication adherence ($p = 0.003$ and $p = 0.024$, respectively).

Table 3 shows the association of diabetes intermediate clinical outcomes with immigration status. While the prevalence of poor glycemic, blood pressure and lipid control was high, with 40–60 % having poor glycemic control, US-born Mexican Americans and undocumented and documented Mexican immigrants did not differ significantly in either mean glycemic, blood pressure, or lipid control, measured via means or proportion in poor control.

Table 4 provides the results of separate multivariable logistic and linear regression analyses for each clinical outcome. Undocumented immigrants, documented immigrants, and US-born Mexican Americans had similar odds of poor control (glycemic, blood pressure, and lipids). They also show comparable results in the continuous clinical outcome variables. Documented Mexican immigrants had lower A1C values and were at lower odds of having uncontrolled diabetes (A1C ≥ 8.0 %) than US-born Mexican Americans. Other clinical outcomes did not differ. Power calculations determined that the study sample size has over 80 % power to detect differences in good versus poor control for each comparison.

Discussion

We report on the experience of diabetes care among Mexican immigrants receiving care in two immigration sanctuary areas [42, 43] in the US where people seeking health services are not asked about immigration legal status, nor is immigration status reported to immigration officials. In this setting, we found that undocumented immigrants achieved comparable clinical outcomes and reported similar experiences of health care as documented immigrants and US-born Mexican Americans. Undocumented immigrants did not differ from documented immigrants in their ability to manage and control their blood sugar, blood pressure, or blood lipids. While we are underpowered to detect small yet significant differences in doctor patient interactions and trust, we note that undocumented immigrants reported similar perceived doctor-patient interactions and diabetes self-management-related behaviors. Perhaps contributing to the rest of our findings, we found that these undocumented immigrants were as likely as documented immigrants and US-born Mexican Americans to report trust in their primary care physician.

Table 1 Socio-demographic characteristics, acculturation, limited English proficiency and food insecurity by immigration status (N = 401)

	US-born Mexicans N = 124 N (%)	Mexican immigrants		p value ^a	
		Documented N = 166 N (%)	Undocumented N = 111 N (%)	Undocumented versus US-born Mexicans	Undocumented versus documented immigrants
Clinic Site				0.19	0.44
San Francisco	38 (30.7)	72 (43.4)	43 (38.7)		
Chicago	86 (69.3)	94 (56.6)	68 (61.3)		
Age (years), mean ± SD	51.8 ± 13.9	55.7 ± 10.8	49.8 ± 12.5	0.24	<0.001
Gender				0.71	0.51
Female	64 (51.6)	83 (50.0)	60 (54.0)		
Educational level				<0.001	0.36
Incomplete high school	44 (35.5)	108 (65.1)	78 (70.3)		
Completed high school/GED	47 (37.9)	30 (18.1)	13 (11.7)		
Some advanced degree	33 (26.6)	28 (16.9)	20 (18.0)		
Employment status				0.036	0.023
Full or part-time	32 (25.8)	39 (23.5)	43 (38.7)		
Unemployed	67 (54.0)	75 (45.2)	42 (37.8)		
Retired/willingly unemployed	25 (20.2)	52 (31.3)	26 (23.4)		
Annual household income				0.094	0.072
<\$10,000	42 (33.9)	34 (20.5)	34 (30.6)		
\$10,000–\$24,999	49 (39.5)	73 (44.0)	38 (34.2)		
≥\$25,000	27 (21.8)	44 (26.5)	23 (20.7)		
Unsure/declined	6 (4.8)	15 (9.0)	16 (14.4)		
Type of residence				0.46	0.081
Rent	68 (54.8)	79 (47.6)	68 (61.2)		
Own/with family	53 (42.7)	78 (47.0)	39 (35.1)		
Shelter/homeless	3 (2.4)	9 (5.4)	4 (3.6)		
Marital status				<0.001	0.25
Married/living together	36 (29.0)	103 (62.1)	62 (55.9)		
Divorced/separated/widowed	49 (39.5)	47 (28.3)	31 (27.9)		
Single, never married	39 (31.45)	16 (9.6)	18 (16.2)		
Years in US, mean ± SD	–	31.95 ± 11.63	14.60 ± 8.44	N/A	<0.001
Acculturation				<0.001	0.082
Anglo oriented	88 (80.0)	15 (9.5)	4 (3.9)		
Limited English proficiency	–	105 (63.2)	86 (77.5)	N/A	0.012
Food insecurity	54 (43.5)	80 (48.2)	54 (48.6)	0.43	0.94
BMI				0.305	0.088
Obese (≥ 30.0 kg/m ²)	82 (66.1)	96 (57.8)	65 (59.6)		
Diabetes duration (years), mean ± SD	11.75 ± 10.35	11.27 ± 9.71	9.24 ± 9.92	0.059	0.094
Number of comorbidities ^b , mean ± SD	2.26 ± 1.20	2.13 ± 1.08	1.78 ± 1.03	0.001	0.007

^a Significant differences (*p* < 0.05) indicated in bold type

^b Comorbidities included past myocardial infarction, transient ischemic attack/stroke/cerebrovascular accident, cancer, hypertension, arthritis, and hypercholesterolemia

Previous studies have shown that undocumented immigrants are at heightened risk of not having health insurance or access to health care services [7, 8, 12, 13]. This results in limited use of these services and a decreased likelihood of having a regular source of care and a primary care provider [9–11, 14, 15]. Although Cavazos-Rehg et al. [16]

found that Latino immigrants with concerns about deportation reported poorer subjective health status, to our knowledge our study is the first of its kind that investigates the association between immigration status and a chronic disease health outcomes. Contrary to our hypothesis, we found that undocumented immigrants’ health outcomes

Table 2 Participant report of patient perception of culturally competent care and diabetes-related behaviors

	US-born Mexicans N = 124 Mean ± SD	Mexican immigrants		<i>p</i> value ^a	
		Documented N = 166 Mean ± SD	Undocumented N = 111 Mean ± SD	Undocumented versus US-born Mexicans	Undocumented versus documented immigrants
CAHPS-CC ^{b,c}					
1. Trust				0.36	0.31
Optimal	50 (48.5)	66 (48.9)	33 (41.8)		
Suboptimal	53 (51.5)	69 (51.1)	46 (58.2)		
2. Positive communication				0.13	0.45
Optimal	41 (39.8)	46 (34.1)	23 (29.1)		
Suboptimal	62 (60.2)	89 (65.9)	56 (70.9)		
Diabetes self-care (0–7 days/week)					
1. Healthy diet					
General diet	4.17 ± 2.32	4.24 ± 2.48	3.93 ± 2.46	0.44	0.30
Specific diet	4.20 ± 2.38	3.67 ± 2.37	3.62 ± 2.46	0.068	0.87
2. Exercise	4.13 ± 2.55	3.97 ± 2.62	3.86 ± 2.54	0.43	0.74
3. Blood glucose testing	5.11 ± 2.48	4.42 ± 2.58	4.51 ± 2.53	0.062	0.69
4. Foot-care	5.08 ± 2.64	5.05 ± 2.71	5.14 ± 2.72	0.87	0.81
Diabetes self-care barriers/supports (0–5, low–high)					
1. Barriers to following a diabetic diet and taking medications	2.74 ± 0.77	3.04 ± 0.76	3.15 ± 0.69	<0.001	0.19
2. Social support for diet	3.58 ± 0.92	3.58 ± 0.97	3.75 ± 0.86	0.15	0.13
3. Impact of job on therapy	2.43 ± 0.77	2.72 ± 0.96	2.76 ± 0.89	0.013	0.75
4. Benefits of therapy	4.14 ± 0.49	4.14 ± 0.37	4.14 ± 0.35	0.90	1.00
5. Control of effects of diabetes	3.16 ± 1.24	3.35 ± 1.20	3.29 ± 1.15	0.42	0.67
Diabetes self-efficacy (1–10, low–high)	7.59 ± 1.40	7.47 ± 1.66	7.61 ± 1.68	0.91	0.50
Medication adherence (0–4, good–poor)	1.04 ± 1.10	1.16 ± 1.13	1.02 ± 1.06	0.87	0.30

^a Significant differences ($p < 0.05$) indicated in bold type

^b Dichotomous variables are given as number (percentage)

^c CAHPS-CC, The California Assessment of Healthcare Providers and Systems – Cultural Competency. A validated tool used to measure patient perception of culturally competent care for those with a steady primary health care provider (N = 317)

were comparable to those of both documented Mexican immigrants and US-born Mexican Americans in this setting, despite having several risk factors such as younger age [7] and limited English proficiency that are known to be associated with poorer glycemic control [44]. Our finding that reports of trust in physician and positive communication among doctor-patient interactions were also similar among the three groups may help explain the comparable clinical results achieved [45–48], though again we note sample-size limitations. It is possible that the high levels of physician trust reported are an indirect consequence of immigration sanctuary policies that help create a safe environment where undocumented immigrant populations can seek out health care and manage their diseases. However, as we did not study immigrants in non-sanctuary cities, we can only speculate about the connection between these policies and physician trust or clinical outcomes we report.

With the exception of employment status, the demographic characteristics of the undocumented immigrants in this study were consistent with socio-demographical profiles of this population from previous studies [28]. The fact that undocumented immigrants in our study are more likely to be employed may reflect issues related to (un)employment in San Francisco and Chicago. Our survey instrument did not specify employment in the formal sector. Undocumented immigrants are more likely to hold informal, low-skilled jobs and less likely to be in white-collar occupations [49], and the somewhat higher reported employment rate in our study reported by undocumented immigrants may represent sporadic informal employment. We found no differences in income among the three groups, reinforcing this interpretation. This lack of difference in income may partly account for the lack of difference in clinical outcomes we report.

Table 3 Clinical outcomes by immigration status (N = 401^a)

	US-born Mexican	Mexican immigrants		<i>p</i> value ^b	
	N = 124 Mean ± SD	Documented N = 166 Mean ± SD	Undocumented N = 111 Mean ± SD	Undocumented versus US-born Mexicans	Undocumented versus documented immigrants
HbA1c ≥ 8.0 % ^c	67 (60.9)	63 (41.2)	50 (49.5)	0.096	0.19
HbA1c (%)	8.70 ± 2.22	7.98 ± 1.76	8.45 ± 2.11	0.41	0.063
Systolic BP ≥ 130 mmHg ^c	54 (43.9)	83 (50.3)	47 (42.3)	0.81	0.19
Systolic BP (mmHg)	130.46 ± 18.07	130.2 ± 17.03	126.07 ± 18.58	0.069	0.063
LDL ≥ 100 mg/dL ^c	40 (42.1)	48 (35.6)	30 (33.7)	0.24	0.78
LDL (mg/dL)	94.28 ± 33.26	89.70 ± 33.67	88.29 ± 33.49	0.23	0.76

^a The number of subjects in each clinical outcome is limited to those whose lab values were present during chart review

(HbA1c N = 364, Systolic BP N = 399, LDL N = 319)

^b Significant differences (*p* < 0.05) indicated in bold type

^c Dichotomous variables are given as number (percentage)

Table 4 Adjusted and unadjusted odds ratio and beta coefficients (95 % CI) for clinical outcomes by immigration status

	Undocumented versus documented Mexican Immigrants		Undocumented Mexican immigrants versus US-born Mexicans		Documented Mexican immigrants versus US-born Mexicans	
	Unadjusted β/OR (CI)	Adjusted ^b β/OR (CI)	Unadjusted β/OR (CI)	Adjusted ^a β/OR (CI)	Unadjusted β/OR (CI)	Adjusted ^a β/OR (CI)
HbA1c ≥ 8.0 %	1.4 (0.85,2.32)	1.5 (0.75,3.04)	0.63 (0.36,1.09)	0.57 (0.31,1.07)	0.45 (0.27,0.74)	0.51 (0.29,0.90)
HbA1c, mean (%)	0.47 (−0.03,0.98)	0.53 (−0.09,1.14)	−0.24 (−0.79,0.30)	−0.39 (−0.96,0.18)	−0.72 (−1.21,−0.22)	−0.59 (−1.10,−0.07)
Systolic BP ≥ 130 mmHg	0.73 (0.45,1.18)	0.83 (0.43,1.61)	0.94 (0.56,1.58)	1.39 (0.77,2.50)	1.29 (0.81,2.07)	1.56 (0.92,2.65)
Systolic BP, mean (mmHg)	−4.13 (−8.42,0.17)	−3.57 (−9.02,1.87)	−4.38 (−8.96,0.20)	−1.12 (−5.93,3.69)	−0.26 (−4.42,3.91)	1.22 (−3.11,5.55)
LDL ≥ 100 mg/dL	0.92 (0.53,1.62)	1.04 (0.45,2.37)	0.7 (0.38,1.27)	0.69 (0.35,1.35)	0.76 (0.44,1.30)	0.86 (0.47,1.57)
LDL, mean (mg/dL)	0.84 (−7.64,9.33)	2.93 (−8.16,14.02)	−5.94 (−15.11,3.23)	−6.45 (−15.99,3.10)	−6.79 (−15.10,1.53)	−4.82 (−13.43,3.80)

^a Model adjusted for age, gender, highest level of education achieved, employment status, marital status, diabetes duration, BMI, and number of comorbidities

^b Adjusted model additionally includes limited English proficiency and number of years in the US

Significant differences (*p* < 0.05) indicated in bold type

The generalizability of this study is limited. First, all participants were receiving clinical care at community clinics in sanctuary areas, where immigration status is not ascertained or shared with immigration enforcement. Therefore, the results are only representative of an immigrant population that has access to health care services and can receive care in a legally safe environment. As importantly, the study enrolled patients in a primary care setting; undocumented immigrants with diabetes who have great

mistrust of the health system may refuse all but episodic care and their clinical outcomes would likely differ from those enrolled in primary care. Third, the cross-sectional design of the study provides only one snapshot in time. As national debates on immigration continue, the lack of association between immigration status and health status or perception of patient-doctor interaction may change. Finally, the relatively small number of participants enrolled cannot allow us to exclude small yet statistically significant

differences in clinical outcomes. This is particularly true of our analysis of reports of diabetes self-care behaviors where we had less than 80 % power to detect statistically significant differences. The study also has several strengths. It involves a relatively large number of undocumented immigrants, has detailed patient report on the physician-patient relationship and on self-care behavior, and includes measures of diabetes outcomes.

In conclusion, this analysis suggests that undocumented Mexican immigrants are able to achieve comparable clinical outcomes and diabetes self-management behaviors as documented immigrants and US-born Mexican Americans, at least in some environments. While this may reflect the impact of legally safe access to health care, much more research, in many different environments, is needed before that conclusion can be drawn. Future studies should investigate the association between immigration status and health outcomes when immigrants do not reside in sanctuary cities and should draw participants from community settings. Yet, while rates of poor clinical control were high among all three groups—underscoring the need for improvement in Latino diabetes outcomes overall—it is noteworthy that despite the many social burdens associated with illegal immigration status, undocumented patients and their clinicians are able to successfully partner in diabetes care at least in some settings. As the Patient Protection and Affordable Care Act, which promises to expand health care coverage to millions of Americans, excludes undocumented immigrants, these patients are likely to continue to concentrate in relatively few health care delivery settings. It may be reassuring to clinicians and policy makers to know that, at least in some settings, undocumented immigration status need not result in worse diabetes outcomes.

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Appendix

Details on the different measures discussed in the methods section.

CAHPS-Cultural Competency

The CAHPS-CC has seven subdomains: positive doctor communication, negative doctor communication, health promotion, alternative medicine, shared decision-making,

equitable treatment, and trust. Internal consistency for the Immigration, Culture and Health Care (ICHC) study population was determined by Cronbach alpha (0.82 for positive communication, 0.77 for trust, 0.72 for preventive care counseling). Negative communication and equitable treatment were not included in this study due to their low Cronbach alpha in the Spanish-speaking population. Shared decision-making and alternative medicine are also excluded due to their overall low Cronbach alpha. Due to highly skewed distributions and as a proof of concept, scores for the two domains included in the study were dichotomized into two categories [26]: the upper 25 % (optimal) and the lower 75 % (suboptimal). Scores for each of the CAHPS-CC subscales range from 0 to 100.

Diabetes Self-Management

(1) *Diabetes self-care* is measured through a brief version of the Summary of Diabetes Self-Care Activities (SDSCA) scale [27]. It is a self-report questionnaire that measures levels of self-management across different components of the diabetes regimen: general diet (2 items), specific diet (2 items), exercise (2 items), blood-glucose testing (2 items), foot care (2 items), and smoking (not included in the ICHC Study survey). Due to issues of recall, we decided to use only the item of each measure that asked about behaviors within the immediate past week. For the foot care measure, we only used the item that asked about checking feet and not inspecting the inside of shoes. Responses range from 0 to 7 (days a week) with higher scores indicating better diabetes self-management. (2) *Diabetes self-care barriers/supports* were measured using a diabetes-related health belief instrument translated for use with Spanish-speaking Mexican Americans [29]. It is a 25-item health belief instrument from Starr County, Texas consisting of five subscales: Social support for diet, Impact of job on therapy, Benefits of therapy, Control of effect of diabetes, and Total barriers to diet and taking medications. Responses were given in a Likert-scale format, ranging 1 (strongly disagree) to 5 (strongly agree). The higher the score on an item, the stronger the belief. (3) *Diabetes self-efficacy* was measured through an 8-item scale originally developed and tested in Spanish for the Diabetes Self-Management study [32]. Responses range from 1 (not at all confident) to 10 (completely confident) and the score for this scale is the average of the eight items. Higher averages indicate higher self-efficacy. (4) *Medication adherence* was measured using the Morisky scale, a four-item self-reported adherence measure (Cronbach alpha = 0.61) that addresses barriers to medication-taking. Responses are yes/no categories and the score is calculated by assigning 1 point for each “yes” answer, thus ranging from 0 to 4. Higher scores indicate poorer medication adherence [34].

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Exhibit D

The power of local autonomy: expanding health care to unauthorized immigrants in San Francisco

Helen B. Marrow

(First submission June 2010; First published August 2011)

Abstract

I analyse the mechanisms through which an inclusive local policy environment in the integrated city-county of San Francisco operates to improve unauthorized immigrants' access to and utilization of health care. Within – but not outside – the bounds of this inclusive local context, committed providers reported being able to provide attention to unauthorized immigrants without worrying about the direct costs of doing so; to buffer, marshal resources, and advocate for individual unauthorized patients; and to exert substantial autonomy in deciding how to approach lack of legal status in their patient–provider interactions. These results highlight the potential and limitation of sub-national policies seeking to ameliorate unauthorized immigrants' health vulnerability in a hostile US federal context.

Keywords: Immigration; incorporation; unauthorized; health care; safety net; autonomy.

Introduction

The federal and state health care policy context toward the estimated 11.1 million unauthorized immigrants living in the USA today has been described as so decidedly hostile that it leaves little leeway for government officials, health care providers, and immigrant advocates to make the situation more inclusive, even when they want to (Newton and Adams 2009). With few exceptions, restrictive government policies have rendered unauthorized immigrants ineligible for most federally funded public health insurance – such as Medicare, regular Medicaid, and State Children's Health Insurance Program (SCHIP) – since the

early 1970s (Schwartz and Artiga 2007; Fox 2009). All unauthorized immigrants qualify for select public health and nutrition measures – including immunizations, the Special Supplemental Nutrition Program for Women, Infants and Children (WIC), and testing and treatment for communicable diseases – but they can only qualify for a limited form of Emergency Medicaid (which covers labour and delivery and other designated emergencies) if they fall into certain categories like low-income children or pregnant women, and they can only qualify for non-emergency care in a handful of states that use their own state funds to offer it.

In addition, unauthorized immigrants face a range of indirect eligibility restrictions. Many are effectively barred or deterred from seeking care even in federally funded institutions that do not in theory restrict care based on legal status. This is because they are employed in informal jobs, move constantly between jobs, and live in overcrowded housing, so they often have difficulty producing income tax forms or utility bills that can serve as proof of local residency and low income – two bureaucratic criteria that *are* required for admission into such institutions (Portes, Light, and Fernández-Kelly 2009; Portes, Fernández-Kelly, and Light 2011).

Together with other barriers like fear, direct and indirect eligibility restrictions lead to some of the most severe disparities in access to and utilization of care among comparable populations in national, state, and local studies (Goldman, Smith and Sood 2005; Ortega et al. 2007). Moreover, under the Health Care and Education Reconciliation Act of 2010, unauthorized immigrants will not be eligible to receive federal subsidies to purchase their own private insurance, nor will they be allowed to purchase health insurance through new state-based health insurance exchanges, even if they pay with their own money. In fact, unauthorized immigrants are projected to become a full one-third of the remaining 23 million uninsured Americans by 2019 (Pear and Herszenhorn 2010).

If government officials, health care providers, immigrant advocates, and other actors want to reduce disparities by legal status – whether to help prevent the spread of infectious diseases, reduce the cost of preventable emergency care, or help institutions comply with ethical stances that support the provision of care to all humans, all residents of their communities, or all workers – they must look to other creative alternatives. One viable alternative is the national network of federally qualified health centres (FQHCs), which offer a variety of primary, mental, and dental services to unauthorized immigrants across the country and which, like public hospitals, do not in theory restrict care based on legal status. The Health Care and Education Reconciliation Act of 2010 did increase federal funding to FQHCs, and this will

certainly help to reduce some, but not most, disparities in access to and utilization of care for unauthorized immigrants.

Other creative alternatives are bi-national, although these too may be problematic since unauthorized immigrants face increasing restrictions on moving back and forth across international borders.

A third set of creative alternatives consists of inclusive sub-national policies that may be enacted at the state and local levels in receiving communities – especially since new patterns of geographic dispersion have brought unauthorized immigrants into an unprecedented array of states and localities, all of which are now struggling to determine how best to respond to their presence. In this article, I ask: what are the *mechanisms* through which inclusive local policy environments can operate to improve unauthorized immigrants' access to and utilization of health care, specifically via the actions of providers and staff working in public health care safety nets that they govern?

Site selection and methods

To identify such mechanisms, I conducted a case study of thirty-six safety net health care providers and staff who work in a large, residency-training, outpatient clinic – hereafter called Hospital Outpatient Clinic (HOC). HOC is associated with the public safety net hospital of the integrated city and county of San Francisco, which exhibits a uniquely inclusive local policy environment toward unauthorized immigrants but which continues to be embedded in the more restrictive federal and state context described above. Examining providers and staff in a public safety net clinic such as HOC is valuable because it is they who constitute the front-line or street-level bureaucratic arms of local governments, and who have some discretion to interpret, enact, and enforce government policies during the execution of their work, even while remaining heavily influenced by rules and bureaucratic processes (Lipsky 1980).¹ HOC provides comprehensive primary care and select specialty services – most FQHCs do not provide the latter – and is one of the city's Healthy San Francisco (HSF) medical homes. Like its parent hospital, HOC serves a diverse patient population that is predominantly low income, uninsured, and racially, ethnically, or linguistically in the minority.

Between May and September 2009, I sought out a variety of providers and staff in HOC through a combination of purposive and snowball sampling. Purposively, I wanted to include a range of types (from physicians to non-physician staff) who come into contact with unauthorized immigrants in different statuses and roles. Respondents included five physicians; seven resident physicians-in-training; and twenty-four non-physician providers and staff members, including eight registered nurses, three nurse practitioners, seven medical evaluation

assistants, four clerical staff, one social worker, and one health worker. I also conducted interviews with an additional eighteen safety net providers and staff (including two hospital Medi-Cal eligibility staff) working in other hospital clinics and departments, a nearby Latino-oriented FQHC, and a nearby Latino day labourer-oriented free clinic in order to uncover their perspectives on how unauthorized immigrants view and interact with providers and staff at HOC and its parent hospital.

Interviews lasted between forty-five and ninety minutes and over two-thirds (thirty-eight of the fifty-four respondents) were conducted in isolation, although due to their workday time constraints the remainder (sixteen) were interviewed in small sets of focus groups. I tape-recorded, transcribed, cleaned, coded, and analysed all interviews using ATLAS.ti, a qualitative analysis software program. To ensure anonymity, I have changed all names and identifying characteristics of individual respondents.

Creating an inclusive policy climate

Local government officials in San Francisco have worked hard to create an inclusive and less stigmatizing environment for unauthorized immigrants than exists at the federal level or in most other localities, one that is consistent with the city's vanguard reputation for being on the leading edge of progressive social and political change. They have allocated relatively generous funds to the city's public safety net, which stands at the country's leading edge of promoting culturally and linguistically competent care and is anchored by a community-oriented acute care public teaching hospital affiliated with a well-respected academic medical centre. This public teaching hospital gets referrals for specialty care from its own internal outpatient clinics, a system of closed satellite public outpatient clinics, and another system of affiliated non-profit FQHCs. Providers and staff working within the infrastructure are paid on public salaries with local Department of Public Health funds.

Local government officials in San Francisco have also enacted measures that separate lack of legal status from the provision and receipt of public services and benefits. First, they have strengthened their commitment to an official sanctuary policy. Originally passed as a symbolic resolution in 1985 to declare the city a refuge for, and to prohibit discrimination against, Salvadoran and Guatemalan refugees, San Francisco's sanctuary policy has evolved into an active ordinance in the city's Administrative Code. Recently, the ordinance has been subjected to a federal grand jury investigation (ongoing) to determine whether or not it violates federal immigration law but, through it, San Francisco has joined over fifty other American localities to actively

prohibit: (a) the asking or collection of any information on legal status other than that required by state/federal statute, court decision, or regulation, or by federal, state, or local public assistance criteria; and (b) the cooperation of public service providers with federal immigration officials regarding any persons not under investigation or convicted of felonies (Tramonte 2009).

Second, local government officials recently approved a municipal ID ordinance (effective 15 January 2009), making San Francisco the second city in the country after New Haven, Connecticut, to offer a municipal identification card to all city residents regardless of legal status. The ordinance's originators were primarily interested in the benefits it would bring to the city's approximately 40,000 unauthorized immigrants, yet they were also careful to design and frame the ordinance inclusively to better withstand public criticism and avoid stigmatizing the card's future holders (de Graauw 2009). Thus, although the ID card does not grant any new services or benefits to unauthorized immigrants, it makes them easier to access. Both the sanctuary and municipal ID ordinances acknowledge unauthorized immigrants' *de facto* legitimacy to be part of San Francisco's civic community, based on what Ridgley (2008) and de Graauw (2009) term a conception of local 'inhabitation' or 'residence' (e.g. *jus domicili*) rather than birthright, ancestry, or legalistic citizenship.

Third, local government officials enacted and committed substantial local public funds to San Francisco Healthy Kids (SFHK) (effective 2002) and Healthy San Francisco (HSF) (effective April 2007). SFHK provides subsidized health care plans to all local resident children aged up to eighteen who do not qualify for other forms of federal or state public insurance (including regular Medi-Cal and Healthy Families – California's regular Medicaid and SCHIP programmes) regardless of legal status. Similarly, HSF provides 'universal access' to primary medical care to all local resident adults aged eighteen to sixty five who have incomes under 500 per cent of the federal poverty line but do not qualify for other forms of federal or state public insurance coverage, regardless of legal status. Participation is free if residents' incomes fall below the federal poverty line; otherwise it is based on designated quarterly participation and point-of-service fees. However, services covered in the HSF universal access model are not equivalent to insurance coverage. They are limited to those primary care services provided by participating health care institutions (to date, almost exclusively public safety net ones) or otherwise funded by HSF monies, and a range of specialty and select primary care services are not covered, including dental, vision, organ transplants, and long-term care.

Thus, although San Francisco is not immune to the conservative pressures that have increased class and racial inequality and put severe

pressure on the public social safety net nationwide; even though its two main policy efforts to divorce lack of legal status from the provision and receipt of local public services and benefits have come under strong attack; and even though its HSF universal access model remains ‘categorically unequal’ (Light 2011), the city exemplifies a much more inclusive and less stigmatizing environment than does either the state of California or the nation as a whole. HOC respondents, especially those who have worked in other states and localities, including some in the surrounding Bay area, noted such ‘exceptionalism’ frequently and emphatically.

Local bureaucratic autonomy: self-selecting into the safety net and providing primary care

HOC providers feel that they have actively self-selected themselves into the San Francisco safety net environment. Over the course of their medical training, all selected: (1) primary care, which is lower paying and less prestigious than specialty care; (2) the American social safety net, which is devoted to serving under-served populations; and (3) living and working in San Francisco, which is one of the most politically liberal cities in the country. Taken together, self-selection shapes their positive attitudes toward unauthorized immigrants, whom many considered to be equally deserving of care either because they are human beings (human rights perspective), members of a disadvantaged and under-served population (social justice perspective), members of the local community (public health and community perspective), positive contributors to the American economy (deserving worker perspective), or simply ‘sick’ and in need of care (humanitarian perspective). While some variation did exist among respondents in the degrees to which – and various rationales for why – they supported providing care to unauthorized immigrants, all exhibited an inclusive attitude, and several reported that public safety net hospital’s institutional culture imposes sanctions on providers and staff who openly disagree.

San Francisco’s inclusive policy climate helps HOC providers put their attitudes into practice in several ways. First, it allows them to provide care to unauthorized immigrants without having to worry about direct costs. As physician Charlotte explained, San Francisco’s public-salaried payment structure insulates them from having to ‘eat’ the direct costs of treating uninsured patients, making them less reluctant to treat them than many providers working in private practice. Likewise, San Francisco’s generous funding of public health care insulates these public safety net providers from the ‘frustration’ of unfunded mandates to treat unauthorized immigrants who are uninsured, which HOC providers view as a more pressing issue in

other localities with more restrictive policy environments. As Charlotte stated:

We all take a pay cut to work in a safety net institution. . . We do it because it frees us from some of the structural problems of private practice. And there is. . . a whole [San Francisco] city understanding for investing in this infrastructure. [It is] a place where you don't have [that] level of frustration. . . like "Okay, so we have to deal with the unfunded patients and do not get any resources from the local government to do so."

Indeed, local HSF investment – which, as clerical worker Shana reported 'kicks in the money' for many services that federal and state policies do not fund for poor people and unauthorized immigrants – allows HOC providers, in nurse practitioner Sarah's words, to offer 'access to better than 90 per cent' of primary care services without thinking or asking about patients' legal statuses. According to Sarah:

There's just once in a while something you can't do. And I feel lucky that I don't really care [about legal status]. It doesn't, you know, for the most part it doesn't really affect what we can do for people.

HOC providers knew that their ability to disregard patients' legal statuses would disappear if local sanctuary or insurance policy were to become more restrictive, since, according to physician Joseph, it would:

become much more germane to know if someone's unauthorized because you want to know what benefits you can try to get people access to. If that's [a] criterion for excluding people from benefits then, you know, we would probably start asking [patients about their legal statuses].

Physician Mary agreed that providers:

often don't know [legal status] because we are very lucky in San Francisco in having no [legal or financial constraints placed on us] for anything we can provide on-site [at the public safety net hospital] to anyone who lacks health insurance.

She went even further than Charlotte or Sarah to explain how additional local investment even allows providers to link patients to care at other area institutions through a system of city contracts if the public safety net hospital does not provide a particular service on site: 'If we don't have a whole department that provides it here, the city

actually has a contract where they pay for it, usually at [another nearby academic medical centre], to buy the care for patients there.' As Mary showed, San Francisco's inclusive local policy, which includes a generous allocation of local funding to the city's safety net, allows HOC providers to more effectively marshal resources for individual uninsured patients.

This inclusive context also allows providers to more effectively muster resources and advocate for such patients in other ways. For instance, the city's sanctuary policy reaffirms many providers' beliefs that unauthorized immigrants are often scared to seek health care services because of the restrictive federal policy toward unauthorized immigrants. Sanctuary policy supports them in their efforts to engage in what Horton (2006) and Lamphere (2005) call 'buffering' strategies as they try to smooth and compensate for such fear (Konczal and Varga 2011). At an institutional level, buffering strategies include attempts by hospital administrators to create trust in the local immigrant community (by advertising a 'safe' hospital context, in which data on lack of legal status will not be unlawfully collected or transmitted to authorities) and the creation of a standard, neutrally coloured hospital 'gold card' (which outpatient clinic providers and staff can use to view patients' medical record numbers instead of requesting their citizenship and legal status information directly).

At the individual level, buffering strategies include attempts by hospital Medi-Cal eligibility workers to reassure applicants that they only ask about citizenship and legal status insofar as it is required to determine plans and payers (e.g. federal or state public insurance programmes or the two local initiatives, SFHK and HSF), never for disqualification purposes. As medical evaluation assistant Marta attested, front-desk clerks and medical evaluation assistants reported accepting alternative documents (e.g. medical record numbers) instead of social security numbers when checking in patients for appointments; sometimes they also 'run after' patients whom they notice are visibly fearful and so 'turn around and leave', in order to reassure them that 'it is safe here'.

In the more insulated back rooms of the clinic, physicians, residents, registered nurses, and nurse practitioners also reported going to great lengths to advise and advertise to patients that San Francisco is a 'safe' context where it is okay to utilize services and programmes. Likewise, they reported encouraging patients to collaborate with 'safe' social workers (who understand eligibility rules and can help both providers and patients 'work around' confusing legal status restrictions to access more resources) and drawing on their professional networks to request compassionate assistance from external non-safety net providers when they are unable to provide certain services internally. As nurse practitioner Lynne described:

I really do encourage people. “It’s okay. You’re not going to get arrested. You’re not going to get deported just because you’re seeking health care. You can use your real name.” Or, “If you’re really scared, go to the refugee clinic.” Or I’ll try to send them to the social worker to get some referrals to a Spanish-speaking advocacy agency where they can get reassurance if that’s what they need.

Throughout the clinic, providers and staff all reported engaging in buffering strategies to reduce unauthorized immigrants’ fear, including not asking patients about their legal statuses directly, heavily downplaying such requests when they do (e.g. prefacing requests with ‘It doesn’t matter to me...’), never documenting patients’ lack of legal status directly in patients’ records, and utilizing patients’ social networks (both inside and outside the clinic) to encourage greater utilization of resources.

Perhaps most importantly, San Francisco’s inclusive policy grants these providers substantial autonomy to decide if, how, and why they will approach lack of legal status in their patient–provider interactions in order to offer unauthorized patients with the most effective medical care. Some providers choose to actively ‘ignore’ or ‘look beyond’ patients’ legal statuses, to comply not only with the city’s sanctuary policy but also with their dominant professional norm to ‘suspend judgment’ and ‘not disenfranchise’ patients. As physician Charlotte explained, ‘We try to treat people the same no matter what... do our damndest not to think about [legal status].’ In fact, registered nurse Jane emphatically described a strategy of never asking patients about legal status ‘not because are trying to avoid the issue, but rather because we are trying to get around it to help people and give them equal care. It just interferes with medical care to bring [legal status] up.’ For this group of providers, San Francisco’s inclusive context not only strengthens the dominant professional norm of ‘don’t ask, don’t know, don’t care’ regarding legal status but also legitimates their cognitive beliefs that ideally lack of legal status should not matter to health care delivery. Resident Eduardo even interpreted this as an additional directive to ‘follow the same algorithm no matter what’ and treat all patients equally.

Other providers choose different approaches to offer culturally competent and compensatory care. San Francisco’s inclusive local policy environment assists them by creating a secure environment in which they can, according to physicians Mary and Elena, more easily seek out patients’ ‘social histories of migration’ to help ‘contextualize their medical conditions’. Most providers in this group continued to refrain from asking patients directly about their legal statuses, fearing that doing so would give them a false impression of stigmatization or service restriction. Instead, they tried to elicit the information from

patients indirectly, often making inference to it through ‘related’ characteristics such as their recent arrival, day labourer or caregiver occupational status, lack of English language skills, separation from family members abroad, and/or inability to travel internationally. Context-oriented providers saw such characteristics associated with conditions of illegality, as causing patients stress and trauma, and as compromising patients’ health and ability to follow care recommendations.

While San Francisco’s inclusive policy climate does not solve the internal provider debate as to whether to ‘ignore’ or ‘acknowledge’ lack of legal status, it does set both approaches within a more protective and enfranchising context.

Where autonomy ends: referring to specialty and ancillary care

The restrictive federal and state context in which San Francisco’s inclusive local policy is embedded does not necessarily change HOC providers’ desires to provide care for unauthorized immigrants. They are, after all, part of the heavily self-selected social safety net. Nonetheless, restrictive federal and state policy does limit the range of resources that HOC providers can offer to unauthorized patients, force providers to directly engage patients’ legal statuses when they might not otherwise do so, and depress providers’ strategies for buffering and advocating for individual unauthorized patients.

This important set of limits on providers’ bureaucratic autonomy is most clearly visible at two critical junctures – the first between primary medical care and specialty medical care, and the second between primary medical care and ancillary social support care. Government officials have enacted and committed substantial local public funds to two programs (SFHK and HSF) that in theory expand access to care to all low-income children and adults who are San Francisco city residents. Nevertheless, as a universal access model, HSF remains categorically unequal (Light, 2011) with respect to other forms of public health insurance – even Medi-Cal and Healthy Families – in that it only includes primary care provided by participating health care institutions or otherwise funded by HSF monies. HSF does not cover certain specialty care services (including dental and vision) or other ancillary services (including public housing, General Assistance (GA), Supplemental Security Income, food stamps, disability, or hospice). Unauthorized immigrants’ access to these services lies outside the domain of local San Francisco policy and continues to be delimited by more restrictive federal and state policies (WIC is a notable exception).

Consequently, HOC providers’ ways of dealing with patients’ lack of legal status change dramatically as they cross the line separating locally covered primary medical care services from other specialty care

and ancillary services. They are suddenly forced into thinking and asking about lack of legal status. According to health worker Mariana, clerical workers and medical evaluation assistants learn about patients' legal statuses not only when they 'need to know [what insurance is] going to cover some specific test we are setting up, or if patients need a pre-authorization to do that' (specialty services), but also when they 'need to send patients to the social worker to see if there are any [social support] resources available.' Similarly, physician Elena does not usually have to ask about legal status and is 'able to provide standard of care for the majority of my patients who are chronically ill' without knowledge of it since 'the city and county of San Francisco commits amazing, amazing resources to provide an enormous amount of things.' However, for the small group of patients who do become 'severely ill, or have the wrong thing', it matters because they 'just can't get [specialty] care' and 'it becomes really hard, depending on what the service is.' It is rare that Elena has 'to come flat out and ask a patient, 'Are you documented?'. Nevertheless, in a 'clinically exigent situation when patients need a specialty service that requires they are U.S. citizens or legal immigrants', she is forced to ask.

As a result, providers like Elena see clear patterns of 'blocked access' emerging for unauthorized patients regarding select high-tech specialty procedures such as organ transplants, open MRIs, nuclear medicine tests, coronary bypass or bariatric surgeries, endoscopies, cystoscopies, screening colonoscopies, intervention cardiology procedures, and PET or DEXA scans, because such services are either not offered on site at the public safety net hospital or not covered by HSF or other local, state, or federal monies. Coming up against these barriers, HOC providers reported going into advocacy mode, trying desperately to 'twist some arms' and find ways to link their unauthorized patients to care. In a few cases their efforts have been successful, but as resident doctor Laura explained of the time when an external allergist agreed to see one of her unauthorized patients who had recurrent anaphylaxis, such success is 'voluntary' and 'discretionary' rather than systemic, and it declines as the cost of the specialty procedure rises. In most situations, providers reported that their 'hands are tied' and that their efforts to buffer and advocate for their unauthorized patients fall short, as happened to physician Mary:

[My patient] is someone who by . . . every criterion would get a liver transplant. She's socially stable, she's married, she's adherent to absolutely everything that you ask her to do, there's like nothing wrong. And I asked the liver specialist here to see her [but] as soon as they found out she didn't have papers it was like very clear [that she would not be treated]. . . That's just a devastating conversation to have [with a patient].

Likewise, physician Elena argued that lack of legal status quickly becomes ‘determinant of the care one receives’ at the point of transition into high-tech specialty care:

If I advocate hard enough for an African-American patient who needs a particular service outside the ones we provide [at the public safety-net hospital], usually I can get it. There’s usually all sorts of hoops to jump through but I can get it.

However, with unauthorized patients her advocacy strategies prove ineffective: ‘I just can’t.’ As registered nurse Harriet confirmed, in the context of high-tech specialty care, ‘When you’re unauthorized,’ providers have even less [ability to] ‘work around.’ At this point providers described the frustration of watching unauthorized patients unable to access needed services, or only able to access insufficient stopgap or (in resident Kate’s words) ‘band-aid’ emergency services that do not constitute a ‘long-term solution’. Several even began debating the pros and cons of advising patients to return to their home countries to try to obtain specialty medical care services there.

The restrictive federal and state policy context also depresses these public safety net providers’ strategies for buffering and advocating for individual unauthorized patients in the realm of ancillary services, where rules governing access are strict and strongly enforced. As physician Mary said, even in remarkable cases, where the city does fund certain specialty medical care services for unauthorized immigrants, HOC providers’ ‘hands get tied’ when accessing critical support services like unemployment, disability, or public housing that would allow patients to support themselves and their families as they heal:

When I sent a patient to the social workers, I asked them, “Is there any miracle we can pull off here [hooking him up to unemployment or disability benefits]?” And they basically said “No.” And at this point, you know, the city’s about to pay \$100,000 to get an ICD [implantable cardioverter-defibrillator] implanted in him [for cardiac arrhythmia]. So it’s hard. We work to send him to the food bank and stuff, but he’s basically losing his housing and it’s just a mess. He wound up having to send his children, who are American-born and are U.S. citizens, and his wife back to his home country, because he can’t afford to keep them fed or anything. He’s someone who, because he can get this procedure, should be able to recover, be a productive member of our society, and be able to raise two kids who will be, too. But there’s nothing we can do right now.

In fact, restrictive policy context and the ever-looming threat of budget cuts keeps many HOC providers’ constantly aware of, in Mary’s words,

the ‘power of the state’. It curtails their willingness to ‘rock the boat too much’ or to encourage unauthorized patients to apply for services they ‘know they can’t get’, lest such actions bring about a restrictive backlash that could jeopardize what access to primary care unauthorized immigrants do have.

Conclusion

I have examined the mechanisms through which inclusive local policy environments can operate to improve unauthorized immigrants’ access to and utilization of health care, specifically via the actions of street-level bureaucratic providers and staff working in public health care safety nets that they govern. HOC providers have come to their jobs both strongly selected and heavily committed to expanding access, and providing culturally competent care to vulnerable patient populations, including unauthorized immigrants. By and large they reported that the inclusive San Francisco policy context allows them to give care to unauthorized immigrants without worrying about the direct costs of doing so; to buffer, marshal resources, and advocate for individual unauthorized patients; and to exert substantial autonomy in deciding how to approach lack of legal status in their patient–provider interactions – to the point that some even go beyond the official bounds of the city’s sanctuary ordinance to extend what they view as more effective medical care to unauthorized patients in ways they believe to be consistent with the ordinance’s broader spirit.

Nevertheless, HOC providers also reported that their advocacy efforts and bureaucratic autonomy break down at two critical junctures during the transition from an inclusive local to a more restrictive federal and state policy climate, especially as the cost of high-tech specialty medical services rises or when federal and state regulations regarding ancillary services are strictly codified and enforced. In these realms, care becomes more ‘discretionary’ and ‘voluntary’ – successful only in a few ‘miracle’ cases and frustratingly unsuccessful most of the time.

These results carry important practical and theoretical implications for policymakers, health care providers, and advocates. Most importantly, they demonstrate that sub-national strategies such as San Francisco’s are imperfect substitutes for including unauthorized immigrants within the bounds of federal and state health insurance and social welfare programmes. Even in San Francisco, it is ‘access’ rather than insurance that is the goal, since full insurance is still deemed to be unaffordable. The continued exclusion of unauthorized immigrants from national and state programmes means that even in San Francisco, local providers still face difficulties working around specialty and ancillary problems in order to care for unauthorized

immigrants. ‘San Francisco is not paradise,’ physician Elena reported, and ‘if these problems exist here,’ resident Carla said, ‘you know they’re everywhere else.’ To fully overcome these barriers, HOC respondents noted, the American public must ultimately change its mindset about unauthorized immigrants to see them as more deserving of inclusion and financial investment.

Yet the results of my study also highlight the real potential for sub-national actors to play a positive role in enacting and implementing local strategies that can help overcome some of the barriers to access and utilization. Such strategies may be politically and financially difficult to enact elsewhere. They will likely require supportive, or at least neutral, backing from local communities and a fiscal base large enough to support redistribution. San Francisco is an extremely wealthy and politically liberal city whose public has proven willing to support and contribute taxes to progressive local policies, and whose politicians have committed what physician Elena describes as ‘amazing’ and ‘generous’ resources to its health care infrastructure.

Still, government officials in San Francisco note that even prior to the implementation of HSF, the city was already paying substantial amounts to care for the uninsured, including unauthorized immigrants, and so the programme does not necessarily represent an infusion of new money into the safety net system. Rather, it was conceived as a way to integrate, further de-stigmatize, and make more efficient the robust safety net that the city already had in place (SF DPH and SF OLSE 2010). In this regard, San Francisco can serve as an important model for other localities throughout the USA as they search for practical ways to respond to unauthorized immigration. Unless these localities are willing to let unauthorized immigrants die in the streets, they already pay for their treatment somehow – and usually in ways that are unduly expensive and less efficient than in San Francisco. If local actors are concerned about reducing disparities by legal status, the unique San Francisco case demonstrates how creating a protective civic environment and focusing on expanding and integrating access to primary care can help. This gives providers greater ability to help reduce disparities by legal status and, by extension, it allows patients greater access to and utilization of care at a systemic level.

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Exhibit E



Original article

Change in birth outcomes among infants born to Latina mothers after a major immigration raid

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Abstract

Background: Growing evidence indicates that immigration policy and enforcement adversely affect the well-being of Latino immigrants, but fewer studies examine ‘spillover effects’ on USA-born Latinos. Immigration enforcement is often diffuse, covert and difficult to measure. By contrast, the federal immigration raid in Postville, Iowa, in 2008 was, at the time, the largest single-site federal immigration raid in US history.

Methods: We employed a quasi-experimental design, examining ethnicity-specific patterns in birth outcomes before and after the Postville raid. We analysed Iowa birth-certificate data to compare risk of term and preterm low birthweight (LBW), by ethnicity and nativity, in the 37 weeks following the raid to the same 37-week period the previous year ($n = 52\,344$). We model risk of adverse birth outcomes using modified Poisson regression and model distribution of birthweight using quantile regression.

Results: Infants born to Latina mothers had a 24% greater risk of LBW after the raid when compared with the same period 1 year earlier [risk ratio (95% confidence interval) = 1.24 (0.98, 1.57)]. No such change was observed among infants born to non-Latina White mothers. Increased risk of LBW was observed for USA-born and immigrant Latina mothers. The association between raid timing and LBW was stronger among term than preterm births. Changes in birthweight after the raid primarily reflected decreased birthweight below the 5th percentile of the distribution, not a shift in mean birthweight.

Conclusions: Our findings highlight the implications of racialized stressors not only for the health of Latino immigrants, but also for USA-born co-ethnics.

Key words: immigration enforcement, birth outcomes, stress, Latinos/Hispanics, nativity

Key Messages

- We compare risk of adverse birth outcomes before and after a major federal immigration raid in Postville, Iowa.
- Whereas there was no change in risk of low birthweight for infants born to White mothers in Iowa, infants born to Latina mothers in Iowa had a 24% higher risk of low birthweight in the period following the Postville raid.
- Analyses including gestational age reveal an elevation in risk of moderate-preterm birth (PTB) after the raid among Latina mothers, rather than an increase in very-PTB.
- These findings are consistent with theories linking immigration enforcement to the health of Latino immigrants and their USA-born co-ethnics.

Introduction

Investigators theorize that unintended consequences of social policies affecting disadvantaged groups contribute to entrenched US health disparities.^{1–5} A growing literature examines effects of US immigration policy on immigrants (particularly Latino immigrants),⁵ documenting links between immigration policy and health care utilization,^{6–9} Medicaid participation^{10,11} or food insecurity.¹² A smaller, but growing number of studies examine links between immigration enforcement and psychosocial well-being,^{13,14} self-rated health¹⁵ and enforcement-related distress.^{15–17}

Many existing studies of immigration policy/enforcement and health focus on immigrant (or specifically undocumented-immigrant) samples¹⁸ or examine Latinos regardless of nativity.^{6,7,15} Whereas some studies have documented effects of immigration policy and enforcement on USA-born children of immigrants,^{9,11,19} far fewer examine implications specifically for co-ethnic USA-born adults.^{8,12,16} Although USA-born Latinos are not subject to immigration deportation, many are embedded in communities targeted by immigration enforcement^{20,21} and may experience discrimination, ‘othering’²⁰ or chronic identity-related vigilance²² in response to racialized exclusion.^{5,23–26}

Measuring causal relationships between immigration policy/enforcement and health outcomes has proved challenging: policy changes usually occur after an extended deliberation period that makes exposure classification difficult, and enforcement practices are often diffuse and covert.^{10,21} In contrast, the 2008 Immigration and Customs Enforcement (ICE) raid on a meat-processing plant in Postville, Iowa, was the largest single-site raid yet seen in the USA, and occurred without warning, allowing a clear before-and-after comparison.

We compare risk of adverse birth outcomes among Latina and non-Latina White mothers in the state of Iowa before and after the Postville raid. Birth outcomes, and particularly low birthweight (LBW), are well suited as health outcomes in this study because birth-certificate data

are publicly available and collected for all births regardless of the mother’s immigration status, and birthweight has little measurement error. Previous studies have documented increased LBW risk after population-level stressors such as terrorist attacks or natural disasters^{27–31} (although some studies report null or mixed findings).^{32,33}

Economic and demographic commonalities across Latino population clusters in Iowa (many, like Postville, centre on meat processing) and social and affective ties between foreign-born and USA-born Latinos lead us to hypothesize effects for Latinos across the entire state. We hypothesize that, among Iowa births, the association between LBW and birth after the raid will be modified by mother’s ethnicity, such that foreign-born and USA-born Latina mothers will have higher LBW rates after the raid, whereas non-Latina White mothers will have no change in LBW. We anticipate that this effect modification will be independent of potential socio-economic confounders and traditional risk factors for LBW.

Exposure: the Postville raid

The ICE raid on a meat-processing plant in Postville, Iowa, on 12 May 2008 was implemented without advance warning to local or state officials. ICE deployed 900 agents using military tactics, including armed officers and a UH-60 Black Hawk helicopter, to arrest 389 employees, 98% of whom were Latino.³⁴ Agents used presumed race/ethnicity to identify suspected undocumented immigrants, allegedly handcuffing all employees assumed to be Latino until their immigration status was verified.³⁵

Male arrestees were detained at the National Cattle Congress in Waterloo, Iowa (80 miles from Postville), whereas women were detained in county jails. Mothers of small children were allowed to return to Postville with ankle monitors but, barred from working, survived on charitable aid.^{34,36} Detainees were chained together and arraigned in groups of 10 for felony charges of aggravated identity theft (knowingly working under a false Social Security Number). A plea bargain led nearly all to plead

guilty, although few were technically guilty of the crime, and 297 arrestees were deported after serving a 5-month prison sentence.³⁴

The raid separated hundreds of families, most often from their primary breadwinner. Fear of follow-up home raids kept many Postville families from staying in their own homes, choosing instead to sleep in church pews or leave town altogether.³⁶ News of the raid immediately spread throughout the state. *La Prensa*, a Spanish-language newspaper in western Iowa, published eyewitness testimony of arrestees detained at a cattle fairground, cuffed and chained together from the waist to the ankles.³⁷

Methods

We obtained birth-certificate data for all births in Iowa from 2006 to 2010 ($n = 209\,389$). We classified infants as 'exposed' to the post-raid environment if they were born in the 37 weeks following the Postville raid (12 May 2008–26 January 2009) and 'unexposed' if they were born in same period one year earlier (12 May 2007–26 January 2008). We chose 37 weeks because it was the minimum length of a normal gestation.

The primary outcome variable, LBW, was defined as birthweight <2500 g. We used self-reported race and Hispanic ethnicity to categorize mothers as Latina or non-Latina White, creating a 'Latina' category by restricting to mothers in any Hispanic subgroup except Hispanic/Spaniard. Latina mothers were predominantly of Mexican descent (81%), although 11% were of Central American origin and 8% were of other Hispanic origin. We used self-reported birthplace to categorize mothers as USA- or foreign-born. Immigration status is not collected in birth-certificate data. We included data on maternal age (<20 , 20–25, 26–30, 31–35, 36–40, 41+ years), education (<8 th grade, 9th–11th grade, high-school diploma/equivalent, some college/Associate's degree, college diploma), marital status (married/unmarried at conception) and parity (first live birth/second or higher). We also divided maternal education into tertiles within strata of ethnicity/nativity. We included data on prenatal maternal smoking (no smoking, <10 , 10–19, 20+ cigarettes/day) and prenatal care utilization (Kessner index for adequate, intermediate and inadequate prenatal care).³⁸

We used a data-cleaning algorithm to create a gestational age (GA) variable, which we categorized into preterm birth (PTB) and categories of GA. We took this step to address previously reported data-quality issues for GA estimation in vulnerable populations, including immigrant, Latina or low-English-proficient mothers and mothers with late prenatal care initiation.^{39–42} The algorithm used a LMP-based estimate of GA wherever possible, and the

clinical estimate when a LMP-based estimate was unavailable or implausible for the infant's birthweight; for more information, see Basso and Wilcox.⁴³ PTB was defined as $GA < 37$ weeks. We further categorized GA as very-preterm (<32 weeks), moderate-preterm (32–36 weeks), early-term (37–38 weeks) and full-term (≥ 39 weeks).^{44,45}

We used the cleaned GA variable to estimate the stage of gestation at the time of the raid (or the comparison date), classifying infants as not yet conceived, or in the first, second or third trimester on the date of interest.

We restricted our analysis to singletons born in the 37 weeks following the raid or the same period one year earlier ($n = 57\,850$), although we include data from the same period 2 years earlier ($n = 26\,531$) for description. We excluded 4659 infants born to mothers who were not Latina or non-Latina White, and those missing data on birthweight ($n = 20$), GA ($n = 115$), maternal nativity (Latina mothers only, $n = 11$), age ($n = 2$), education ($n = 332$), marital status ($n = 6$), parity ($n = 256$) and prenatal smoking ($n = 105$). Excluded infants ($n = 847$) were more likely to be LBW, both among Latina and non-Latina White mothers. The final sample included 52 344 infants, 25 979 born in the 37 weeks following the Postville raid and 26 365 born during the same 37-week period 1 year earlier.

Statistical methods

We used modified Poisson regression⁴⁶ to estimate risk ratios (RRs) comparing risk of LBW among infants born after Postville to those in the comparison period, and used Knol and VanderWeele's recommended methods for presenting analyses of effect modification.⁴⁷ This involved presenting: (i) RRs for each stratum of maternal ethnicity and birth timing with a single reference category; (ii) RRs for being born after the raid, stratified on maternal ethnicity; and (iii) measures of effect modification on the additive scale (relative excess risk due to interaction: RERI) and multiplicative scale (ratio of RRs).^{48,49} We estimated a second set of models with Latina mothers further stratified on nativity.

To confirm that findings were not confounded by changes in the population of mothers, we re-estimated all models, first with adjustments for maternal risk factors for LBW (age, education, marital status and parity). We further adjusted for measured health behaviours that could have mediated changes in LBW after Postville: maternal smoking and prenatal care utilization.

We conducted additional analyses to better understand observed changes in LBW. We stratified our initial models on PTB to evaluate whether shifts in LBW were operating primarily on term or preterm births. We used conditional

quantile regression^{50,51} to analyse the distribution of birthweight among Latinas by exposure period. Quantile regression models the association of the exposure with the full range of the birthweight distribution, not merely above or below the set cut-off of 2500 g for LBW.^{51,52} Quantiles were specified to evaluate changes in birthweights lower than the 2500-g cut-off as well as changes throughout the full distribution of birthweight: the 2nd, 5th, 10th, 25th, 50th, 75th, 90th, 95th and 98th percentiles were considered. We estimated the association of birth post-raid with the distribution of birthweight, bootstrapping results 1000 times to estimate standard errors and confidence intervals.

We also examined changes in categories of GA (very-preterm, moderate-preterm, early-term, full-term) before and after the raid, among Latina mothers, using multinomial logistic regression with robust standard errors.

To examine differences in LBW risk according to stage of pregnancy at the time of the raid, we repeated initial analyses with the sample further stratified by stage of gestation at the time of the raid.^{30,53,54} We estimated RRs for LBW after the raid compared with before the raid, by ethnicity and gestational category. To determine whether changes in risk of LBW varied by social position within strata of ethnicity/nativity, we also estimated LBW models stratified on within-group tertiles of education. Analyses were conducted with STATA 13.

Results

Traditional risk factors for LBW and PTB varied by maternal ethnicity and nativity; however, within ethnicity/nativity groups, the distribution of maternal socio-demographic characteristics remained consistent before and after the raid, as did mean birthweight (Table 1). Prior to the raid, Latina and White mothers had similar prevalence of LBW (4.7% for both) and PTB (7.5% for both), which is consistent with other reports of ethnicity-specific birth outcomes in Iowa in this period.^{55,56}

Figure 1 displays temporal trends in LBW, by ethnicity and nativity, including the two time periods in the study sample and also extending an additional year earlier (12 May 2006–26 January 2007). Among White mothers, rates of LBW declined slightly (as has been the trend nationwide since 2006).⁵⁷ Among Latina mothers, rates of LBW were stable in 2006–07, but rose among USA- and foreign-born Latina mothers after the raid.

As displayed in Table 2, the RRs [95% confidence intervals (CIs)] comparing risk of LBW after the raid to before the raid were 1.24 (0.98–1.57) among Latina mothers and 0.95 (0.87–1.03) among White mothers. The measure of effect modification on the additive scale, the RERI, was

0.30 (95% CI 0.03–0.57) and the measure of effect modification on the multiplicative scale, the ratio of RRs, was 1.31 (1.02–1.68). RRs and effect modification measures were robust to adjustment for potential confounders and mediators (Supplementary Tables 1 and 2, available as Supplementary data at *IJE* online).

Table 3 displays the same models with Latina mothers further stratified by nativity. Although confidence intervals widen because of the smaller sample in each group, the RRs (95% CIs) for LBW after the raid among foreign-born (1.25, 0.93–1.67) and USA-born Latina mothers (1.22, 0.83–1.81) were similar in magnitude to the RR from the pooled model, as were the effect modification measures. Adjustment for potential confounders or mediators did not affect these findings (Supplementary Tables 3 and 4, available as Supplementary data at *IJE* online).

In models stratified by term/preterm births, LBW was more strongly associated with birth post-raid among term infants born to Latina mothers (RR, 95% CI = 1.49, 0.95–2.33) than among preterm infants (1.08, 0.88–1.33) (results not shown).

Multinomial logistic regression comparing categories of GA, by ethnicity, before and after Postville, reveals an elevation in risk of moderate-PTB after the raid among Latina mothers (relative risk ratio, 95% CI = 1.11, 0.89–1.38), but no change in risk of very-PTB (0.81, 0.46–1.41) (Table 4).

Quantile regression on the distribution of birthweight indicated that, among Latina mothers, birth post-raid was associated with reduced birthweight only at the left tail of the birthweight distribution, where infants below the 5th percentile of birthweight (corresponding to 2518 g before the raid) were 88 g lighter after the raid (95% CI –168g to –8g). Birth post-raid was not associated with differences in birthweight among infants below the 2nd percentile of birthweight, which corresponded to 2084 g before the raid (6 g heavier, 95% CI –224g to –236g) or at any other point in the birthweight distribution.

In models examining risk of LBW among Latina mothers stratified by stage of gestation at the time of the raid, we found the strongest association between LBW and birth post-raid among mothers in the first trimester at the time of the raid (RR, 95% CI = 1.39, 0.97–1.98) (Table 5). In LBW models stratified by within-group tertiles of education, we observed the strongest association between LBW and birth post-raid in the lower two tertiles of education for both immigrant and USA-born Latina mothers (Table 6).

Discussion

We used the Postville raid, a large-scale immigration raid implemented without warning, as a natural experiment to

Table 1. Descriptive statistics by mother's ethnicity/nativity, during the 37 weeks following the Postville raid (12 May 2008–26 January 2009) and during the same time period 1 year earlier (12 May 2007–26 January 2008) ($n = 52\,344$)

Time period	White		Foreign-born Latina		USA-born Latina	
	Before raid ($n = 23\,878$)	After raid ($n = 23\,379$)	Before raid ($n = 1689$)	After raid ($n = 1746$)	Before raid ($n = 798$)	After raid ($n = 854$)
	Mean	%	Mean	%	Mean	%
Infant sex						
Male	51.3		51.5		50.4	48.7
Female	48.7		48.5		49.6	51.3
Mother's age (years)						
<20	7.7		7.8		9.9	9.3
20–25	32.5		31.1		33.3	33.1
26–30	33.2		34.1		27.5	27.7
31–35	18.6		18.9		19.7	21.0
36–40	6.9		6.9		8.1	7.9
41+	1.1		1.1		1.5	1.0
Education						
8th grade or less	1.3		1.2		34.2	33.7
Some high-school education	8.2		8.2		35.5	36.2
High-school diploma/equivalent	21.4		20.4		18.1	18.4
Some college	38.5		38.8		8.2	7.8
College degree+	30.7		31.4		4.1	3.9
Maternal marital status						
Mother unmarried	31.3		31.7		44.9	47.0
Mother married	68.7		68.3		55.1	53.0
Parity						
0 previous	40.0		39.8		28.4	27.8
1 or more previous	60.0		60.2		71.5	72.2
Prenatal care (Kessner Index)						
Inadequate	2.2		2.2		5.0	4.9
Intermediate	7.7		7.7		19.2	17.5
Adequate	90.1		90.1		75.7	77.6
Smoking in pregnancy						
No smoking	80.0		80.7		98.7	99.1
<10 cigarettes/day	10.3		10.2		1.1	0.9
10–19 cigarettes/day	7.4		6.9		0.2	0.1
20+ cigarettes/day	2.4		2.2		0.1	—
Low birthweight						
Mean birthweight (g)	3401		3407		3349	3339
Preterm birth	7.5		7.5		7.8	8.0
					7.5	8.9

investigate the effects of immigration enforcement on birth outcomes among Latina mothers in a Mid-western state. We found that rates of LBW were steady among White and Latina mothers in the 2 years preceding the raid, but that rates of LBW rose only among Latina mothers after the raid. The association between birth post-raid and LBW was modified by maternal ethnicity on both the additive ($RERI > 0$) and multiplicative scales (ratio of RRs > 1). This association was evident among both foreign-born and USA-born Latina mothers and persisted after adjustment for maternal risk factors, maternal smoking and prenatal care utilization.

We found that the increases in LBW were greatest among term births, but that there was also a higher

prevalence of moderate-preterm (not very-preterm) infants after the raid. Previous studies of psychosocial stressors and birth outcomes have found that LBW increased both through increased PTB^{30,53} and through intrauterine growth restriction^{58,59}; it appears that both mechanisms operated in Iowa, which is plausible given the diversity of economic and psychosocial pathways by which the raid may have affected Latina mothers.

Comparing births after Postville to births in the same period 1 year earlier accounted for seasonality in birth outcomes and avoided the 'mechanical correlation' between pregnancy duration and risk of exposure to stressful events—a methodological pitfall in studies using the time

period immediately preceding an event as the comparison period.³³

Our examination of births in the entire state of Iowa makes this a conservative analysis as one might hypothesize stronger effects in or near Postville compared with Latino communities farther away. Previous studies have examined dose–response relationships based on geographic distance from a natural disaster or attack^{28,33} but, for priv-

acy reasons, the Iowa Department of Public Health does not release microdata with date of birth and geographic information. However, we do not have reason to believe that stressors resulting from Postville raid would emanate by geographic distance in as dramatic a way as a geographically confined natural disaster or attack. Many Latino communities in Iowa are economically similar to Postville, and communication networks between communities make it plausible that Latinos across the state would feel connected to an enforcement event targeted at a single workplace. Lauderdale's finding of increased LBW among Arabic-named mothers in California after the attacks of 11 September 2001 that occurred across the country in New York City lends plausibility to the view that social identity threats can affect co-ethnics at remote distances.

LBW risk increased most among Latina mothers with lower educational attainment (less than high school for the foreign-born and less than college for the USA-born). This could be because low-educated mothers were more vulnerable to the economic and psychosocial fallout of the raid or had fewer coping resources. Reports from throughout Iowa after the Postville raid include evidence of individuals and families preparing for the possibility of further immigration enforcement,^{37,60–62} avoiding public space,^{60,63} restricting spending,^{63,64} losing income or economic security

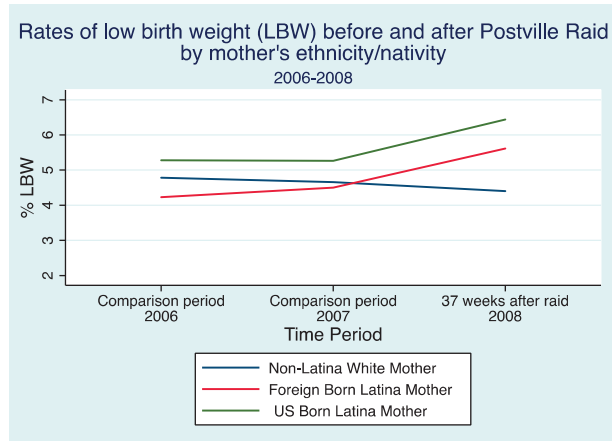


Figure 1. Descriptive graph: rates of low birthweight (LBW) in the 37 weeks following the Postville raid compared with the same time period 1 and 2 years earlier.

Table 2. Modified Poisson regression results for risk of LBW by time period of birth (before/after Postville raid) and mother's ethnicity (White/Latina) ($n = 52\ 344$)

	Before raid		After raid		RR (95% CI); P for after raid vs before within strata of ethnicity
	N LBW/non	RR (95% CI); P	N LBW/non	RR (95% CI); P	
White mother	1112/22 766	1.0 (Reference)	1029/22 350	0.95 (0.87, 1.03); $P = 0.18$	0.95 (0.87, 1.03); $P = 0.18$
Latina mother	118/2369	1.02 (0.84, 1.23); $P = 0.84$	153/2447	1.31 (1.02, 1.68); $P = 0.03$	1.24 (0.98, 1.57); $P = 0.07$

Measure of effect modification on additive scale: RERI (95% CI) = 0.30 (0.03, 0.57); $P = 0.03$.

Measure of effect modification on multiplicative scale: ratio of RRs (95% CI): 1.31 (1.02, 1.68); $P = 0.03$. RRs and measures of effect modification are unadjusted.

Table 3. Modified Poisson regression results for risk of LBW by time period of birth (before/after Postville raid) and mother's ethnicity/nativity (White/foreign-born Latina/USA-born Latina) ($n = 52\ 344$)

	Before raid		After raid		RR (95% CI); P for after raid vs before within strata of ethnicity
	N BW/non	RR (95% CI); P	N LBW/non	RR (95% CI); P	
White mother	1112/22 766	1.0 (Reference)	1029/22 350	0.95 (0.87, 1.03); $P = 0.18$	0.95 (0.87, 1.03); $P = 0.18$
Foreign-born Latina mother	76/1613	0.97 (0.77, 1.21); $P = 0.77$	98/1648	1.32 (0.97, 1.79); $P = 0.07$	1.25 (0.93, 1.67); $P = 0.14$
USA-born Latina mother	42/756	1.13 (0.84, 1.53); $P = 0.42$	55/799	1.29 (0.87, 1.93); $P = 0.20$	1.22 (0.83, 1.81); $P = 0.31$

Measure of effect modification on additive scale: RERI (95% CI) = 0.29 (−0.03, 0.62); $P = 0.07$ (for Foreign-born Latinas), 0.31 (−0.18, 0.80); $P = 0.22$ (for USA-born Latinas).

Measure of effect modification on multiplicative scale: ratio of RRs (95% CI) = 1.32 (0.97, 1.79); $P = 0.07$ (for Foreign-born Latinas), 1.29 (0.87, 1.93); $P = 0.20$ (for USA-born Latinas). RRs and measures of effect modification are unadjusted.

Table 4. Multinomial logistic regression results, categories of gestational age at birth in 37 weeks following the Postville raid compared with same period 1 year earlier, by maternal ethnicity ($n = 52\,344$)

Gestational age at birth	White ($n = 47\,907$) RR (95% CI); P	Latina ($n = 5149$) RR (95% CI); P
Full-term (reference) (39+ weeks)	1.00	1.00
Early-term (37–38 weeks)	0.91 (0.87, 0.95); $P < 0.01$	0.92 (0.81, 1.04); $P = 0.20$
Moderate-preterm (32–36 weeks)	0.97 (0.90, 1.04); $P = 0.39$	1.11 (0.89, 1.38); $P = 0.34$
Very-preterm (<32 weeks)	0.96 (0.79, 1.17); $P = 0.70$	0.81 (0.46, 1.41); $P = 0.45$

Table 5. Modified Poisson regression results for risk of LBW by time period of birth (before/after Postville raid) and mother's ethnicity (White/Latina), stratified by stage of gestation at time of Postville raid ($n = 52\,344$)

Stage of gestation at time of Postville raid	White mothers	Latina mothers	Measures of effect modification	
	RR (95% CI); P	RR (95% CI); P	Ratio of RRs (95% CI); P	RERI (95% CI); P
Not yet conceived ($n = 359$)	1.12 (0.93, 1.35); $P = 0.24$	1.03 (0.65, 1.63); $P = 0.89$	0.92 (0.56, 1.52); $P = 0.75$	-0.08 (-0.70, 0.54); $P = 0.81$
First trimester ($n = 14\,302$)	0.89 (0.78, 1.02); $P = 0.10$	1.39 (0.97, 1.98); $P = 0.07$	1.55 (1.06, 2.27); $P = 0.02$	0.49 (0.07, 0.92); $P = 0.02$
Second trimester ($n = 23\,355$)	0.98 (0.87, 1.11); $P = 0.75$	1.12 (0.79, 1.59); $P = 0.54$	1.14 (0.79, 1.65); $P = 0.49$	0.14 (-0.26, 0.55); $P = 0.49$
Third trimester ($n = 14\,687$)	1.00 (0.81, 1.23); $P = 0.98$	1.12 (0.58, 2.13); $P = 0.74$	1.12 (0.58, 2.16); $P = 0.74$	0.12 (-0.58, 0.81); $P = 0.74$

Table 6. Modified Poisson regression results for risk of LBW by time period of birth (before/after Postville raid) and mother's ethnicity and nativity, stratified by approximate within-group tertiles of education ($n = 52\,344$)

Non-Latina White mothers		Foreign-born Latina mothers		USA-born Latina mothers	
$(n = 47\,257)$		$(n = 3435)$		$(n = 1652)$	
Within-group tertiles of education (n)	RR for birth after Postville raid	Within-group tertiles of education (n)	RR for birth after Postville raid	Within-group tertiles of education (n)	RR for birth after Postville raid
High-school diploma ($n = 14\,334$)	0.95 (0.83, 1.08)	Less than 8th grade ($n = 1165$)	1.42 (0.90, 2.25)	Less than high school ($n = 591$)	1.18 (0.68, 2.06)
Associate's degree or some college ($n = 18\,261$)	0.98 (0.86, 1.12)	Some high school ($n = 1232$)	1.40 (0.84, 2.35)	High-school diploma ($n = 511$)	1.48 (0.78, 2.83)
College diploma or higher ($n = 14\,662$)	0.91 (0.76, 1.09)	High school or greater ($n = 1038$)	0.89 (0.51, 1.57)	Some college or greater ($n = 550$)	0.90 (0.32, 2.54)

due to changing employment practices^{62,65–68} and experiencing increased discrimination, stereotype threat or racialized exclusion as public discourse frequently conflated Latino/Hispanic phenotype with undocumented status.^{35,65} These reports align with findings from a recent quasi-experimental study in Michigan: after a local immigration raid led to several arrests and deportations, Latinos were more likely to report that they feared the consequences of deportation, and that their immigration status impeded social relationships.¹⁵ In the wake of the Postville

raid, similar restrictions in social support and increases in day-to-day fear may have coalesced to increase psychosocial stress and reduce coping resources among Latino immigrants and USA-born co-ethnics. Following the raid, Latino Iowans likened the experience to a flood or earthquake, reflecting the profound impact of this stressor on their lives and on their health.^{69,70}

Quantile regression indicated that the higher risk of LBW among Latina mothers after Postville resulted from decreased birthweight at the left tail of the distribution,

not a shift in mean birthweight. This is similar to Lauderdale's findings for ethnicity-specific change in birthweight after 9/11.⁷¹ Lower birthweights at the left tail of the birthweight distribution are more likely to be associated with infant mortality than a leftward shift of the entire distribution.^{71,72}

Post-raid increases in LBW risk were greatest for Latina mothers in the first trimester of gestation at the time of the raid. Several other studies have also found stronger effects among first-trimester exposures,^{27,29,30,73} but others have not.^{31,33,53,54} Our finding in Iowa could suggest that early-gestation infants were more vulnerable, or it may be that those infants were simply exposed to the post-raid environment for a larger proportion of gestation.

Several complex immune, inflammatory and endocrine pathways are proposed to link psychosocial stressors and birthweight. One hypothesis is that maternal psychosocial stress disrupts the balance between maternal glucocorticoid levels and 11 beta-hydroxysteroid dehydrogenase type 2 (HSD2), an enzyme that metabolizes cortisol into inactive cortisone.^{74,75} Placental HSD2 typically up-regulates in tandem with serum glucocorticoid levels during gestation, protecting the fetus from 80–90% of circulating maternal glucocorticoids.⁷⁶ However, psychosocial stress and disruption of maternal emotional support have been linked to both higher prenatal glucocorticoid concentrations and lower placental HSD2,^{75,77–79} both of which are linked to LBW.^{76,80–84} The psychosocial, economic, communal and identity-based stressors activated by the Postville raid may have interfered with Latina mothers' neuroendocrine balance and coping resources, leaving infants vulnerable to a dysregulated endocrine environment.

Limitations

If healthy pregnant Latinas left Iowa after Postville, increased LBW among Latinas might reflect selection effects. However, analysing Census data,⁸⁵ we found no evidence that the raid was associated with a change in the size of Iowa's Latino population, overall or among women of reproductive age. And, as noted, we found no difference in demographic characteristics among Latina mothers before or after the raid.

There is random year-to-year variation in LBW prevalence, especially in small populations, which raises concerns that the observed increase in LBW among Latina mothers was a chance finding. We do not have access to birth microdata pre-2006, but we used publicly available data⁵⁶ to calculate crude LBW prevalences among singleton births to non-Hispanic White and Hispanic mothers during May–January for the 5 years preceding and following the raid. LBW prevalence among infants born to Hispanic mothers is higher from May 2008 to January

2009 than in any other May–January period from 2003 to 2013 ([Supplementary Figure 1](#), available as [Supplementary data](#) at *IJE* online).

Birth-certificate data for birthweight, maternal ethnicity and maternal birthplace have high validity relative to medical records.^{86–89} However, data on GA are of lower quality,⁸⁶ particularly for Latina and non-English-proficient mothers,^{39,41} which affects our classification of PTB and stage of gestation at the time of the raid. We used a data-cleaning algorithm to mitigate data-quality issues, but this entails several assumptions⁹⁰ and, whereas it is unlikely that remaining misclassification of GA differs by raid timing, even non-differential misclassification may have biased findings for PTB and stage of gestation towards the null. Birth-certificate data for our hypothesized mediators, prenatal smoking and prenatal care are also of lower quality,^{86–88} which reduces our ability to observe mediation by changed health behaviours.

Conclusions

Our findings are consistent with studies observing changes in adverse birth outcomes after a major population-level stressor^{28,30,53,71} and contribute to literature on racialized stressors and ethnicity-specific birth outcomes.^{32,71} We extend the literature on immigration policy/enforcement and health by specifically examining a physical outcome and by examining both immigrant and USA-born Latinos.

The Postville raid was an extreme example of diffuse and pervasive racialized economic and psychosocial stressors that Latinos face throughout the USA. The scale and temporality of this event created conditions that lend insight into the pervasive effects of these stressors, which are often difficult to measure. Exclusive immigration policies and their militarized enforcement exacerbate the racialized exclusion of Latinos in the USA, which may contribute to a cumulative health burden for immigrant and USA-born Latinos alike.

Supplementary Data

[Supplementary data](#) are available at *IJE* online.

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Exhibit F

SCIENCE AND SOCIETY

Stress-induced immune dysfunction: implications for health

Ronald Glaser and Janice K. Kiecolt-Glaser

Abstract | Folk wisdom has long suggested that stressful events take a toll on health. The field of psychoneuroimmunology (PNI) is now providing key mechanistic evidence about the ways in which stressors — and the negative emotions that they generate — can be translated into physiological changes. PNI researchers have used animal and human models to learn how the immune system communicates bidirectionally with the central nervous and endocrine systems and how these interactions impact on health.

The central nervous system (CNS), the endocrine system and the immune system are complex systems that interact with each other. Various stressors — from parachute jumping to academic examinations to bereavement — can dysregulate the immune response by affecting the interplay of these systems. Psychoneuroimmunology (PNI) is the broad interdisciplinary research field that addresses the interactions of these three systems^{1,2}. Studies undertaken during the past two decades have provided evidence that immune alterations that are stimulated by stressful events, ranging from commonplace daily hassles to chronic calamities, can provoke health changes. One definition of a stressor is a stimulus that activates the hypothalamic–pituitary–adrenal (HPA) axis and/or the sympathetic nervous system (SNS) to help an organism to adapt physiologically to deal with a threat³. More broadly, psychological stress ensues when events or environmental demands exceed an individual's perceived

ability to cope⁴. Researchers often categorize stressors by their duration and course (discrete versus continuous)⁵ (BOX 1). For example, chronic stressors, such as suffering a traumatic injury that leads to physical disability, can force people to restructure key aspects of their daily lives. Whereas chronic stressors are deleterious to immune function, some investigators have suggested that very brief stressors, lasting less than 2 hours, might enhance some aspects of immune function, such as trafficking of cells from lymphoid organs to the peripheral blood and the skin (BOX 2).

Stressors can increase susceptibility to infectious agents, influence the severity of infectious disease, diminish the strength of immune responses to vaccines, reactivate latent herpesviruses and slow wound healing. Moreover, stressful events and the distress that they evoke can also substantially increase the production of pro-inflammatory cytokines that are associated with a spectrum of age-related diseases. Accordingly, stress-related immune dysregulation might be one core mechanism behind a diverse set of health risks^{1,3}.

CNS–immune–endocrine interactions

Modulation of the immune response by the CNS is mediated by a complex network of bidirectional signals between the nervous, endocrine and immune systems (FIG. 1). The HPA axis and the autonomic nervous system provide two key pathways for immune-system dysregulation: stressors can activate the sympathetic–adrenal–medullary (SAM) axis, as well as the HPA axis, and thereby provoke the release of pituitary and adrenal

Box 1 | How is stress assessed?

When events or environmental demands exceed an individual's ability to cope, the ensuing psychological stress response typically includes negative thoughts and emotions⁴. Studies of stress and immunity often use measures of negative mood that assess symptoms of general distress, anxiety or depression. Researchers might also assess the number and type of recent significant stressful life changes, or they might ask participants to rate their perceptions of stress on a scale by answering certain questions, such as how frequently in the past week did you feel you could not control important things in your life, or how often did you feel that things were piling up so high that you could not overcome them⁴.

In addition, researchers often study the psychological and immunological responses of individuals who are experiencing a distress-generating event (for example, students taking an examination or spouses going through a divorce) or a more chronic stressor (such as caring for a husband or wife who has Alzheimer's disease)⁵. Other longer-term stressors that are associated with immune alterations have included 'burnout' at work, job strain, unemployment, and isolation and exposure to the hostile climate of Antarctica⁸¹. Adverse immunological changes have also been documented for weeks or months following such natural disasters as earthquakes and hurricanes, with more persistent immune dysregulation among those who suffered greater personal losses⁸². Stressors that are perceived as unpredictable and/or uncontrollable might continue to be associated with increased levels of stress hormones, even after repeated exposures⁸³. The ability to 'unwind' after stressful events — that is, to return to one's neuroendocrine baseline in a relatively short time — is thought to influence the total burden that stressors place on an individual⁸⁴.

hormones. For example, the catecholamines (adrenaline and noradrenaline), adrenocorticotrophic hormone (ACTH), cortisol, growth hormone and prolactin are all influenced by negative events and negative emotions (BOX 1), and each of these hormones can induce quantitative and qualitative changes in immune function. Furthermore, depression can substantially boost cortisol levels, and increases in cortisol levels can provoke multiple adverse immunological changes.

Almost all immune cells have receptors for one or more of the hormones that are associated with the HPA and SAM axes; these are called 'stress' hormones (TABLE 1). Immune modulation by these hormones might proceed through two pathways: directly, through binding of the hormone to its cognate receptor at the surface of a cell; or indirectly — for example, by inducing dysregulation of the production of cytokines, such as interferon- γ (IFN- γ), interleukin-1 (IL-1), IL-2, IL-6 and tumour-necrosis factor (TNF). Cytokines such as IFN- γ have many functions and affect different target cells. Therefore, there are secondary effects of many stress hormones on the immune response^{6,7}.

Moreover, communication between the CNS and the immune system is bidirectional. For example, IL-1 influences the production of corticotropin-releasing hormone (CRH) by the hypothalamus. In turn, CRH can affect the HPA axis and thereby trigger increases in stress hormone levels, which results in dysregulation of immune function (FIG. 1). In addition, lymphocytes can synthesize hormones such as ACTH, prolactin and growth hormone⁸. The role of lymphocyte-derived hormones in immune responses is not well understood, although they might have a role in modulating cell function within the microenvironment of lymphoid organs. Furthermore, studies that show nerve fibres in the spleen and thymus provide evidence of direct connections or 'hard-wiring' between the SNS and lymphoid organs⁹. Therefore, there are many pathways through which stressors might influence immune function^{1,6}. Moreover, many individuals working in the field of PNI are now focusing their efforts on immune-system-to-brain communication and how the activation of inflammatory-cytokine networks might shape mood, cognition and behaviour^{10,11}.

In addition to the direct influences of psychological states on endocrine and immune function, stressed individuals are more likely to have health habits that put them at greater risk, including poorer sleep patterns, poorer nutrition, less exercising and a greater propensity for abuse of alcohol, cigarettes and other

Box 2 | Can stress be beneficial?

The best evidence that stress might be good for the immune system comes from studies of mice that are exposed to very brief stressors. Delayed-type-hypersensitivity skin responses following either primary or secondary cutaneous antigen exposure were augmented following stressors lasting 2 hours, compared with the response of non-stressed control animals. These effects seem to be mediated by glucocorticoid- and adrenaline-induced stress responses⁸⁵. It has been argued that such immunoenhancement would be beneficial to survival, because skin wounding and infection can result from brief aggressive encounters in nature⁸⁵. In humans, short-term stressors, such as public speaking, briefly increase natural-killer-cell activity^{5,86} and increase the numbers of some types of leukocyte⁵. The latter change probably reflects transient alterations in lymphocyte migration from lymphoid organs and peripheral blood, which is mediated by receptors at the cell surface of lymphocytes (TABLE 1) or through sympathetic-nervous-system innervation of lymphoid organs such as the spleen⁹. However, the same short-term stressors also produce transitory changes in humans that would generally be seen as maladaptive: they reduce lymphocyte proliferation⁵, increase pro-inflammatory cytokine production⁸⁶ and impair the ability of the skin to repair abrasions⁸⁶. Further studies need to be carried out to help to clarify health outcomes that are associated with short-term acute stressors.

drugs. Although these health behaviours have immune and endocrine consequences, these indirect effects of stress are not addressed here; we focus on immune dysregulation by stressors and the health consequences of these changes.

Stress and infectious-disease risks

Stressors can enhance the risk of developing infectious disease, and they can also prolong infectious illness episodes. For the mouse models used to explore this relationship, restraint is a commonly used stressor. Mice are placed in tubes such that they can move forwards or backwards but cannot turn around; holes in the tubes ensure that the mice do not overheat. Restraint is often applied overnight, because this is the most active time for mice. One example of data obtained using a mouse model of influenza-virus infection shows that restraint stress altered the immune response to the virus, including the kinetics of the antibody response and suppression of both pro-inflammatory and anti-inflammatory cytokine responses^{12,13}. Mononuclear-cell trafficking to virus-infected lungs was significantly reduced in stressed animals, as was the size of the draining lymph nodes. Virus-specific cytokine responses of T cells in restraint-stressed mice were restored in the draining lymph nodes by pharmacological blockade of the glucocorticoid receptor with the glucocorticoid receptor antagonist RU486. These and related studies have shown that the HPA axis and the SNS are the main immunoregulatory pathways that can influence the pathophysiology of a viral infection^{12,13}.

Consistent with the mouse data on stress and influenza-virus infections, influenza-virus vaccine studies with human participants show that stress can influence infectious-disease

risks. For example, men and women who were chronically stressed by caring for a spouse with dementia showed clear deficits in both their cellular and humoral immune responses to an influenza-virus vaccine compared with well-matched control individuals who were not carers^{14,15}. The protective capacity of antiviral vaccines depends on their ability to induce both humoral and cell-mediated immune responses¹⁶, both of which were poorer in the stressed carers compared with control individuals. Stress-associated impairments in antibody responses after vaccination with influenza virus have also been shown in younger adults¹⁷.

Further studies have confirmed the finding that stressful events and the negative emotions, such as anxiety and depression, that accompany them can modulate the antibody and T-cell responses to other antiviral vaccines, including the vaccines against infection with hepatitis B virus and rubella virus^{18,19}. Moreover, antibody responses to antibacterial vaccines are also influenced by stress: for example, following vaccination, antibody titres to a pneumococcal vaccine decreased during a 6-month period in the carers of spouses with dementia, whereas antibody titres were stable in non-carers²⁰. Similarly, undergraduates who had received a meningitis C conjugate vaccine and who reported greater stress had a poorer antibody response 1–12 months after vaccination²¹.

Responses to vaccines show clinically relevant alterations in immunological responses to challenge under well-controlled conditions; accordingly, they function as a proxy for a response to an infectious agent. Individuals who were more distressed and more anxious had immune responses to vaccines that were delayed, substantially weaker and/or shorter-lived. As a consequence, it is reasonable to

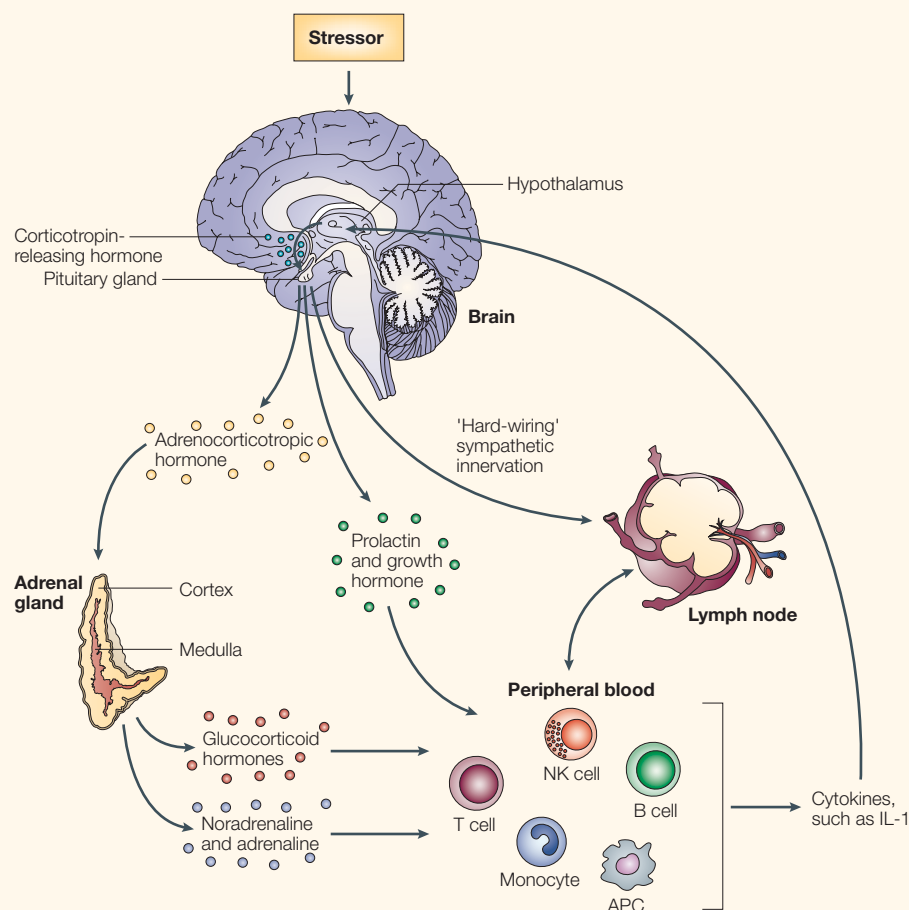


Figure 1 | Stress-associated modulation of the hormone response by the central nervous system. Experiencing a stressful situation, as perceived by the brain, results in the stimulation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic–adrenal–medullary (SAM) axis. The production of adrenocorticotropic hormone by the pituitary gland results in the production of glucocorticoid hormones. The SAM axis can be activated by stimulation of the adrenal medulla to produce the catecholamines adrenaline and noradrenaline, as well as by ‘hard-wiring’, through sympathetic-nervous-system innervation of lymphoid organs. Leukocytes have receptors for stress hormones that are produced by the pituitary and adrenal glands and can be modulated by the binding of these hormones to their respective receptors. In addition, noradrenaline produced at nerve endings can also modulate immune-cell function by binding its receptor at the surface of cells within lymphoid organs. These interactions are bidirectional in that cytokines produced by immune cells can modulate the activity of the hypothalamus. APC, antigen-presenting cell; IL-1, interleukin-1; NK, natural killer.

assume that these same individuals would also be slower to develop immune responses to pathogens; therefore, they could be at greater risk of developing more severe illness. Consistent with this argument, adults who show poorer responses to vaccines also experience higher rates of clinical illness²².

In agreement with these vaccine studies, researchers have also shown that distress can alter an individual's susceptibility to infection with respiratory viruses^{4,23,24}. In a group of 394 healthy volunteers who were inoculated with one of five strains of respiratory virus, severity of both respiratory infection and clinical cold symptoms increased in a dose–response relationship as scores increased on a psychological stress index. The stress index was a

compilation of three common measures: the number of stressful life events, the degree that a participant felt that current demands exceeded his or her ability to cope, and scores from a negative-emotion word list (including words such as sad, angry and nervous). Importantly, the risk did not differ across the five strains of respiratory virus studied. In further related work from the same laboratory, stressors that lasted for 1 month or more were the best predictors of developing colds; volunteers who reported more enduring interpersonal difficulties with family or friends were substantially more likely to develop a cold after inoculation with a rhinovirus²³. Similarly, other researchers reported that individuals who

developed cold symptoms following inoculation with rhinovirus had higher numbers of recent stressful life events than those who did not²⁴.

Studies carried out with human participants in which individuals have been exposed to a pathogen or a vaccine give researchers a means of controlling exposure and dosage; moreover, because immune function can be assessed before the infectious challenge, these studies provide excellent data on causality, thereby complementing evidence from research that addresses the course of naturally occurring infections^{25–35}. The similarity of the data from human and rodent studies provides strong evidence that stress can dysregulate the humoral and cellular immune responses to pathogens and increase the risk of developing infectious disease.

HIV and the herpesviruses are different from many other viruses, such as rhinoviruses and influenza virus, in that they remain in a latent state in the body after primary infection. To investigate the possibility that social stress was a contributor to the rate of progression in HIV-associated disease, rhesus macaques were inoculated with simian immunodeficiency virus (SIV)³⁶. Animals that were assigned to the stable social condition (the same three animals met every day) had lower concentrations of SIV RNA in plasma early after inoculation and survived longer than those in the unstable social condition (different two-, three- and four-member groups were formed every day).

Studies of HIV-infected men have also indicated that stress increases the rate of disease progression. For example, in a longitudinal study of HIV-positive men who were asymptomatic at entry to the study, faster progression to AIDS was associated with more stressful life events and less social or interpersonal support²⁵; indeed, at 5.5 years after entry into the study, the probability of developing AIDS was two- to threefold higher in men who were above the median level for stress or below the median level for support compared with those who were below the median level for stress or above the median level for support. Other researchers reported that the course of HIV infection was accelerated in gay men who concealed their homosexual identity compared with men who did not²⁶.

Considerable anecdotal evidence has supported the relationship between psychological stress and the development, duration and recurrence of herpesvirus infections. The cellular immune response has an important role in controlling the pathophysiology of both lytic herpesvirus infections and the expression

Table 1 | Interactions of hormones and immune cells

Hormone	Expression of receptors by immune cells	Examples of effects on cell function	References
Glucocorticoids	T and B cells, neutrophils, monocytes and macrophages	Inhibit inflammation; inhibit the production of IL-12 by antigen-presenting cells; induce a shift from production of T _H 1 to T _H 2 cytokines	87,88
Substance P	T and B cells, eosinophils, mast cells, monocytes and macrophages	Stimulates mitogen-induced blastogenesis; increases trafficking of cells from lymph nodes to peripheral blood; stimulates monocytes to produce several cytokines, such as IL-1, IL-6 and TNF	89
Neuropeptide Y	T and B cells, dendritic cells, monocytes and macrophages	Can downregulate antibody production to T-cell-dependent antigens by its effect on dendritic cells, and T and B cells	90
Corticotropin-releasing hormone	T cells, monocytes and macrophages	Increases production of IL-1 by monocytes; evidence for autocrine and/or paracrine modulation of inflammation	91
Prolactin	T and B cells, granulocytes, NK cells, monocytes and macrophages	Can stimulate lymphoid-cell clonal expansion; might function as an <i>in vitro</i> co-mitogen for NK cells and macrophages	92,93
Growth hormone	T and B cells, NK cells, monocytes and macrophages	Helps to maintain competence of T and B cells, and macrophages; stimulates antibody production and NK-cell activity	94
Catecholamines (adrenaline and noradrenaline)	T and B cells, NK cells, monocytes and macrophages	Induce a shift to a T _H 2 response, involving antigen-presenting cells and T _H 1 cells	95
Serotonin	T and B cells, NK cells, monocytes and macrophages	Modulates the synthesis of IFN- γ by NK cells; stimulates the production of IL-16 (a chemotactic factor) by T cells	96

IFN- γ , interferon- γ ; IL, interleukin; NK, natural killer; T_H, T helper; TNF, tumour-necrosis factor.

and/or replication of latent herpesviruses. When the cellular immune response is impaired, one or more herpesviruses can be reactivated, and herpesvirus infections are often more severe.

Herpes simplex virus (HSV) is a natural human pathogen that is characterized by its ability to cause an acute infection at a peripheral site and to establish a latent infection in the local sensory ganglia, and stress can exacerbate HSV lytic infection. Mouse models have been developed to study the effect of stress on the pathophysiology of HSV latent and lytic infections. Indeed, several studies carried out during the past 15 years have provided compelling experimental evidence that stress not only increases the development and severity of HSV infection, in both the peripheral nervous system^{13,37–39} and the CNS, but also suppresses components of primary^{13,37,39–41} and memory^{13,38,41} cytotoxic T lymphocyte (CTL) responses to HSV infection.

Surgical and pharmacological approaches have shown the ability of both the HPA¹³ and the SAM⁴¹ axes to mediate stress-induced

modulation of immunity and HSV-associated pathology. For example, mice treated with 6-hydroxydopamine (6-OHDA) to induce peripheral sympathetic denervation were inhibited in their ability to generate primary HSV-1-specific CTLs when infected with the virus⁴¹. The suppression of CTL production could result from a large release of noradrenaline induced by 6-OHDA and increased levels of corticosterone. In another study, surgical removal of the adrenal gland blocked the suppression of HSV-1-specific CTLs that was induced by restraint stress and also blocked the production of IL-6 and IFN- γ ¹³.

Relationships between neuroendocrine activity, immune function and latent HSV reactivation have also been documented^{42,43}; infected mice that were exposed to a stressor showed reactivation of the latent virus, whereas non-stressed controls showed no reactivation⁴³. It is important to keep in mind that these experiments were carried out using mice in a laboratory setting; however, the data still provide some insight into how stress

could modulate the immune response to HSV in humans.

Indeed, psychological stressors have been linked to more frequent recurrences of lesions in individuals who are latently infected with HSV-1 or HSV-2. For example, women who reported greater persistent stress from events that lasted longer than 1 week also had more recurrences of genital herpes²⁸. Similarly, more chronically distressed individuals had more frequent recurrences of re-activation of HSV-1 (REF 29) and HSV-2 (REF 30).

The incidence of Herpes zoster (also known as shingles), which is caused by the reactivation of latent varicella-zoster virus (VZV), increases with age, presumably owing to a decline in cell-mediated immunity to VZV⁴⁴. A case-control study indicated that psychological stress in healthy community-dwelling older adults was associated with the occurrence of herpes zoster³¹. Other researchers evaluated the possibility that VZV-specific immunity could be altered by means of a behavioural intervention, such as T'ai chi (also known as 'meditation through movement')⁴⁴. Older adults who

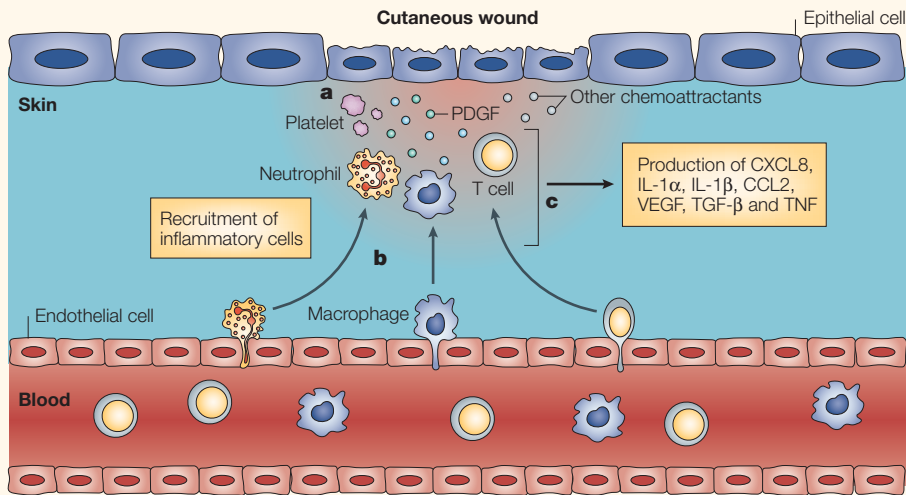


Figure 2 | Influence of stress on pro-inflammatory cytokine responses in wound healing. Stress can influence key pro-inflammatory cytokine responses in the early phase (the first 24 hours) of the healing of skin wounds, through dysregulation of cytokine secretion at the wound site and recruitment and activation of circulating peripheral-blood leukocytes that traffic to the wound site^{48,52,54}. Using a skin wound as an example, blood platelets at the wound site produce platelet-derived growth factors (PDGFs) (a). Other chemoattractants are also produced by activated parenchymal cells. A concentration gradient is established, with higher levels of chemoattractants at the wound site attracting immune cells, such as neutrophils and macrophages. These cells have important roles in the early phases of wound healing. For example, neutrophils clean the area of bacteria and, together with activated macrophages, they phagocytose the bacteria and produce cytokines that stimulate the growth of fibroblasts. The leukocytes transmigrate through the endothelium of the blood-vessel wall to the wound site in the skin (b) and are activated to proliferate and produce cytokines and chemokines, such as CXC-chemokine ligand 8 (CXCL8; also known as IL-8), IL-1 α , IL-1 β , transforming growth factor- β (TGF- β), vascular endothelial growth factor (VEGF), CC-chemokine ligand 2 (CCL2; also known as MCP1) and tumour-necrosis factor (TNF), at the wound site (c). These cytokines continue to function as chemoattractants for the continued migration of cells to the site. The proliferative phase of wound healing involves the recruitment and replication of cells that are required for tissue regeneration and capillary growth. Therefore, the downregulation of the early inflammatory response by an increase in serum cortisol levels can help to explain how stress affects wound healing⁴⁹.

were randomly assigned to Tai chi showed a 50% increase in VZV-specific cellular immunity between the start and the end of the 15-week intervention compared with no change in the 'waiting-list' control group.

Epstein-Barr virus (EBV) — the aetiological agent of infectious mononucleosis — is another herpesvirus that establishes latent infection and can be modulated by psychological stressors. In one early study, West Point Military Academy (New York, United States) cadets who were seronegative for EBV on entry into the academy were followed for 4 years²⁷. Men with particular psychosocial risk factors (high motivation for a military career in the face of poorer academic performance) were more likely to develop infectious mononucleosis and were likely to be hospitalized for longer periods. In addition, these risk factors were also associated with increased EBV-specific antibody titres in cadets who had been infected with EBV but had not developed obvious clinical symptoms.

A series of studies provided mechanistic data that revealed the effect of stress on EBV

latency. Medical students had substantially higher titres of IgG specific for EBV capsid antigen, and these were associated with more stressful examination periods compared with lower-stress periods⁴⁵. In a further study of medical students, examination stress produced a significant decrease in the ability of EBV-specific CTLs to kill EBV-infected autologous B cells⁴⁵. The results of several studies have shown that various psychological stressors — including examination stress, caring for a spouse with dementia and spaceflights by astronauts — can reactivate latent EBV and cytomegalovirus (CMV)^{32–35,45}. Together, these human and animal studies show that stress can modulate the steady-state expression of latent HSV, EBV and CMV, downregulating the specific T-cell response to the virus to an extent that is sufficient to result in viral reactivation. Although the mechanisms that underlie stress-associated reactivation of latent herpesviruses are not fully understood, *in vitro* studies of cells that are latently infected with EBV have shown that glucocorticoid hormones can reactivate the virus.

For example, a glucocorticoid hormone, dexamethasone, can reactivate latent EBV and enhance the lytic replication of the virus in EBV-superinfected cells *in vitro*, but the catecholamine hormones do not induce such a response. Other stress hormones — CRH and ACTH — cannot induce reactivation of latent EBV, but they can enhance lytic replication in EBV-superinfected cells⁴⁶.

Different types of stressor can have different effects on reactivation of latent HSV-1 and EBV^{43,47}. For example, although restraint-stressed mice did not show evidence of reactivation of latent HSV-1, infectious HSV-1 was isolated from approximately 50% of the mice that were subjected to social reorganizational stress, despite both stressors resulting in similar increases in serum corticosterone levels⁴³. Data from studies of students at West Point Military Academy also showed that different types of stress could have an impact on the reactivation of latent HSV-1 and EBV⁴⁷. The mechanisms underlying these differences are not understood, but clearly, a factor as obvious as disparities in glucocorticoid hormone levels is not sufficient to explain variations in viral reactivation. Together, these studies highlight the complex interactions that underlie the relationships between stress, neuroendocrine activity, immune function and herpesvirus pathogenesis, and they indicate the many ways in which these relationships are central to a lifelong defence against herpesvirus infections.

Stress and wound healing

Wound repair progresses through several overlapping stages⁴⁸. In the initial inflammatory stage, vasoconstriction and blood coagulation are followed by platelet activation and the release of platelet-derived growth factors (PDGFs), as well as the release of chemoattractant factors by injured parenchymal cells. Cytokines and chemokines — such as IL-1 α , IL-1 β , transforming growth factor- β (TGF- β), vascular endothelial growth factor (VEGF), TNF and CXC-chemokine ligand 8 (CXCL8; also known as IL-8) — are important in the early stages of wound healing. These factors function as chemoattractants, promoting the migration of phagocytes and other cells to the wound site, thereby starting the proliferative phase, which involves the recruitment and replication of cells that are required for tissue regeneration and capillary regrowth. The final step, wound remodelling, might continue for weeks or months. So, the healing process is a cascade, and success in the later stages of wound repair depends to a large extent on initial events⁴⁸.

Immune function has a key role in the early stages of this cascade (FIG. 2). CXCL8 and pro-inflammatory cytokines, such as IL-1 and TNF, are essential to this effort; they help to protect against infection and prepare injured tissue for repair by enhancing the recruitment and activation of phagocytes⁴⁹. Furthermore, cytokines that are released by recruited cells regulate the ability of fibroblasts and epithelial cells to remodel the damaged tissue⁴⁹. IL-1 that is produced early after tissue injury can regulate the production, release and activation of metalloproteinases that are important in the destruction and remodelling of the wound. IL-1 also regulates fibroblast chemotaxis and the production of collagen⁴⁹. Moreover, IL-1 stimulates the production of other cytokines that are important for wound healing, including IL-2, IL-6 and CXCL8 (REF. 49). Accordingly, IL-1 deficits early in the wound-repair cascade can have adverse consequences downstream.

Stress disrupts the production of pro-inflammatory cytokines that are important for wound healing, a mechanism that produces substantial delays in wound repair. For example, in a clinical study, women who were experiencing the long-term stress of caring for a relative with Alzheimer's disease took 24% longer than sociodemographically matched controls to heal a small, standardized dermal wound. Consistent with these differences in wound repair, peripheral-blood leukocytes (PBLs) obtained from carers also produced less IL-1 β in response to lipopolysaccharide (LPS) stimulation⁵⁰. In a subsequent study in a different population, wounds produced in the hard palate 3 days before important examinations healed an average of 40% more slowly than identical wounds made during summer holidays: no student healed as rapidly during examinations as during the holiday period, and no student produced as much IL-1 β when his or her PBLs were stimulated with LPS⁵¹.

Mouse models have also been developed to study the effect of stress on wound healing. These studies have confirmed and extended the data obtained by studying humans. Mice that were subjected to restraint stress and had a standardized 3.5-mm full-thickness cutaneous punch-biopsy wound healed this wound an average of 27% more slowly than control mice⁵². Analysis of the cellularity of wound sites using cross-sections of dermal and epidermal layers showed less leukocyte infiltration of the wound sites in restraint-stressed mice at 1 and 3 days after wounding, compared with controls⁵². Serum corticosterone levels in the restraint-stressed group were more than fourfold higher than those

of control animals⁵². Blocking glucocorticoid receptors in restraint-stressed animals, using RU40555, resulted in healing rates that were similar to those of control animals⁵². Accordingly, these data provide evidence that disruption of neuroendocrine homeostasis modulates the early stages of wound healing.

Higher levels of glucocorticoids have several adverse effects on various components of the wound-healing process. For example, they might slow wound healing by altering local levels of pro-inflammatory cytokines. Hübner *et al.*⁴⁸ showed that the strong and early induction of IL-1 α , IL-1 β and TNF expression at the site after wounding was significantly reduced after pretreatment of mice with glucocorticoids. Similarly, human studies have also shown that stress-induced increases in glucocorticoids can transiently suppress IL-1 β , TNF and PDGF production⁵³. Accordingly, dysregulation of glucocorticoid secretion provides one obvious neuroendocrine pathway through which stress alters wound healing.

In humans, a suction-blister model enabled investigators to measure immune responses that are central to the early stages of wound healing *in vivo* and occur at the wound site, providing key data on the inflammatory response that have direct clinical relevance^{54,55}. The suction-blister model provides an excellent mechanism to study the migration of neutrophils and macrophages and the production of cytokines at wound sites for the first 2 days after wounding. Commonly, after raising several blisters and removing their roofs (the epidermis), plastic templates with wells containing a salt solution and autologous serum are placed over the lesions, and cells migrate to the wound sites and collect in the wells. The serial collection of samples from the wells as time progresses allows for cell phenotyping and cytokine measurement as the local immune response evolves. Using this approach to study stress and wound healing, women who reported more stress produced significantly lower levels of two pro-inflammatory cytokines (IL-1 α and CXCL8) that are important for the early stages of wound healing⁵⁴.

Therefore, convergent data from mouse and human studies have shown that stress has substantial adverse effects on wound repair. In agreement with these laboratory findings, several studies have shown that greater fear or distress before surgery is associated with poorer outcomes, including longer hospitalization, more post-operative complications and higher rates of rehospitalization^{56,57}.

Stress and inflammation

The pro-inflammatory cytokine IL-6, which is produced by T cells, B cells, monocytes and several non-lymphoid cell types, has an important role in the acute-phase response³. IL-6 is an important inducer of C-reactive protein (CRP) by the liver, and the combination of IL-6 and CRP is important in the process that leads to the development of cardiovascular disease^{3,58}. As previously discussed, stress induces immune dysregulation partly through alterations in the production of pro-inflammatory cytokines. Both physical and psychological stressors can provoke transient increases in pro-inflammatory cytokines, particularly in IL-6 (REFS 53,59). In animal models, both stress and administration of adrenaline increase levels of IL-6 in the plasma, which is consistent with evidence that IL-6 production is stimulated by β -adrenergic receptors, as well as through other pathways³.

Importantly, negative emotions, such as depression and anxiety, augment the production of IL-6 (REFS 60–62). Indeed, both stressors and depression can sensitize the inflammatory response, thereby producing heightened responsiveness to subsequent stressful events, as well as to antigen challenge^{59,61–63}. For example, individuals who reported more depressive symptoms showed increases in serum IL-6 levels 2 weeks after vaccination against influenza-virus infection, whereas there was little change in IL-6 levels in those individuals who reported few or no symptoms⁶¹. This is consistent with other evidence of cross-sensitization between cytokines and stressors in human and animal studies^{59,62,63}. These stress-related changes have broad implications for health: increased levels of pro-inflammatory cytokines, such as IL-6, have been linked to various age-related diseases and conditions (including cardiovascular disease, osteoporosis, arthritis, type 2 diabetes, frailty and functional decline) and to certain cancers (such as chronic lymphocytic leukaemia)⁶⁴.

Stress, inflammation and ageing

One recent longitudinal study highlighted the deleterious longer-term immunological consequences of chronic stress: the average annual rate of increase in serum IL-6 was about fourfold higher in men and women who were chronically stressed by caring for a spouse with dementia than in similar individuals who did not have caring responsibilities⁶⁵. Possible consequences of these different trajectories are indicated by epidemiological studies of individuals of 65 years of age or older⁶⁴; within these population studies, individuals whose IL-6 values fell within the highest quartile had

a twofold greater risk of death within the following 4–5 years compared with those whose IL-6 values were in the lowest quartile⁶⁴. Application of the epidemiological risk values to the data from carers indicated that carers would, on average, have values that crossed into the highest quartile around the age of 75, whereas the IL-6 values of control individuals would not reach that level until after the age of 90.

Another recent study also supports the hypothesis that chronic stress might be associated with premature ageing of immune cells. Telomerase activity and telomere length — two cellular markers that are associated with ageing — were measured in peripheral-blood mononuclear cells obtained from mothers caring for a chronically ill child, as well as from mothers of healthy children⁶⁶. Carers reported greater stress than controls, but reports of a higher level of perceived stress were associated with lower telomerase activity and shorter telomere length, regardless of whether the mother's child was ill or healthy. Reports of high stress levels were also associated with higher oxidative-stress activity, as measured by levels of F₂-isoprostanes, another independent measure associated with ageing⁶⁶.

Taken together, the data regarding the IL-6 levels of carers of spouses with dementia⁶⁵ and the data regarding telomerase activity and length⁶⁶ provide evidence of mechanisms through which chronic stressors might accelerate the risk of developing many age-related diseases by 'premature ageing' of the immune response. Indeed, a prospective population-based cohort study found that the relative risk for all-cause mortality over a 4-year period in strained carers was 63% higher than in control individuals who were not carers⁶⁷.

Conclusions and future directions

Great strides have been made in the field of PNI towards understanding some of the interactions between the CNS, endocrine system and immune system, as well towards understanding how distress modulates these three complex systems. Although the mechanisms that underlie these interactions are complex, and although it will probably take many years to fully understand how these three systems interact, there are already clear translational implications from laboratory data.

Herpesvirus infections carry substantial human costs because the latent viruses are linked to considerable pain and suffering. Moreover, the evidence that psychological stressors can reactivate latent herpesviruses might have the most notable implications for

people who are already immunosuppressed (such as patients who have received an organ transplant or patients infected with HIV), owing to the risk of these individuals developing EBV-associated B-cell lymphomas. Indeed, reactivation of latent EBV, HSV-1 and CMV is associated with significant morbidity and mortality of immunosuppressed patients.

Furthermore, on the basis of speculation that chronic inflammation might be a contributing factor in up to 15% of all cancer cases⁶⁸, stress-induced increases in the inflammatory response could be a broader pathway that links stress with cancer. Although it is beyond the scope of this article, the possibility that the physiological changes associated with stress could be key factors in cancer risk and progression has recently been reviewed⁶⁹.

The results of the vaccine studies are particularly important for individuals who might be at a higher risk of developing complications that are associated with respiratory-virus infections, such as older individuals for whom increased susceptibility to pathogens is a serious health problem: together, influenza and pneumonia are the fifth leading cause of mortality in individuals aged 50 or older¹⁶. Biologically, the largest deleterious or enhancing consequences of stress are likely to occur when biological vulnerability is greatest: that is, early and late in life⁷⁰. Older adults seem to show greater immunological impairments associated with distress or depression than younger adults^{14,57}. However, the studies indicate that vaccine efficacy can be compromised by psychological stress, even in younger adults — an important public-health finding in its own right. These studies should be considered in the planning of clinical studies using cancer vaccines. The efficacy of such vaccines will depend on an optimum immune response.

The possibility that stressors might have a long-term impact on the developing endocrine and immune systems of infants and young children is an important question that has not been well studied in the PNI field. Indeed, excellent developmental studies of primates indicate that early stressors can reverberate for the life of an individual⁷⁰.

In accordance with the evidence that stress delays wound healing, more than 200 studies published in the past 3 decades have shown beneficial effects from pre-surgical interventions. These beneficial effects include decreased anxiety and stress reductions when hospitalized, fewer post-operative complications, better treatment compliance, less pain and reduced use of analgesics, and alterations in various physiological indices^{56,57}. Given the substantial consequences of stress for wound

repair, even small reductions in anxiety could have substantial clinical consequences, both directly and indirectly⁵⁷.

More broadly, researchers have used several diverse strategies to modulate immune function, including relaxation, hypnosis, exercise, classical conditioning, self-disclosure and cognitive behavioural interventions. These interventions have generally produced positive endocrine and immune changes^{5,44,71–74}. Although it is not yet clear to what extent these positive immunological changes translate into any concrete improvements in relevant aspects of health, such as alterations in the incidence, severity or duration of infectious and/or malignant disease, the preliminary evidence seems to be promising.

The role that genetics might have in these complex relationships is unknown, and this is an important new area that deserves exploration. For example, do individuals who have one or more variants of the polymorphisms associated with increased production of cortisol show greater immunological dysregulation when faced with stressful events?

Several studies have provided convincing evidence linking stress-induced immune dysregulation with morbidity and mortality. Animal models that involve viral infections have confirmed that stress can exacerbate morbidity that is associated with a viral infection^{37,75–77}. Stress can also exacerbate bacterial infections, such as infections with *Listeria monocytogenes*^{78,79}. In both humans and mice, studies of wound healing show a direct link between stress-associated immune dysregulation and health outcome, with well-documented relationships occurring between stress hormones, the immune response and the rate of wound healing^{50–52,54}. Together, these studies support the hypothesis that morbidity can be directly linked to stress-induced immune dysregulation.

Using a mouse model, it was also shown that stress-induced immune dysregulation can cause mortality⁸⁰. Restraint-stressed mice infected with Theiler's murine encephalomyelitis virus (TMEV) had an increased risk of dying. TMEV is a Picorna virus, which can cause CNS lesions. Higher titres of the virus were observed in the stressed mice compared with the control mice, and the underlying mechanism that accounted for the increased mortality in restraint-stressed mice was related to corticosterone-induced immune suppression.

The field of PNI is improving our understanding of the complex physiological changes that take place in stressful situations and providing new insights into various clinical applications. This research field is

also contributing to our knowledge of how the immune system operates in an environment in which there is bidirectional communication with other bodily systems. Despite the remarkable complexities of the interactions between the CNS, the immune system and the endocrine system, the researchers are making good progress at the molecular, cellular and organ-system levels. And, with that knowledge, the potential for new approaches to treatment is evident.

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Competing interests statement

The authors declare no competing financial interests.

 Online links

DATABASES

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OPINION

Consensual immunity: success-driven development of T-helper-1 and T-helper-2 responses

Pawel Kalinski and Muriel Moser

Abstract | Non-germline-encoded T- and B-cell receptors allow humans to effectively deal with rapidly mutating pathogens. Here, we argue that, in addition to determining the antigenic specificity of immune responses, the same receptor systems can also regulate the T-helper-1/T-helper-2 profile of immunity. Such a mechanism — based on feedback from distinct effector cells to dendritic cells, rather than on instruction from pathogens — uses the effectiveness of particular effector cells at targeting and destroying a pathogen as a reliable, experience-based criterion to induce and maintain the appropriately polarized response.

Distinct subsets of CD4⁺ T cells preferentially support cell-mediated (type 1) versus humoral (type 2) immunity¹. Type 1 T helper (T_H1) cells promote the cytotoxic effector functions of natural killer (NK) cells, CD8⁺ T cells and macrophages. They also promote antibody-dependent cell-mediated cytotoxicity (ADCC) by supporting B-cell production of IgG2a in mice and IgG1 in humans. By

contrast, T_H2 cells promote humoral immunity, mediated by B-cell-produced IgG4 and IgE in humans (and IgG1 and IgE in mice). Although the proper balance of T_H1 and T_H2 immunity is as important for the success of an immune response as its specificity and overall magnitude¹, it still remains unclear how the T_H1/T_H2-response profile is matched to distinct pathogens and to particular affected tissues.

The previously identified ‘instructive’ mechanisms of the induction of T_H1- versus T_H2-dominated responses by dendritic cells (DCs) use germline-encoded receptors to identify both distinct sets of conserved pathogen-specific motifs and endogenous mediators of tissue damage that are induced by different pathogen types invading distinct tissues^{2–6}. Here, we discuss recent evidence for the existence of an additional highly reliable mechanism that assures the correctness of such a match. We propose that the intrinsic ability of different effector cells to discriminate between different pathogen classes and to differentially affect DC functions is a

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Exhibit G

Trauma and Psychological Distress in Latino Citizen Children Following Parental Detention and Deportation

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The mental health impact of parental detention and deportation on citizen children is a topic of increasing concern. Forced parent–child separation and parental loss are potentially traumatic events (PTEs) with adverse effects on children's mental health. **Objective:** This study examines posttraumatic stress disorder (PTSD) symptoms and psychological distress among 91 Latino U.S.-born children (ages 6 to 12), living in mixed-status families with a least 1 undocumented parent at risk for detention or deportation. **Method:** Multiagent (child, parent, teacher, clinician) and standardized assessments were conducted at baseline to assess for child trauma and psychological distress. **Results:** Analyses indicate that PTSD symptoms as reported by parent were significantly higher for children of detained and deported parents compared to citizen children whose parents were either legal permanent residents or undocumented without prior contact with immigration enforcement. Similarly, findings revealed differences in child internalizing problems associated with parental detention and deportation as reported by parent as well as differences in overall child functioning as reported by clinician. In addition, teachers reported higher externalizing for children with more exposure to PTEs. **Conclusions:** These findings lend support to a reconsideration and revision of immigration enforcement practices to take into consideration the best interest of Latino citizen children. Trauma-informed assessments and interventions are recommended for this special population.

Keywords: PTSD, Latino children, citizen children, immigration, deportation, detention

Adverse childhood experiences (Alegría, Green, McLaughlin & Loder, 2015) and immigration status (Castañeda et al., 2015) are important social determinants of mental disorders. In children, potentially traumatic events (PTEs) may lead to the development of posttraumatic stress disorder (PTSD; Finkelhor, Ormrod, & Turner, 2009). PTSD has debilitating effects on child development and functioning and is a costly public health issue (U.S. Department of Health & Human Services, 2003). This study examines the intersection of parental immigration status and children's mental

health. Specifically, we examined U.S.-born Latino children's mental health, including PTSD and psychological distress, following parental detention or deportation.

Children of immigrants represent 25% of the 69.9 million children in the United States (Zong & Batalova, 2015). Over 88% of immigrant-origin children (4.5 million) are U.S.-born with a foreign-born parent (Passel, Cohn, Krogstad, & Gonzalez-Barrera, 2014). Many of these foreign-born parents are unauthorized immigrants at chronic risk of arrest, detention, and/or deportation. Enforcement efforts have taken the form of worksite and home raids that sweep undocumented immigrants from families and communities. From 2002 to 2014, the Office of Immigration Statistics (2013) reported record-high deportations. In just over 2 years (July 2010 to September 2012), nearly 250,000 parents of citizen children were deported (Wessler, 2012). The majority of the deportees had migrated from Latin American countries, including Mexico, Honduras, El Salvador, Guatemala, Cuba, and Brazil (Office of Immigration Statistics, 2013).

Forced parent–child separation and parental loss are PTEs with adverse effects on child mental health and academic functioning (Finkelhor et al., 2009). Children may experience the loss or potential loss of a parent as particularly traumatic if it occurs in the context of contact with legal authorities, such as in the case of incarceration or deportation. Parental incarceration, a recognized PTE in childhood (Felitti, 2009), is distinguished from other adverse childhood experiences by the unique combination of trauma, ambiguity, lack of social support, shame, and stigma (Hairston,

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2007). Mounting evidence has indicated that arrest and imprisonment of a parent disrupts parent–child relationships, alters familial support networks, and impairs children’s mental health (Roberts et al., 2014). We speculate that the detention and deportation of unauthorized parents may have similar unintended negative effects on their U.S.-born progeny.

Emerging research has indicated that parental detention and deportation increase risk for mental health problems such as severe psychological distress, anxiety, and depression (Allen, Cisneros, & Tellez, 2015; Zayas, Aguilar-Gaxiola, Yoon, & Rey, 2015); for underutilization of care (Chen & Vargas-Bustamante, 2011); and for involvement with Child Welfare (Rabin, 2011). A few empirical and qualitative studies have examined the effects of parental legal status on child and adolescent development (e.g., Allen et al., 2015; Brabeck & Xu, 2010; Dreby, 2012), but this research has been largely descriptive or retrospective, relying primarily on parent report of child outcomes (Allen et al., 2015; Brabeck & Xu, 2010; Chaudry et al., 2010).

To the best of our knowledge, only two empirical studies have examined citizen children and their increased risk for psychological distress subsequent to parental detention or deportation (Allen et al., 2015; Zayas et al., 2015). Allen and colleagues (2015) recruited immigrant caregivers who either were in deportation legal proceedings, had been deported, or were unauthorized without contact with immigration enforcement. In this sample of primarily U.S.-born children, Allen et al. found that children with a deported parent exhibited more internalizing problems after controlling for trauma history than did children without a deported parent.

In a recent binational study using child self-report, Zayas and colleagues (2015) examined the psychological distress of three groups of citizen children (ages 8–15 years) who had at least one parent of Mexican origin. The groups consisted of (a) children living in Mexico with their deported parents, (b) children living in the United States with parents affected by detention or deportation, and (c) children living in the United States whose undocumented parents were not affected by detention or deportation. Two significant group differences emerged. First, children with parental history of detention or deportation reported possible attention deficits. Second, citizen children living in Mexico with deported parents displayed more depressive symptoms than did other children. Furthermore, all three groups scored within the range of probable anxiety problems. Notably, no measures of trauma were reported. To the best of our knowledge, no studies have systematically assessed child PTSD symptoms and overall psychological distress in this vulnerable population using extrafamilial informants. Using multiple informants (i.e., child, parent, teacher, clinician) and standardized measures, the present study was designed to examine the psychological impact of parental detention and deportation on U.S.-born Latino children.

Children of unauthorized parents have been shown to be disproportionately poor and in disadvantaged neighborhoods at risk for exposure to violence, victimization, and further marginalization (e.g., Ross & Mirowsky, 2009). In fact, unauthorized status is highly associated with poverty and low parental education (Yoshikawa, Kholoptseva, & Suárez-Orozco, 2013). Emerging evidence, however, has proposed that precarious parental immigration status puts citizen children at risk for a gamut of socioemotional disadvantages beyond the ill effects of poverty and related risk

factors (Yoshikawa et al., 2013). Immigration enforcement is a multifaceted social issue, and its effects on Latino children’s development need further research.

The Present Study

This study sought to build on prior research on the unintended mental health consequences of immigration enforcement on Latino citizen children. To address the intersectional nature of cumulative risks, we included two comparison groups of citizen children whose immigrant parents had no contact with U.S. Immigration and Customs Enforcement (ICE): (a) children of unauthorized parents with no history of detention or deportation and (b) children of U.S. legal permanent residents (LPRs). We planned to control for child lifetime exposure to PTEs and for maternal education as the best indicator of family’s socioeconomic status (SES). Income was not included as an SES indicator, because family income was expected to be substantially reduced following parental detention or deportation. We examined baseline multiple informant assessment data to test the central hypothesis that Latino U.S.-citizen children whose parents have been detained and/or deported would have significantly more psychological distress and PTSD symptoms than would children of parents who had no contact with ICE.

Method

Study Sample

From 2013 through early 2015, undocumented and legal permanent resident parents born in Mexico or Central America (e.g., Nicaragua, Honduras, El Salvador, Guatemala), regardless of race or socioeconomic status, were recruited. Specifically, this study targeted mixed-status Latino families with U.S.-born citizen children between ages 6 and 12 living in the Southwest. Citizen children with a current major medical, neurological, or mental health disorder (e.g., psychosis, autism, Down’s syndrome) were excluded.

Procedures

Families with precarious legal status were recruited through a broad network of trusted immigration advocacy agencies, community-based programs, and churches that work with such families. Three primary methods were used in recruiting mixed-status families: (a) individual agency referral, (b) oral presentations at various community-based programs and Latino churches serving the immigrant community, and (c) a short video advertising the study. Staff at these agencies identified potential study participants. Using provided scripts, staff invited caregivers who had at least one child who was born in the United States to participate. Once a release of information was obtained, contact information was passed on to the research staff, who then contacted potential participants by phone to explain the study, validate the child’s age, and schedule the initial visit. Caregivers and children were interviewed simultaneously in separate rooms at trusted community agencies or churches. Interviewers were bilingual or bicultural (English or Spanish) master’s-level clinicians. Interviews lasted approximately 2 hr, including snack breaks.

Consent and assent forms were reviewed and signed, including parental consent to obtain school records and to mail a survey to the child's teacher. Adult and child participants were informed that they could choose not to answer any question or to stop the interview at any time. Confidentiality was discussed, including the exception for reporting child abuse and neglect. Given the vulnerable legal status of this study's participants, a "certificate of confidentiality" was deemed important and obtained. Participants were compensated with \$30 for parents or caregivers, \$10 gift card for teachers, and \$15 gift cards for children. All parent and child measures were available in Spanish and English and were read to participants.

Measures

Child report. Children were assessed using the UCLA Posttraumatic Stress Disorder Reaction Index (UCLA PTSD-RI; Steinberg, Brymer, Decker, & Pynoos, 2004). This 22-item, clinician-administered measure is among the more extensively studied and widely used assessments of childhood PTSD. The UCLA PTSD-RI has strong convergent validity with the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 1994) diagnosis criteria of experiencing a traumatic event (Criterion A) and reporting symptoms related to reexperiencing/intrusive thoughts (Criterion B), avoidance (Criterion C), and hyperarousal (Criterion D). This measure has excellent psychometric properties, with internal consistencies of .82 (Criterion B), .83 (Criterion C), and .71 (Criterion D). It has been used across a variety of trauma types, age ranges, settings, and languages, including Spanish (Rodríguez, Steinberg, & Pynoos, 1999; Steinberg et al., 2013). The UCLA PTSD-RI provides PTSD symptom severity and screens for 13 PTEs among children of 7–18 years of age, including accidents, physical and sexual abuse, and domestic violence. In our sample, PTEs were positively skewed (1.50), with observed scores ranging from 0 to 8. To normalize this distribution, we recoded the five scores above 4 to 4.

Children also completed the Center for Epidemiologic Studies Depression Scale for Children (CES-DSC), a 20-item self-report depression inventory with scores ranging from 0 to 60 and a clinical cutoff of ≥ 15 (Weissman, Orvaschel, & Padian, 1980). The Spanish version of the CES-DSC has been widely used in epidemiological research (González et al., 2016). Cronbach alpha in this study was .81.

Parent report. Parents completed the Behavior Assessment System for Children–2nd Edition, Parent Rating Scales–Child (BASC-2 PRS-C; Reynolds & Kamphaus, 2004). The BASC-2 PRS-C is a widely used and well-validated caregiver-report measure of 160 items on a Likert-type scale ranging from 1 (*never*) to 4 (*almost always*). It yields scores on a wide range of empirically based syndrome scales and two composite scales (Internalizing Problems and Externalizing Problems). Scores are reported in *T* scores, and percentiles based on age-specific norms (clinical cutoff ≥ 70), standardized using samples of clinical and nonclinical populations sampled to reflect the general population (Reynolds & Kamphaus, 2004). The Spanish version of the BASC-2 PRS-C has reliability and validity support with Spanish-speaking parents (McCloskey, Hess, & D'Amato, 2003). In the current study, composite score reliabilities for the BASC-2 PRS-C Externalizing Problems and Internalizing Problems were strong, with Cronbach alphas of .88 and .76, respectively.

Parents also completed the Trauma Symptom Checklist for Young Children—Spanish Version (TSCYC–SP; Briere, 2005), a standardized 90-item caregiver report developed to assess trauma-related symptoms in children ages 3–12 (*T* scores with clinical cutoff ≥ 70). The reliability and validity of the TSCYC–SP has been established in a sample of outpatient children from Spanish-speaking families, with reported Cronbach alphas from .67 to .93 (Wherry et al., 2014). Reliability for the TSCYC–SP scales in the current study were strong (alphas of .79 to .85).

Teacher report. Teachers completed the BASC-2 Teacher Rating Scales–Child (BASC-2 TRS-C; Reynolds & Kamphaus, 2004). The BASC-2 TRS-C is a 139-item scale that evaluates children's behavioral and emotional functioning. Like the BASC-2 PRS-C, scale scores are reported as *T* scores, and percentiles are based on normative data (clinical cutoff score ≥ 70). In this study, composite score reliabilities for BASC-2 TRS-C Externalizing Problems and Internalizing Problems were strong, with Cronbach alphas of .89 and .82, respectively.

Clinician evaluation. Clinicians used the Child and Adolescent Functional Assessment Scale (CAFAS; Hodges, 2006) to rate the child's lowest level of day-to-day functioning across critical life domains (School, Home, Community, Moods/Emotions, and Total Dysfunction). Cutoff scores indicating severe, moderate, and mild impairment are 30, 20, and 10, respectively. The CAFAS has been widely used in community mental health across the United States as part of statewide assessments of mental health outcomes (Bates, 2001). After being trained to 80% agreement using CAFAS training materials and assessment (Hodges, 2006), two master's-level clinicians jointly rated each child participant on the basis of information collected in the structured interviews with parent and child, as well as the BASC-2 TRS-C scale (teacher report) and school records.

Results

Descriptive data and correlations for main study variables are presented in Table 1. Gender was not significantly related to outcome variables, so it was dropped from all analyses. Surprisingly, neither maternal education nor family income was correlated with most outcome variables. Higher maternal education was associated with lower parental TSCYC–SP depression reports ($p = .01$), and lower income was significantly correlated with more PTEs ($p = .03$). Thus, these SES variables were included as covariates in analyses of only those specific outcomes. Demographic characteristics of the participant children, grouped by parental immigration status comparisons, are presented in Table 2. As expected, groups significantly differed on family income ($p = .002$), with legal permanent resident (LPR) families reporting significantly higher incomes than did either unauthorized group, and families with a detained or deported parent having both lower maternal education than did LPR families and more father unemployment than did either LPR or unauthorized without ICE contact families ($p = .002$ and $p < .001$, respectively).

Risk Exposure for PTEs

After controlling for family income, the groups significantly differed on lifetime exposure to PTEs on the UCLA PTSD-RI index by parental immigration status, as shown in Table 3, with

Table 1
Bivariate Correlations, Means, and Standard Deviations for Major Study Variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Sex ^a	—																
2. Education ^b	.04	—															
3. Income ^c	.12	.10	—														
4. PTE	.11	.02	.22*	—													
5. PTSD	-.19 ^a	.05	.10	.26**	—												
6. CES-DSC	-.09	.01	.06	.26**	.52***	—											
7. PTS total	-.00	-.17	.01	.08	.02	.08	—										
8. Anxiety	.03	-.19 ^a	.05	.07	-.08	-.06	.71***	—									
9. Depression	-.06	-.25*	-.04	.06	-.02	.08	.77***	.59***	—								
10. Parent int	.03	-.12	.09	.04	-.03	.04	.40***	.32**	.54***	—							
11. Parent ext	.01	.10	.11	.34**	.21*	.13	.27**	.07	.27**	.48**	—						
12. Teacher int	-.02	.08	-.04	-.07	.01	-.03	-.13	-.14	-.12	-.03	.22*	—					
13. Teacher ext	.01	.00	-.13	.21	.10	-.07	-.03	-.01	.01	.03	.38***	.55***	—				
14. Total dys	-.01	-.19 ^a	.11	.20	.21*	.17	.47***	.43***	.53	.16	.42***	-.02	.27*	—			
15. Home	.04	-.08	.10	.10	.05	.04	.26*	.16	.35***	.24*	.57***	-.01	.27*	.77***	—		
16. School	.13	-.07	-.01	.18	.02	.05	.49***	.37***	.46***	.08	.31**	.15	.37***	.57***	.26*	—	
17. Mood	-.07	-.20 ^a	.09	.22*	.42***	.31**	.35***	.41***	.33**	.06	.19 ^a	-.14	.10	.75***	.37***	.29**	—
M	.61	.42	1.27	1.69	20.40	22.97	51.72	54.51	50.32	51.16	47.41	48.17	49.49	13.59	1.74	2.07	6.52
SD	.49	.50	1.35	1.27	16.01	10.12	10.68	11.89	10.82	11.43	10.49	10.56	10.51	19.08	4.83	5.04	7.77
n	97	95	95	97	96	97	92	92	92	96	96	83	83	92	92	92	92

Note. PTE = potentially traumatic event; PTSD = UCLA PTSD Reaction Index total score; CES-DSC = Center for Epidemiological Studies Depression Scale for Children; PTS total = Trauma Symptom Checklist for Young Children (TSCYC) posttraumatic stress total score; Anxiety = TSCYC anxiety score; Depression = TSCYC depression score; Parent int = Behavior Assessment System for Children-2nd Edition, Parent Rating Scales-Child (BASC-2 PRS-C) internalizing score; Parent ext = BASC-2 PRS-C externalizing score; Teacher int = BASC-2 Teacher Rating Scales-Child (BASC-2 TRS-C) internalizing score; Teacher ext = BASC-2 TRS-C externalizing score; Total dys = clinician report of Total Dysfunction score from the CAFAS; Mood = clinician report of Mood score from the CAFAS).

^a Child gender (0 = female, 1 = male). ^b Maternal education (0 = less than high school, 1 = high school, GED, or some college). ^c Parental income (1 = less than \$15,000, 2 = \$15,000–\$34,999, 3 = \$35,000 or more).

* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 2
Demographic Characteristics of Citizen Children and Their Families

Variable	Parental immigration status			Inferential statistic
	Detained or deported (<i>n</i> = 39)	Unauthorized no history of detention or deportation (<i>n</i> = 42)	Legal permanent resident (<i>n</i> = 16)	
Child sex				2.13
Male	21	29	9	
Female	18	13	7	
Mother education				12.69***
<High school	29	22	4	
High school or higher	9	19	12	
Family income				17.11**
<\$15,000	19	24	2	
\$15,000–\$34,999	16	13	7	
≥\$35,000	4	3	7	
Father current employment				50.43***
Full-time	4	28	11	
Part-time	3	8	3	
Unemployed	29	3	1	
Mother current employment				4.48
Full-time	9	5	4	
Part-time	12	10	5	
Unemployed	16	27	7	
Parents' marital status				5.16 [†]
Married	23	33	14	
Never married	14	8	2	
Father's country of origin ^a				2.16
Mexico	23	28	10	
El Salvador	9	3	2	
Guatemala	4	6	2	
Honduras	3	1	0	
Nicaragua	0	1	0	
United States	0	2	1	
Mother's country of origin ^a				9.89**
Mexico	14	33	8	
El Salvador	3	2	3	
Guatemala	4	4	3	
Honduras	10	2	0	
Nicaragua	0	0	0	
United States	6	1	2	
Parent years in U.S.				2.75 [†]
<i>M</i>	14.79	17.67	20.00	
<i>SD</i>	9.91	5.41	8.42	
Child age				.40
<i>M</i>	9.05	9.12	8.63	
<i>SD</i>	1.82	2.03	1.78	

Note. Inferential statistics are χ^2 for count data and $F(2, 94)$ for means.

^a Due to small cell counts, χ^2 was computed on Mexico versus Central America countries.

[†] $p < .10$. * $p < .05$. ** $p < .01$. *** $p < .001$.

children of detained or deported parents experiencing significantly more lifetime PTEs than did children of LPRs ($p = .02$). Even when child reports of parental deportation or detention as a PTE were excluded, the groups significantly differed on PTEs, $F(2, 91) = 3.62$, $p = .03$, $\eta_p^2 = .07$, again with children of detained or deported parents reporting significantly more PTEs than did children of LPRs ($p = .03$). Children of unauthorized parents with no contact with ICE were not significantly different from children with detained or deported parents but tended to have more PTEs than did children of LPRs ($p = .06$). Overall, exposure was high across groups, with 35% of the sample reporting exposure to one PTE, 21% to two, 14% to three, and 12% to four or more PTEs in their lifetime, with an average exposure of 1.69 PTEs ($SD = 1.27$).

PTSD and Psychological Distress

Child outcomes by parental immigration status were examined in a series of univariate and multivariate analyses of variance (ANOVAs), controlling for maternal education when indicated, with Bonferroni pairwise post hoc comparisons (see Table 3). Analyses were conducted both with and without controlling for lifetime exposure to PTEs, and the results were essentially identical. Thus, for ease of interpretation, only analyses not controlling for lifetime exposure are presented here.

Child report of PTSD symptoms. Per the UCLA PTSD-RI child report, 29% of all child participants met criteria for full (19%) or partial (10%) PTSD diagnoses. There were no significant

Table 3
Citizen Children PTSD and Psychological Distress by Parental Immigration Status

Measure	Parental immigration status									F	η_p^2
	Detained or deported			Unauthorized no history of detention or deportation			Legal permanent resident				
	n	M	SD	n	M	SD	n	M	SD		
Child reports											
UCLA PTSD-RI	38			42			16				
Lifetime PTEs ^a		1.97 _a	1.33		1.67	1.23		1.19 _b	1.11	3.84*	.08
Total severity score		21.92	14.39		20.12	16.92		17.50	18.11	.43	.01
Criterion B		6.92	4.45		5.90	5.84		5.19	6.67	.66	.01
Criterion C		7.68	6.54		7.79	7.13		6.63	7.02	.18	<.01
Criterion D		7.32	4.99		6.43	4.99		5.69	5.55	.65	.01
CES-DSC		23.95	11.33		23.32	9.94		19.69	6.77	1.05	.02
Parent reports											
TSCYC ^b	37			39			14				
PTS overall total		57.62 _a	12.40		48.56 _b	7.64		46.14 _b	5.35	9.70***	.18
Anxiety		60.57 _a	14.44		51.54 _b	7.97		48.07 _b	6.04	7.73***	.15
Depression		56.59 _a	11.76		47.18 _b	8.64		43.79 _b	4.04	10.21***	.19
Anger/Aggression		51.59 _a	8.37		47.15 _b	5.23		45.93	3.85	4.67*	.10
PTS Intrusion		56.49 _a	14.27		47.41 _b	8.13		47.36	6.59	5.90**	.12
PTS Avoidance		55.62 _a	11.09		49.44 _b	7.83		47.36 _b	5.40	6.08**	.12
PTS Arousal		57.92 _a	11.69		49.41 _b	8.18		45.71 _b	5.92	9.96***	.19
Dissociation		48.22	8.00		47.69	6.74		44.93	3.36	1.23	.03
BASC-2 PRS-C	39			42			15				
Int Prob total		54.67 _a	12.45		49.90	10.78		45.53 _b	7.25	4.17*	.08
Anxiety		58.00	11.73		54.12	11.45		53.07	11.00	1.56	.03
Depression		54.13 _a	10.84		49.17	10.84		44.47 _b	7.46	5.24**	.10
Somatization		49.05 _a	11.92		46.69	9.69		41.33 _b	4.85	3.14*	.06
Ext Prob total		49.41	10.37		46.81	11.15		43.87	8.07	1.66	.03
Hyperactivity		50.59	11.97		48.64	11.73		45.87	10.69	.92	.02
Aggression		47.62	8.39		44.98	9.16		43.73	6.24	1.54	.03
Conduct problems		50.28	10.50		47.74	11.59		44.00	6.59	2.00	.04
Teacher reports											
BASC-2 TRS-C	33			37			13				
Int Prob total		49.61	13.54		47.49	8.36		46.46	7.24	.55	<.01
Anxiety		47.52	9.57		47.35	7.95		46.62	9.00	.05	<.01
Depression		50.18	10.65		47.59	7.06		46.31	6.10	1.26	.03
Somatization		51.30	15.98		49.35	8.42		48.38	9.07	.36	.01
Ext Prob total		52.48	13.53		48.24	8.15		49.49	10.51	2.66 [†]	.06
Hyperactivity		52.88	13.49		48.68	9.31		47.54	6.17	1.76	.04
Aggression		51.42	12.47		48.24	7.47		45.00	4.16	2.35	.06
Conduct problems		52.36	13.39		48.19	7.87		44.46	3.48	3.25*	.08
Clinician reports											
CAFAS	35			42			15				
Overall dysfunction		25.14 _a	23.44		7.38 _b	12.31		4.00 _b	6.32	13.41***	.23
Home		2.86	6.23		1.19	3.95		.67	2.58	1.60	.03
School		4.00 _a	6.95		1.19 _b	3.23		.00 _b	.00	4.86***	.10
Mood/Emotions		11.71 _a	8.22		3.33 _b	5.26		3.33 _b	6.17	17.10***	.28

Note. Means with differing subscripts are significantly different in Bonferroni corrected pairwise comparisons. PTSD = posttraumatic stress disorder; UCLA PTSD-RI = UCLA PTSD Reaction Index; PTEs = potentially traumatic events; CESD-DSC = Center for Epidemiologic Studies Depression Scale for Children; TSCYC = Trauma Symptom Checklist for Young Children; PTS = posttraumatic stress; BASC-2—PRS = Behavior Assessment System for Children—2nd Edition, Parent Rating Scales-Child; Int Prob = Internalizing Problems; Ext Prob = Externalizing Problems; BASC-2 TRS-C = BASC-2 Teacher Rating Scales-Child; CAFAS = Child and Adolescent Functional Assessment Scale.

^a Analysis of covariance (ANCOVA) controlling for family income was conducted. Raw means and standard deviations reported. ^b ANCOVA of the total score and multivariate analysis of variance of the scale scores were conducted for TSCYC, controlling for maternal education. Raw means and standard deviations are presented here.

[†] $p < .10$. * $p < .05$. ** $p < .01$. *** $p < .001$.

differences by parental immigration status on total PTSD symptoms, $F(2, 93) = 0.43, p = .65, \eta_p^2 = .01$, or individual criteria (Wilks's $\lambda = .96$), $F(6, 184) = 0.68, p = .67, \eta_p^2 = .02$.

Parent report of PTSD child symptoms. Five families had invalid TSCYC–SP Response Level and Atypical Response Scale scores and were dropped from TSCYC–SP analyses. Controlling for maternal education, total symptoms differed by parental immigration status, $F(2, 86) = 9.70, p < .001, \eta_p^2 = .18$. Similarly, a multivariate analysis of covariance of TSCYC–SP Anxiety, Depression, Anger/Aggression, Intrusion, Avoidance, Arousal, and Dissociation controlling for maternal education indicated a significant multivariate effect of parental immigration status (Wilks's $\lambda = .64$), $F(12, 168) = 3.53, p < .001$, with significant univariate effects for all scales except Dissociation. In each case, per parent report, children of detained and deported parents demonstrated higher levels of trauma symptoms than did children of either LPR parents (ps ranging from $< .001$ to $.03$) or unauthorized parents with no ICE contact (ps ranging from $< .001$ to $.01$; see Table 3).

Child reports of psychological distress. There was no effect of parent immigration status on child self-reports of depression on the CES-DSC, $F(2, 94) = 1.05, p = .35, \eta_p^2 = .02$.

Parent report of child psychological distress. As shown in Table 3, there was a significant univariate effect of parent immigration status on BASC-2 PRS-C total internalizing, $F(2, 93) = 4.17, p = .02, \eta_p^2 = .08$, with children of detained or deported parents reported to have more internalizing problems than did children of LPRs ($p = .02$). Multivariate analysis of variance (MANOVA) analyses revealed a marginal main effect of parent immigration status on the three BASC-2 PRS-C internalizing subscales (Wilks's $\lambda = .88$), $F(6, 182) = 2.05, p = .06$, with children of detained or deported parents scoring higher on Depression ($p = .009$) and Somatization ($p = .04$) per parent report than did children of LPRs.

In contrast, there were no significant effects of parent immigration status on parent-reported total externalizing, $F(2, 93) = 1.67, p = .20, \eta_p^2 = .03$, or on Hyperactivity, Aggression, or Conduct Problems (Wilks's $\lambda = .95$), $F(8, 182) = 0.83, p = .55$.

Teacher report of child psychological distress. Univariate and MANOVA results demonstrated no significant effects for parental immigration status on teacher BASC-2-TRS total internalizing score, $F(2, 80) = 0.55, p = .58, \eta_p^2 = .01$, or on the Anxiety, Depression, or Somatization scales (Wilks's $\lambda = .95$), $F(6, 156) = 0.61, p = .72$ (see Table 3).

Teacher reports of total externalizing symptoms were only marginally different by group, $F(2, 80) = 2.66, p = .08, \eta_p^2 = .06$. A MANOVA analysis of Hyperactivity, Aggression, and Conduct Problems was also not significant (Wilks's $\lambda = .90$), $F(6, 156) = 1.35, p = .24$, but a significant univariate effect was found for Conduct Problems, with children of detained or deported parents tending to have more of these problems than did children of LPRs ($p = .06$).

Clinician report of overall child functioning. There was a significant univariate main effect for parental immigration status on clinician's CAFAS overall child dysfunction, $F(2, 89) = 13.41, p < .001, \eta_p^2 = .23$, with children of detained or deported parents exhibiting poorer functioning than did children of both LPRs and unauthorized parents with no ICE contact ($ps < .001$). Similarly, MANOVA analyses of the Home, School, and Moods scales revealed a significant effect of parent immigration status (Wilks's $\lambda = .69$), $F(6, 176) = 5.87, p < .001$, with children of detained or deported

parents having poorer scores on School Behavior than did children of LPRs ($p = .03$) or unauthorized parents with no ICE contact ($p = .04$), and poorer scores on Moods than did children of either LPRs or unauthorized parents with no ICE contact ($ps < .001$).

Multiple Informant Comparisons

The correlations between ratings of internalizing constructs were typically modest. For instance, teacher, parent, and child ratings of depression were uncorrelated, as were parent and child reports of PTSD symptoms. In contrast, clinician CAFAS ratings of Moods and Emotions were significantly correlated with both parent TSCYC–SP Depression, $r(92) = .36, p < .001$, and child CES-DSC, $r(92) = .31, p = .003$. Adult reports of externalizing problems were more consistently and strongly related, with correlations among parent and teacher BASC-2 Total Externalizing and between BASC-2 and clinician CAFAS Home Behavior and School Behavior ranging from $.37$ to $.57$ (all $ps < .001$). Direct comparisons of means were possible for only parent and teacher BASC-2 scores. Parents reported higher Total Internalizing than did teachers, $t(83) = 3.70, p = .03$, but reports of Total Externalizing did not differ, $t(83) = -1.40, p = .17$.

Discussion

The need to detect children with PTSD-related symptoms and psychological distress is pertinent given the evidence for the detrimental effects of early childhood adversity in the overall mental health of children. This is significant for Latino citizen children whose parents are undocumented and at high risk for detention or deportation, which often lead to forced parent–child separation. In light of complex immigration policies, our findings provide some support for the need for clinical and public policy interventions on behalf of this vulnerable child population.

Impact of Parental Detention or Deportation on Citizen Children's PTSD

Taken together, the reports of multiple informants (parent, teacher, clinician, and child) indicate that citizen children of detained and deported parents experience more psychological distress and trauma compared to peers whose parents had no involvement with immigration enforcement. Higher levels of parent-reported PTSD symptoms in children of detained and deported parents imply that forced parental separation resulting from immigration enforcement is particularly detrimental to children's mental health. The unpredictability and uncertainty associated with such separations may have exacerbated PTSD symptoms (see Grillon et al., 2009). As such, our findings suggest that the current and heightened enforcement of immigration laws poses a serious public health challenge to U.S.-born children of undocumented parents. Not only is PTSD recognized as a high priority public health issue (U.S. Department of Health & Human Services, 2003), but child PTEs, such as losing a parent, pose serious risks for lifelong mental and medical illnesses (Felitti, 2009; Putnam, Harris, & Putnam, 2013).

Specifically, the children of detained and deported parents were rated on the TSCYC–SP as endorsing more symptoms in all three DSM–IV PTSD criterion domains as well in total posttraumatic

symptoms. Although to the best of our knowledge, no other study has used the TSCYC–SP with this population, our results seem congruent with those of prior studies reporting on the validity of the TSCYC–SP (e.g., Wherry et al., 2014). TSCYC–SP scores were significantly correlated with BASC-2 internalizing problems but not with child self-ratings, consistent with research documenting divergence in such child and parent reports (Briere, 2005; De Los Reyes & Kazdin, 2005).

Impact of Parental Detention or Deportation on Citizen Child Psychological Distress

Children of detained or deported parents were rated by parents and clinicians as higher in internalizing problems and in negative moods and emotions compared to children of LPRs and parents who had no contact with ICE. The overlap of depressive and anxious symptoms with PTSD is significant, and thus these findings are consistent with the findings of prior empirical research in showing significantly increased rates of depression and anxiety problems among children with PTSD symptomatology (Samuelson, Krueger, Burnett, & Wilson, 2010). Depression and anxiety pose immediate developmental challenges to child functioning (Kendall et al., 2010) and pose higher risk for future mental health problems (Lopez, Turner, & Saavedra, 2005). Furthermore, our findings corroborate and extend those of Zayas et al. (2015) and Allen et al. (2015) and are also congruent with findings of previous studies documenting the negative mental health outcomes associated with parental separation (Chaudry et al., 2010; Suárez-Orozco, Bang, & Kim, 2011).

Children with more PTEs were also rated by parents and teachers as having more externalizing problems (BASC-2) and by clinicians as having more total dysfunction (CAFAS). This finding aligns with previous research showing that children with trauma-related symptoms are at risk of misdiagnosis (e.g., with attention deficit/hyperactivity disorder or conduct difficulties), particularly in the absence of assessments for complex trauma (e.g., Kletzka & Siegfried, 2008). Our findings underscore the need for educating parents and teachers on symptoms associated with PTEs.

Intersection Between Poverty, Exposure to PTEs, and the Loss of a Parent

Exposure to multiple PTEs was common across our sample, with 35% of the children reporting experiencing one PTE and 47% endorsing two or more PTEs. This high prevalence of PTE exposure is concerning given the negative short- and long-term consequences of childhood PTE exposure (Appleyard, Egeland, van Dulmen, & Sroufe, 2005). Consistent with the literature, more PTEs were related to increased child PTSD scores. Although there were no differences by parental immigration status, the PTSD prevalence in our sample was high (19% of the children meeting all *DSM-IV* criteria and 10% meeting partial criteria) per child report.

Emerging research in childhood adversity describes synergy as the interaction of two or more PTEs, or adverse events, so that their combined effect is greater than the sum of their individual effects (Putnam et al., 2013). Putnam and colleagues (2013) documented the synergy of adverse events with loss of a parent among adult males with three or more PTEs. They found that poverty, the

most potent adverse childhood event in males, is synergistic with the loss of a parent. Putnam and colleagues' research is particularly relevant to citizen children of detained or deported parents who have lost, or have the impending possibility of losing, a parent due to U.S. immigration enforcement. These findings thus call for a reconsideration and reduction of unnecessary detention of undocumented parents and consequent parent–child separation.

Implications for Health Services, Policies, and Future Directions

Researchers have argued that child PTEs are the most preventable causes of debilitating mental illnesses, such as PTSD, depression, and anxiety (Finkelhor, Ormrod, & Turner, 2007; National Research Council & Institute of Medicine, 2009). Particularly for children who have been multiply victimized, preventing future PTEs may be the most effective intervention (Finkelhor et al., 2007). This is notable for our sample of citizen children. A call for action to prevent forced parental separation and constant threat of potential loss of a parent due to immigration enforcement is gravely needed.

Given the high endorsement of PTEs in our sample, more trauma-informed, developmentally appropriate systems placed at multiple levels (e.g., home, school) would assist Latino citizen children and their families. Trauma-informed intervention and prevention programs for this vulnerable population should target synergistic adverse events, such as poverty and loss of a parent. Furthermore, affordable and culturally relevant services are warranted not only for children of detained or deported parents but also for citizen children of parents living in the shadows. A reevaluation of immigration policies that have significant effects on access to health services is also extremely relevant to the well-being of Latino citizen children (for a review see Rodríguez, Young, & Wallace, 2015).

On the basis of findings with children of incarcerated parents (Roberts et al., 2014), we suspect that witnessing parental detainment may be particularly detrimental. Future research should investigate the effects of witnessing the arrest or detention of undocumented parents on child PTSD symptoms, and this information should be used in reviewing policies involving undocumented immigrants with children. Arrest protocols should consider the children's best interest.

Study Strengths and Limitations

The cross-sectional nature of this study and its relatively small sample size limit the ability to infer causation and to generalize findings to other ethnic and racial immigrant groups. Future studies should also examine South American Latino groups. Statistics show undocumented South American immigrants tend to fare better economically in the United States, in part due to higher levels of education and different migratory routes than for immigrants coming from the Central American cone (Stoney, Batalova & Russell, 2013). Such SES dynamics would be important to understand in their interaction with immigration enforcement and child well-being.

Finally, some children exposed to PTEs, including parental detention or deportation, do not exhibit high levels of mental

health symptoms. These findings highlight an underlying resilience in the face of adversity that should be understood and supported in all children of immigrants, regardless of parental legal status. Future research should explore mediating factors, such as family or community support, religious coping, hope, and cognitive processing of PTEs.

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24
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26
27
28

Exhibit H



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War exposure, daily stressors, and mental health in conflict and post-conflict settings: Bridging the divide between trauma-focused and psychosocial frameworks

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ABSTRACT

This paper seeks to bridge the divisive split between advocates of trauma-focused and psychosocial approaches to understanding and addressing mental health needs in conflict and post-conflict settings by emphasizing the role that daily stressors play in mediating direct war exposure and mental health outcomes. The authors argue that trauma-focused advocates tend to overemphasize the impact of direct war exposure on mental health, and fail to consider the contribution of stressful social and material conditions (daily stressors). Drawing on the findings of recent studies that have examined the relationship of both war exposure and daily stressors to mental health status, a model is proposed in which daily stressors partially mediate the relationship of war exposure to mental health. Based on that model, and on the growing body of research that supports it, an integrative, sequenced approach to intervention is proposed in which daily stressors are first addressed, and specialized interventions are then provided for individuals whose distress does not abate with the repair of the social ecology.

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As the papers in this special issue of *Social Science and Medicine* make clear, interest in the psychological effects of organized violence has grown tremendously over the past 25 years. As in any growing field of inquiry, a number of controversial issues have emerged in research and practice with war-affected populations. Particularly salient among these issues is the conflict between advocates of what we refer to in this paper as *trauma-focused* versus *psychosocial* approaches to understanding and addressing the mental health needs of communities affected by armed conflict.

Underlying these two approaches are fundamentally different assumptions regarding the factors that most influence mental health in conflict and post-conflict settings. For trauma-focused advocates, the critical factor is direct exposure to the violence and destruction of war—the types of potentially traumatic exposure typically assessed by war-events checklists (e.g., physical assault, the destruction of one's home, the disappearance or death of loved ones in the Harvard Trauma Questionnaire; Mollica et al., 1992). In contrast, for psychosocial advocates attention is focused primarily

on the stressful social and material conditions caused or worsened by armed conflict—conditions such as poverty, malnutrition, displacement into overcrowded and impoverished refugee camps, strife and divisions within communities, the destruction of social networks and the resulting loss of social and material support, and the ostracism and struggle for survival of groups such as former child soldiers, widows, sexual assault survivors, orphans, and people with war-related disabilities (Boothby, Strang, & Wessells, 2006; Miller & Rasco, 2004; Wessells & Monteiro, 2004). Where trauma-focused advocates primarily see evidence of enduring war-related trauma requiring specialized clinical treatment (Neuner & Elbert, 2007; Yule, 2002), psychosocial advocates see distress rooted largely in the stressful conditions of everyday life in settings of organized violence. From a psychosocial viewpoint, altering those stressful conditions is likely to improve people's mental health, while also fostering their inherent capacity to recover—with adequate social support and the passing of time—from the lingering effects of exposure to war-related violence and loss (Betancourt & Williams, 2008; Boothby et al., 2006). Conversely, trauma-focused advocates believe that ameliorating symptoms of war-related trauma will not only improve mental health, but will also enable people to cope more effectively with ongoing environmental stressors.

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The debate between trauma-focused and psychosocial approaches has been fueled in part by differences that are not easily reconciled. Such differences include disagreement over the extent to which people are vulnerable or resilient in the face of extreme and persistent stress (Bonanno, 2004; Kostelny & Wessells, 2004; Neuner & Elbert, 2007); the ethics and efficiency of individualized clinical interventions in settings where distress is widespread and mental health resources are scarce (Inter-Agency Standing Committee, 2007; Miller & Rasco, 2004; Neuner, Karunakara, & Elbert, 2004); and the appropriateness of applying Western psychiatric diagnoses such as post-traumatic stress disorder (PTSD) and trauma-focused clinical treatments such as narrative exposure therapy (Neuner, Karunakara, et al., 2004; Neuner, Schauer, et al., 2004) and EMDR (Shapiro, 2001) to war-affected populations that are overwhelmingly non-Western (Bracken, Giller, & Summerfield, 1995; Kostelny & Wessells, 2004; Miller, Kulkarni, & Kushner, 2006; Summerfield, 1999; Wessells & Monteiro, 2004).

Beyond such differences, we suggest that the debate between advocates of trauma-focused and psychosocial approaches has also been driven by an empirical framework that—until recently—has failed to capture the various pathways by which organized violence impacts mental health. Research on the psychological impact of armed conflict has traditionally focused rather narrowly on examining the relationship between direct war exposure and mental health. Implicit in this focus is a simple direct effects model to explain psychological distress in settings of organized violence. In that model, depicted in Fig. 1, there is a straight line with an arrow leading from war exposure to mental health, reflecting the direct effect that exposure is believed to have on mental health status. The model in Fig. 1 does not include any intervening variables (such as daily stressors) that might either partly or fully explain the impact of war exposure on mental health.

Armed conflict undoubtedly has profound effects on those who experience it directly. However, organized violence also generates or exacerbates a host of highly stressful conditions or daily stressors, such as poverty, social marginalization, isolation, inadequate housing, and changes in family structure and functioning. Only recently have researchers begun exploring what happens when daily stressors are added to the model in Fig. 1. Several studies, in settings as diverse as Afghanistan (Miller et al., 2008; Panter-Brick, Eggerman, Mojadidi, & McDade, 2008), Chad (Rasmussen et al., in press), Sri Lanka (Fernando, Miller, & Berger, in press), Lebanon (Farhood et al., 1993), Algeria (de Jong et al., 2004), and the West Bank (al-Krenawi, Lev-Wiesel, & Sehwal, 2007), have now examined the role of daily stressors in helping to explain the high rates of psychological distress so often found among survivors of armed conflict. Thus far, the data have consistently shown that daily stressors also have powerful effects on mental health outcomes. In our review of those findings in this paper, we suggest that the overly simplistic conceptual model in Fig. 1 has unfortunately led trauma-focused advocates to overestimate the magnitude of the direct effects of direct war exposure in explaining psychological distress within communities. We further suggest that this in turn has contributed to an emphasis on trauma-focused interventions aimed at alleviating war-related PTSD in situations where greater attention to daily stressors may have yielded greater benefits.

At the same time, the available data also suggest that a narrowly psychosocial focus is likely to underestimate the adverse impact that exposure to armed conflict can have on mental health and psychosocial functioning. Interventions that exclusively target daily stressors risk overlooking the need for more specialized treatment for persistently traumatized or depressed individuals (see Hubbard & Pearson, 2004, for an excellent discussion of this issue). To our knowledge, there have been no published studies showing that altering stressful social and material conditions is in and of itself sufficient to foster the resolution of severe and persistent trauma or unresolved grief.

Implicit in much of the discourse regarding the psychosocial framework is a conceptual model that places great emphasis on precisely those variables—daily stressors—that are missing from the trauma-focused model. To the extent that the psychological impact of armed conflict is seen to operate largely or wholly through the stressful social and material conditions it creates, the psychosocial conceptual model may be considered fully mediated—that is, other factors (i.e., daily stressors) largely or fully account for the impact that armed conflict has on mental health. This model is depicted in Fig. 2. The dashed arrow between war exposure and mental health is meant to reflect the fully mediated effect accorded to direct war exposure in explaining psychological distress within a psychosocial framework.

In fact, neither the direct effects model that guides trauma-focused interventions (Fig. 1), nor the fully mediated model that informs many psychosocial programs (Fig. 2), is consistent with what we are learning about the relative contribution of war exposure and daily stressors to mental health. As we discuss below, war exposure does exert a significant direct effect on mental health, beyond the stressful social and material conditions it creates. However, the addition of daily stressors to the model does two important things: (1) it significantly increases the overall explanatory power of the model, and (2) it consistently weakens—though by no means eliminates—the direct relationship between war exposure and mental health. To reflect these findings, we adopt the model recently delineated by Fernando et al. (in press) based on their research with war and disaster-affected youth in eastern Sri Lanka. This model, depicted in Fig. 3, includes both war exposure and daily stressors as predictors of mental health status, and illustrates the role that daily stressors may play in partially mediating the relationship of war exposure to psychological distress. In the model, armed conflict results in exposure to violence and loss, which in turn directly affect mental health and psychosocial functioning. Exposure to armed conflict also gives rise to a constellation of daily stressors, which in turn affect psychological wellbeing (partial mediation). Importantly, the model also includes daily stressors unrelated to armed conflict. This reflects a point to which we return below—namely, that not all distress (including psychological trauma) in situations of armed conflict is related to the violence itself or to the stressful conditions it so often generates.

In the discussion that follows, we draw on an increasingly robust set of empirical findings that support this more complex model, and examine the different pathways through which organized violence appears to exert its effects on psychological wellbeing. We recognize that the utility of any model that purports to explain distress among survivors of armed conflict ultimately lies in its



Fig. 1. Direct effects model of the relationship between war exposure and mental health.

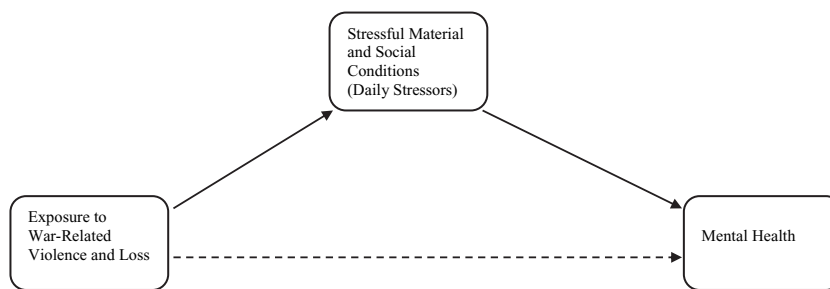


Fig. 2. Mediation by daily stressors of the relationship between war exposure and mental health.

capacity to inform the development of interventions and the allocation of scarce resources. It is our hope that the model discussed here, and the integrative approach to intervention that we propose based on it, will contribute to that end, while also helping to bridge the problematic divide between trauma-focused and psychosocial frameworks.

We begin by examining those factors that have led to a gradual shift among researchers away from the direct effects model, and towards a greater consideration of the ways in which war exposure and daily stressors both contribute to mental health difficulties. Woven into that discussion are findings from recent studies that illustrate and support the partial mediation model in Fig. 3. We then explore why daily stressors are so powerfully linked to mental health, drawing on findings from research on the adverse impact of chronic stress, and on theory concerning the relative importance of proximal versus distal stressors to mental health (Kanner, Coyne, Schaefer, & Lazarus, 1981; Rowilson & Felner, 1988). We also consider shortcomings of the term daily stressors; for example, as we note below, some “daily stressors” do not actually occur on a daily basis. Moreover, the category lumps together chronic low level stressors (e.g., overcrowded housing) with events that are potentially quite traumatic (child sexual abuse). Finally, we suggest an integrated and sequenced model of intervention that addresses the effects both of war exposure and of the stressful social and material conditions to which armed conflict invariably gives rise.

Looking beyond the direct effects model

Recent interest in examining the ways in which war exposure and daily stressors might both contribute to mental health status has its roots in three sets of research findings: (1) the consistently large amount of unexplained variance in mental health outcomes when war exposure is used as the sole predictor of psychological distress (i.e., concern over the limited explanatory power of the direct effects model); (2) research with refugees in developed

nations showing that that post-migration or exile-related stressors such as social isolation, unemployment and discrimination consistently predict levels of psychiatric symptomatology as well as, or better than, pre-migration exposure to organized violence (Steel, Silove, Bird, McGorry, & Mohan, 1999; for a meta-analysis examining pre- and post-migration stressors see Porter & Haslam, 2005); and (3) studies of non-war-affected populations in which so-called “daily hassles” are often more highly associated with mental health symptom severity than major life events (Kanner et al., 1981; Rowilson & Felner, 1988). We consider each of these factors below. First, however, we briefly consider the origin of the direct effects model and the particular context that gave rise to it.

Origin of the direct effects model

Research on the mental health effects of organized violence on civilians began in earnest in the 1980s, and followed two rather distinct tracks. In apartheid era South Africa and in Latin American countries suffering under prolonged state terror and civil war, psychologists adopted a broad view of the pathways by which organized violence influenced mental health (Buitrago Cuellár, 2004; Dawes & Donald, 1994; Gibson, 1989; Martín Baró, 1989; Melville & Lykes, 1992; Straker, 1988). The effects of direct exposure to physical violence were seen against the backdrop of the structural violence that formed that stressful context of everyday life (poverty, discrimination, and marginalization; Farmer, 2004; Dawes & Donald, 1994). In a similar vein, the impact of violence was analyzed at all levels of the social ecology, from individual mental health to the functioning of families and communities (Buitrago Cuellár, 2004; CODEPU, 1989; Martín Baró, 1989).

In contrast, researchers in North America, Europe, and Australia tended to view the mental health needs of refugees recently arrived from Latin America and Southeast Asia through the lens of Western psychiatry and the recently developed diagnosis of PTSD. Although it was developed based on research and clinical work with

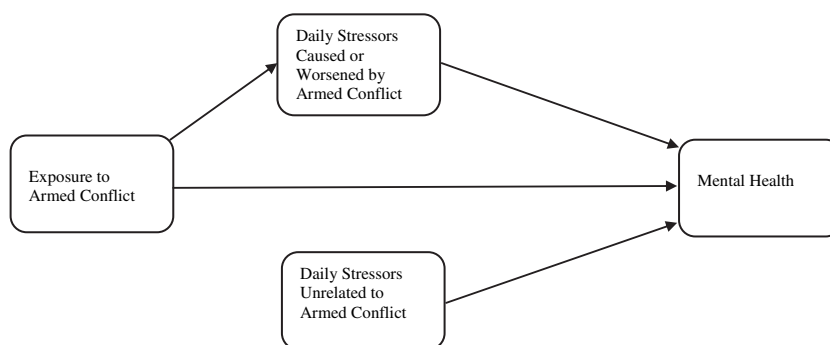


Fig. 3. Daily stressors as partially mediating the relationship of armed conflict to mental health and psychosocial status. Adapted from Fernando et al., in press.

American veterans of the Viet Nam War, the diagnostic criteria for PTSD clearly specified that it was intended as the diagnosis of choice when post-traumatic symptoms arose following any sort of traumatic event that entailed at least the perception of life-threatening danger beyond one's control. For many refugees, who had survived terrifying experiences of extreme violence and showed visible signs of distress, PTSD seemed ideally suited for classifying their experience of distress. Given the salience of their war stories, it was understandably assumed that their high levels of distress were the result of their exposure to the frightening violence and destruction from which they had escaped (Arroyo & Eth, 1986; Kinzie, Sack, Angell, Clarke, & Ben, 1989; Kinzie, Sack, Angell, Manson, & Rath, 1986). Within a short time, research with refugees had become focused heavily on assessing the “dose–effect” relationship between direct war exposure and PTSD symptom levels (Mollica et al., 1998; Smith, Perrin, Yule, Hacam, & Stuvland, 2002); that is, the emphasis was on examining the extent to which degree of war exposure predicted or accounted for severity of PTSD symptoms or the likelihood of receiving a diagnosis of PTSD. As we suggested earlier, underlying this emphasis was an assumption that war exposure represented the critical determinant of distress among survivors of political violence (and that PTSD represented the critical mental health impact of war exposure). Although the strength of the association between exposure and PTSD varied considerably across studies, consistent evidence of a dose–effect relationship emerged over time (Fox & Tang, 2000; Jaranson et al., 2004; Mollica et al., 1999; Tang & Fox, 2001). War exposure was clearly linked to the development of PTSD symptoms, and greater exposure was predictive of greater PTSD symptomatology. Based at least partly on this research, clinical guidelines and recommendations were developed and widely disseminated regarding the treatment of traumatized refugees (Basoglu, 1998; van der Veer, 1999; Varvin & Hauff, 1998). This combination of PTSD-focused research and clinical work with refugees was also critical in launching a worldwide interest in the mental health of war-affected populations, and continues to play a critical role in procuring critical resources in refugee populations in disaster and resettlement settings (Breslau, 2004), much as research and treatment with returning Viet Nam veterans spurred a growth in resources for veterans and active duty soldiers today.

Rapid growth in the field of traumatology has fueled global interest in the study of PTSD. Researchers trained in Western psychiatry and clinical psychology have increasingly adopted the trauma-focused framework developed in the West, shifting the focus of research in non-Western societies affected by armed conflict to the study of PTSD (and related psychopathology) and its relation to war exposure (Fox & Tang, 2000; Lopes Cardozo et al., 2004; Neuner, Karunakara, et al., 2004; Neuner, Schauer, et al., 2004; Thabet & Vostanis, 2000). A similar pattern of results has emerged to that found in earlier studies of refugees resettled in Western societies: greater direct exposure to war events is associated with higher levels of PTSD symptoms (see Barenbaum, Ruchkin, & Schwab-Stone, 2004; de Jong, 2002, for excellent reviews). Although much of our focus in this paper is on the mental health correlates of exposure to the indirect effects of armed conflict (i.e., daily stressors), we also recognize the profoundly distressing nature of direct exposure to armed conflict.

Unexplained variance in the direct effects model and the inclusion of daily stressors

The recent addition of daily stressors to the direct effects model reflects a growing concern that variability in the degree of direct war exposure leaves a substantial proportion of variance in mental health outcomes, including PTSD, unexplained when war exposure

is used as the sole predictor of distress. Having just established that exposure does predict PTSD symptom levels, we also note that such prediction is far from perfect; in fact, war exposure typically accounts for less than 25% of the variance in PTSD symptoms, and often much less than that. For example, in their study of mental health among adults in the Afghan capital of Kabul, Miller et al. (2008) found a correlation of .39 between level of war exposure (as measured by total score on the Afghan War Experiences Scale) and level of PTSD symptomatology (assessed using the Impact of Events Scale-Revised; Weiss & Marmar, 1997). Squaring that correlation coefficient, we find that war exposure in the war-torn city of Kabul accounted for only about 15% of the variance in PTSD symptom levels.

Findings have been similar in other studies. In their study of factors influencing the mental health of youth in eastern Sri Lanka (a region of the country badly affected by civil war and natural disaster), Fernando et al. (in press) found that war and disaster exposure accounted for a mere 8% of the variance in PTSD symptom levels. In a study of Palestinian youth in the West Bank, al-Krenawi et al. (2007) assessed exposure to political violence as well as various forms of violence within the family. They found a correlation of .14 between exposure to political violence and scores on the Brief Symptom Inventory, suggesting that direct exposure accounted for only about 2% of the variance in distress among the youth in their sample (as we note below, family violence was a considerably stronger predictor of distress in their sample). And in a study of predictors of distress among Darfurian refugees in refugee camps in Chad, Rasmussen et al. (in press) found that only about 1% of variance in PTSD symptom levels was attributable to the violence experienced in Sudan.

In all of these studies, only a small proportion of the variance in PTSD symptom severity levels was related to the degree of exposure to armed conflict. This same pattern is found extensively in studies using war exposure as the sole predictor of distress, and it is even more pronounced when outcomes other than PTSD are used as dependent variables (e.g., depression, functional impairment). This robust finding would appear to call into question the widespread assumption that the degree of war exposure is the critical determinant of mental health severity in conflict and post-conflict societies. The large amount of unexplained variance has led researchers to ask what other variables beyond war exposure might be contributing to levels of distress or psychiatric symptomatology. The decision to focus on daily stressors was informed at least partly by recent studies of refugees resettled in developed nations, for whom post-migration stressors have been found to predict mental health status at least as strongly as prior history of war exposure.

The salience of post-migration stressors among refugees in developed nations

As described above, early studies of refugees' mental health needs focused on measuring the “dose–effect” relationship between war exposure and psychopathology, primarily PTSD but also depression, anxiety, and functional impairment. Research lagged behind the experience of clinicians and resettlement workers, however, who noted that the experience of resettlement confronted refugees with a host of stressful challenges, ranging from a lack of culturally relevant competencies to inadequate housing, poverty, social isolation, discrimination, and—for undocumented individuals, a chronic fear of discovery and deportation (Birman et al., 2005; Silove, 1999). As researchers began adding these post-migration or exile-related stressors to their models, they discovered that post-migration stressors accounted for equal or greater variance in symptomatology relative to pre-migration war exposure. Post-migration stressors have been consistently stronger

predictors than war exposure of depression, while war exposure has tended to be more strongly related than post-migration stressors to PTSD (Ellis, MacDonald, Lincoln, & Cabral, 2008; Gorst-Unsworth & Goldenberg, 1998; Miller et al., 2002; Montgomery, 2008; Steel et al., 1999). Nonetheless, post-migration stressors have also consistently been related to PTSD symptom levels among refugees, though the mechanism by which they may affect PTSD symptomatology remains unclear at present (e.g., do they deplete coping resources, thereby leaving people more vulnerable to the impact of prior war exposure? Are some exile-related stressors themselves traumatogenic?). In any case, the significance of these findings for practitioners cannot be overstated. Clearly, a narrow focus on healing war-related trauma among refugees risks overlooking significant sources of current environmental stress that might readily be targeted for intervention (Miller, 1999; Silove, 1999).

There is an interesting similarity between findings regarding the salience of post-migration stressors among refugees and the clinical significance of post-disaster stressors in settings of natural calamities. For example, in the wake of the bushfire disaster in southeastern Australia in 1983, Clayer, Bookless-Pratz, and McFarlane (1985) found that post-disaster stressors such as financial hardship and difficulties rebuilding were as powerfully related to survivors' mental health as their actual exposure to the fire itself. In a similar vein, McFarlane (1995) notes that that post-disaster stressors that ensued from the an earthquake that hit the Yunnan province of China accounted for twice the variance in PTSD symptoms compared with the actual experiences of injury, loss, and threat resulting from direct exposure to the earthquake. And in the previously mentioned study by Fernando et al. (in press), the impact of the tsunami that hit Sri Lanka in 2004 was at least partly mediated by the stressful living conditions it created—that is, daily stressors resulting from the tsunami (e.g., displacement to refugee camps, inability to get basic needs met) were at least as powerful as actual exposure to the tsunami in predicting symptoms of distress.

There is a natural parallel between the concepts of post-migration and post-disaster stressors, on the one hand, and the idea of daily stressors in conflict and post-conflict settings, on the other. In each case, the reference is to constellations of stressors that are generated or exacerbated by highly distressing and potentially traumatic situations. In the case of resettled refugees, armed conflict exposes to people to violence and loss, but it also forces them into exile, where they are confronted with a host of potentially stressful challenges related to adapting to life as refugees or asylum seekers. In conflict and post-conflict settings, armed conflict gives rise to (or worsens) the social and material conditions of everyday life. Survivors of organized violence are thus confronted with a set of enduring and stressful phenomena with which they must contend while also coping with the impact of direct exposure to situations of violent conflict.

As researchers began exploring the salience of daily stressors in conflict and post-conflict settings, two related questions became central:

- 1) To what extent do daily stressors help account for high levels of unexplained variance in levels of distress? That is, to what extent does the addition of daily stressors strengthen the explanatory power of the direct effects model?
- 2) To what extent do daily stressors function to mediate or explain the relationship between war exposure and distress?

Several studies have examined the relative contribution of war exposure and daily stressors to levels of distress without specifically looking at whether daily stressors actually mediate the relation of war exposure to mental health. The findings have generally

been quite consistent: daily stressors have shown strong and significantly related main effects on mental health outcomes, including PTSD (al-Krenawi et al., 2007; Catani, Schauer, & Neuner, 2008; Farhood et al., 1993; Miller et al., 2008). Moreover, in two recent studies (Fernando et al., in press; Rasmussen et al., in press), the addition of daily stressors to the model substantially weakened, though did not eliminate, the relationship of war exposure to mental health status. Perhaps most importantly, the addition of daily stressors significantly increased the explanatory power of models predicting levels of distress, disorder, or functional impairment.

In the Miller et al. (2008) study of mental health in Afghanistan, locally salient daily stressors were first identified through interviews with community members and with input of an expert panel of local Afghans. The Afghan Daily Stressors Scale (ADSS) was created based on these qualitative data. Sample items on the ADSS include overcrowded housing, poverty, unemployment, the security situation, violence in the home, poor health, air pollution, and traffic congestion making public transportation extremely difficult (in a subsequent study of university students in Kabul by Panter-Brick et al. (2008), two subscales were identified in the ADSS, socioeconomic stressors and family stressors; not all items loaded on these two scales, however). The ADSS was then used together with a measure of war exposure to predict levels of PTSD, depression, anxiety, functional impairment, and a locally derived measure of general distress, the Afghan Symptom Checklist (Miller, Omidian, et al., 2006). The addition of daily stressors significantly increased the explanatory power of each model (i.e., the predictive power for each mental health outcome); it also lowered (but did not eliminate) the predictive power of war exposure on all mental health outcomes. Moreover, daily stressors moderated the effect of direct war exposure, so that the effect of war experiences was weaker among those who experienced more severe daily stressors. Had daily stressors not been included in the analysis, the predictive power of war exposure would have been deceptively inflated because it masked the contribution of daily stressors. With regard to specific outcomes, daily stressors were better at predicting depression, functional impairment, and general distress. Among women, war exposure and daily stressors were comparably strong predictors of PTSD, while among men, only daily stressors predicted PTSD.

In their study of Palestinian youth in the West Bank, al-Krenawi et al. (2007) found that family violence, including spousal violence, parental violence against children and violence between siblings, better predicted children's mental health status ($B = .38$) than their level of exposure to political violence in the community ($B = .08$). Family violence, specifically child physical abuse, was also found to strongly predict PTSD symptom levels among Tamil children in the northeast of Sri Lanka (Catani et al., 2008). The likelihood of child abuse was related to paternal substance abuse and war exposure, suggesting that the relationship of war-related violence to children's mental health may have been mediated at least partly through the impact of violence on fathers' substance use and increased likelihood of engaging in violent parenting.

In one of the earliest studies looking at daily stressors and war exposure as predictors of mental health, Farhood et al. (1993) found that among Lebanese families, "daily hassles" associated with the breakdown in community services, economic hardship, and difficulty maintaining contact with family and friends as a result of the war were all better predictors of distress than the constant threat of war-related violence.

To our knowledge, only three studies have looked specifically at the mediating role of daily stressors. Rasmussen et al. (in press) formally tested the role of refugee camp-related daily hassles in mediating the relationship of prior war exposure to mental health

among Darfurian refugees in neighboring Chad. Despite the high level of extreme violence to which the refugees had been exposed, daily stressors related to a lack of basic needs and a lack of safety in the camps were better predictors of PTSD than war exposure; in fact, daily stressors fully mediated the relationship of war exposure to PTSD. Both war exposure and daily stressors predicted levels of depression, while current level of perceived safety mediated the relationship of war exposure to functional impairment. Daily stressors significantly enhanced the overall explanatory power for all mental health outcomes, including the indigenous constructs *majnun* and *hozun*.

As noted earlier, [Fernando et al. \(in press\)](#) examined the role of daily stressors in mediating the relationship of war and disaster exposure to several mental health outcomes including PTSD, depression, anxiety, and psychosocial functioning among Sri Lankan youth in the eastern district of Ampara—a region badly affected by civil war and a tsunami that killed over 35,000 people on the island in December, 2004 ([SAFMA, 2008](#)). Daily stressors were identified through focus groups with youth of all three ethnic groups (Sinhalese, Tamil, and Muslim), and data were used to create the Children's Daily Stressor Scale (CDSS). A factor analysis of the CDSS revealed three subscales or sets of daily stressors: deprivation, child abuse, and inter-parental violence. The addition of these three subscales to the regression model substantially reduced the relationship of war and disaster exposure to all mental health variables; however, the relationship remained significant in all cases, suggesting that war exposure and daily stressors both were contributing significantly to levels of distress and functional difficulties. Mediation analysis further revealed that the relationship of war and disaster exposure to mental health was partially mediated by deprivation and child abuse, a finding consistent with the apparent mediational role of paternal child abuse in the study of Tamil youth cited above ([Catani et al., 2008](#)).

Although the focus of this paper is on the impact of armed conflict and daily stressors on civilians, a recent finding by [Betancourt \(2008\)](#) with former child soldiers in Sierra Leone is germane to our discussion. Based on two waves of data from 156 youth of both sexes, the authors found that having wounded or killed others was significantly related to levels of anxiety and hostility. However, when current stigma (perceived discrimination) related to their status as former child soldiers was added to the analysis, the relationship between wounding or killing and mental health status was no longer significant (i.e., the main effect was no longer significant). That is, the current experience of feeling stigmatized within their communities (a form of chronic daily stress) fully mediated the relationship between the experience of wounding or killing as a combatant and the subsequent development of psychiatric symptomatology. Interestingly, stigma did not mediate the relationship between the experience of rape and self-reported levels of anxiety or hostility. That is, the experience of having been sexually assaulted exerted a main effect on mental health regardless of the level of stigma subsequently experienced in the community.¹

In all of these studies, the addition of daily stressors significantly increased the explanatory power of models predicting psychiatric symptomatology, including symptoms of PTSD in those studies that assessed it. War exposure generally remained an important contributing factor, and as the findings of [Betancourt \(2008\)](#) suggest, it may be that some types of war exposure (e.g., rape) are

particularly likely to influence mental health directly. Clearly, however, the data consistently underscore the importance of taking into account the stressful social and material conditions of everyday life when seeking to understand and address patterns of distress in conflict and post-conflict settings.

The importance of daily stressors to mental health status in non-war-affected populations

The findings we have reviewed above are consistent with research on major life events and “daily hassles” in non-war-affected populations. In a somewhat counter-intuitive yet highly robust set of findings, numerous studies have found that the cumulative effect of daily hassles—the lower level stressors of everyday life—is more strongly predictive of psychological distress than exposure to major life events—the sort of acutely stressful experiences measured by such life events checklists as the widely used [Holmes and Rahe Scale \(1967\)](#) ([Johnson & Sherman, 1997](#); [Kanner et al., 1981](#); [Rowlison & Felner, 1988](#); [Ruffin, 1993](#)). Although both popular and professional attention is consistently drawn to dramatic and potentially traumatic events, whether in peaceful societies or settings of armed conflict, there is a substantial and growing body of evidence which suggests that it may be the less dramatic but more enduring stressful conditions of everyday life that eventually take the greatest toll on people's psychological wellbeing.

Why are daily stressors so stressful?

Having established the important contribution that daily stressors make to mental health and psychosocial functioning in conflict and post-conflict settings, it may be fruitful ask why daily stressors are so impactful. We suggest four reasons. First, daily stressors represent proximal or immediate stressors, whereas war exposure is often more of a distal experience, particular in post-conflict settings or situations of low intensity warfare where violence is episodic rather than constant. Poverty, social isolation, and overcrowded housing confront people on a daily basis; specific acts of political violence, though highly distressing, may have occurred a year or more in the past, and thus simply be less psychologically salient. Research with non-clinical community samples has shown that survivors of traumatic events are generally far more resilient than clinical studies and case reports tend to suggest ([Bonanno, 2004](#)), and that with adequate support and the passing of time, the majority of trauma survivors are likely to regain their psychological equilibrium ([Foa & Rothbaum, 2001](#)). Consequently, distally experienced war exposure may be highly traumatic in the immediate wake of the exposure, but no longer be experienced as traumatic during assessments conducted after a significant period of time has passed ([Thabet & Vostanis, 2000](#)). In contrast, daily stressors represent ongoing and often chronic threats to psychological wellbeing; therefore, their effects are likely to continue being felt even with the passing of time. Because of their chronicity, daily stressors may gradually erode people's coping resources and tax their mental health. [Kubiak \(2005\)](#) has suggested that chronic daily stress may gradually diminish people's capacity to cope effectively with potentially traumatic life events, thereby increasing the likelihood of such events causing enduring symptoms of PTSD. [Sapolsky \(2004\)](#) has documented the numerous ways in which continuous exposure to stressful circumstances—including lower level, non-traumatic stressors—gradually erodes physical and psychological health, and leaves people increasingly vulnerable to both physical and psychological illness. More specifically, research on the psychophysiology of stress suggests that the human stress response is evolutionarily quite well

¹ Betancourt et al. note that their measure of stigma may have failed to adequately capture the particular experience of stigma/discrimination experienced specifically by survivors of sexual assault, which may partly explain the absence of a mediating effect of stigma on the relationship between sexual assault and anxiety or hostility.

adapted to helping us cope effectively with exposure to acute, life-threatening events, which may help explain why, as noted earlier, only a minority of people exposed to potentially traumatic experiences actually develop PTSD or other psychiatric disorders (Bonanno, 2004; Foa & Rothbaum, 2001). In contrast, chronic stress exposure maintains the stress response system (specifically the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis) in a state of continuous activation, which in turn has been linked (via the effects of prolonged exposure to epinephrine, norepinephrine, and glucocorticoids) to increased risk of both physical and emotional disorder (Christopher, 2004; Gunnar & Quevedo, 2007; Sapolsky, 2004).

Second, daily stressors are stressful in part because they are noxious stimuli that are largely beyond people's control (just as direct war experiences are beyond control). Lack of access to clean water, vulnerability to sexual assault while gathering firewood on the outskirts of a refugee camp, overcrowded and unsafe housing, loneliness and a lack of social support because one's family has been killed or dispersed due to violence—these are all stressful circumstances that may lead people to feel a fundamental lack of control over the basic resources on which their physical and psychological wellbeing depend. As Sapolsky (2004) has noted, such lack of control over unpleasant or aversive events contributes powerfully to the perception of those events as stressful. This suggests that psychosocial interventions that foster a greater sense of control over challenging circumstances may hold considerable promise as an approach to reducing stress (and thereby improving mental and physical wellbeing) in conflict and post-conflict settings.

Third, daily stressors are pervasive within conflict-affected populations, whereas direct war exposure is highly variable in many conflict and post-conflict settings (Macksoud & Aber, 1996). Everyone in a refugee camp has been displaced, and everyone must contend with the numerous challenges and hardships of camp life. However, not all camp residents have necessarily been directly exposed to the violence that caused the displacement. This was the case in the previously mentioned study of Darfurian refugees in Chadian refugee camps (Rasmussen et al., *in press*). Fully 25% of the refugees in the study reported having had no direct exposure to organized violence in Sudan; everyone in the study, however, was exposed to the deprivation and vulnerability of life in the camps. The situation was similar among Guatemalan refugees in southern Mexico, many of whom had escaped into Mexico upon hearing of massacres in neighboring villages in the early 1980s (Manz, 1988).

Finally, the term *daily stressors* includes a wide range of stressful phenomena, some of which may be quite traumatic (e.g., child physical and sexual abuse, intimate partner violence). The inclusion of potentially traumatic experiences in the same category as lower intensity chronic stressors such as lack of access to education or overcrowded housing is a problematic issue to which we return below; here we note merely that such potentially traumatic events may account for at least some of the consistently strong relationship that has been found between daily stressors and mental health status, including PTSD.

Are daily stressors really daily? Unpacking the construct

In seeking to broaden the focus of research beyond the effects of direct war exposure, we suggested that research on major life events and daily hassles might offer a useful framework. On closer inspection, however, there are some reasonable objections that might be raised to this parallel. First, daily hassles are generally conceptualized as just that: hassles that occur on a daily basis. However, some of the phenomena we have considered in the category of daily stressors do not necessarily occur daily; in fact,

they may occur only episodically, yet still have a significantly adverse impact on mental health. A child may be sexually abused periodically by a relative or a teacher, a woman may be beaten recurrently though intermittently by her husband, and poisonous snakes may enter homes in refugee camps only occasionally. Though not a daily occurrence, such events are clearly likely to represent significant sources of stress (and distress). What is likely to be daily in these examples is the realistic fear of recurrence and the experience of vulnerability that such intermittent events may elicit.

A second objection is the inclusion under the label *daily stressors* of such a broad range of stressors of highly varied intensity. As noted in the previous section, measures of daily stressors have sometimes included items that may be quite traumatic in their intensity; this does not seem consistent with the lower level types of chronic stress that were intended by the concept of *daily hassles* (Kanner et al., 1981; Rowleson & Felner, 1988). We find merit in this concern, and propose a distinction between lower intensity and potentially traumatic daily stressors. Lower intensity stressors include such experiences as overcrowded housing, lack of access to education and employment, and social isolation resulting from the loss of social networks. Potentially traumatic daily stressors, in contrast, would include experiences such as physical and sexual abuse of children, spousal abuse, and criminal acts not directly related to armed conflict (sexual assault in or around refugee camps by other camp residents or local officials). The concept of potentially traumatic daily stressors is important because it underscores the reality that even in settings of armed conflict, there are sources of psychological trauma other than exposure to the conflict itself. This point was underscored in a recent study of children's mental health in Afghanistan (Panter-Brick, Eggerman, Gonzalez, & Safdar, 2009). Not surprisingly, exposure to violence was strongly predictive of both PTSD and depression symptom levels; however, much of the violence that children reported was not directly related to war exposure, including domestic and community violence, accidents, and medical treatment. In fact, the authors note that "Some children identified severe beatings, a severe accident, or a frightening medical treatment as more traumatic than having witnessed parents or grandparents being killed in rocket attacks" (p. 8). This is a critical point when planning interventions. A focus on healing the effects of previously experienced war trauma may seem profoundly out of sync to a child who is currently being beaten or sexually abused at home or in the community.

Implications for intervention: a sequenced, integrated model

The findings from the literature we have reviewed in this paper suggest the potential utility of an integrated approach to intervention that addresses, in a sequential manner, both daily stressors (low intensity and potentially traumatic) and war exposure. They also suggest the utility of an empirically-informed set of guidelines for the allocation of mental health resources and the development of interventions aimed at improving mental health and psychosocial wellbeing in conflict and post-conflict settings. We note that the guidelines we propose are consistent with those suggested by Barenbaum et al. (2004), Betancourt and Williams (2008), and Bolton and Betancourt (2004).

Guideline 1: It is important to undertake a rapid and contextually grounded assessment of locally salient daily stressors before developing mental health and psychosocial interventions

There are both similarities and differences in the types of daily stressors that are salient in different geographic, economic, cultural, and sociopolitical contexts. Moreover, the salience of

particular stressors is likely to vary by age and gender; for example, children may be particularly vulnerable to school-related problems, parental neglect or abandonment, and physical or sexual abuse, while women may struggle with domestic violence or high rates of reproductive health-related problems. Numerous reports describe quick and efficient methods (focus groups, free-listing, key informant interviews) for identifying locally salient daily stressors, as well as resources available to help people cope with or modify those stressors (Bolton & Tang, 2002; de Jong & van Ommeren, 2002; Miller, Fernando, & Berger, in press).

Guideline 2: Before providing specialized clinical services that target psychological trauma, first address those daily stressors that are particularly salient and can be affected through targeted interventions.

Advocates of psychosocial approaches have long maintained that reducing ongoing sources of stress that tax coping resources, and reestablishing social ties that foster emotional and material support, are likely to go a long way towards improving mental health in war-affected communities. The data we have reviewed are consistent with this position, for several reasons.

First, daily stressors clearly exert a direct effect on mental health. By targeting particularly impactful stressors for change, we can expect to see a direct benefit in terms of reduced distress and improved psychosocial functioning. Second, daily stressors contribute to continuously high levels of stress, and it seems reasonable to infer that coping with continuous stressors—poverty, family violence, unsafe housing, social isolation—is likely to place considerable demands on people's coping resources. To the extent that interventions are able to reduce the occurrence and/or intensity of such stressors, coping resources will be less taxed and thus be more available for healing from any persistent effects of war-related violence and loss. In short, by altering the social and material environments in ways that improve mental health, the need for formal and resource-intensive mental health services may be reduced (Bolton & Betancourt, 2004).

Third, findings from research on stress and social support suggest that strengthening social support networks is likely to exert significant beneficial effects on mental health, and may in fact buffer against the development of PTSD in the wake of exposure to potentially traumatic stress (Norris et al., 2002). This may in turn have the beneficial effect of reducing the need for specialized mental health care.

Finally, as Bolton and Betancourt (2004) have noted, by improving mental health to the extent possible through psychosocial interventions aimed at reducing daily stressors (or, phrased more positively, by improving the quality of the social and material ecology), it will be easier to identify those individuals whose persistent distress does not abate with the reduction of daily stress and who may in fact require specialized assistance.

Guideline 3: When specialized mental health interventions are indicated, interventions should go beyond PTSD to address the diverse forms of distress that may result from exposure to war-related violence and loss.

Although researchers and clinicians have shown a strong interest in PTSD, the studies we have reviewed show that war exposure is also related to a variety of other forms of distress, including depression, anxiety, impaired social functioning, and various local idioms of distress. While recognizing that many symptoms of PTSD are found transculturally and may benefit from clinical intervention, we share Breslau's (2004) concern (see also Barenbaum et al., 2004; de Jong, 2002; Miller, Kulkarni, et al., 2006;

Miller, Omidian, et al., 2006; Summerfield, 1999) that a narrow focus on treating PTSD may reflect the interest of mental health professionals more than it does the actual priorities of community members regarding their own mental health.

Guideline 4: It is essential to take into account that not all symptoms of trauma are necessarily related to conflict exposure. Even in situations of armed conflict, there are other sources of psychological trauma.

Although this may seem intuitive or self-evident, we have been struck by how few studies of mental health in war-affected communities have assessed exposure to forms of traumatic stress other than direct war exposure. Given what is known about the increased risk for PTSD and more complex forms of trauma caused by experiences such as child abuse (Garbarino & Ganzel, 2000; Terr, 1990) and intimate partner violence (Stein & Kennedy, 2001), it seems imperative to us to consider the inclusion of potentially traumatic daily stressors such as these in any assessment of factors contributing to psychological distress in conflict and post-conflict settings. As we suggested earlier, the relevance and impact of mental health or psychosocial interventions are likely to be considerably enhanced when they are seen as targeting those sources of stress that are most immediately and severely affecting people. A programmatic focus on healing the effects of previously experienced war exposure is likely to have limited impact on individuals who are facing ongoing exposure to traumatic stress in their homes or communities.

Conclusion

In this paper, we have sought to bridge the longstanding and unhelpful division between advocates of trauma-focused and psychosocial approaches to understanding and addressing mental health needs in conflict and post-conflict settings. We have suggested that among the various factors underlying this split in the field is a fundamental difference in perception regarding what factors most critically affect mental health in the wake of organized violence. Until recently, there was a paucity of data to inform this largely opinion-based and experience-driven difference in perception. Presently, however, there are sufficient data to permit an empirically-informed discussion. We believe that the findings we have presented make a compelling case for the inclusion of daily stressors in any model purporting to explain patterns of distress in war-affected populations. In fact, the available data suggest that addressing daily stressors should be a priority in the development of mental health policy, the allocation of scarce resources, and the design of interventions to assist war-affected communities. Daily stressors are strongly related to the severity of psychological distress and psychiatric symptomatology; and, because they are ongoing, may be targeted for change through well-designed intervention programs.

The inclusion and prioritization of daily stressors by no means negates the value of more specialized clinical interventions for highly distressed individuals whose symptoms do not abate with the normalization of their environment through the reduction of daily stressors. War exposure does exert a direct and adverse effect on mental health, though the data are not consistent with the current trend towards conceptualizing that effect solely in terms of PTSD. We suggest that a broad range of specialized interventions should be brought to bear, from culturally informed adaptations of Western treatment strategies (Hubbard & Pearson, 2004) to the use of traditional healers whose explanatory models and methods of treatment are more likely to be familiar to community members (de Jong, 2004).

As we suggested in the introduction to this paper, the difference in underlying conceptual models is by no means the only point of disagreement between trauma-focused and psychosocial advocates. Other issues must also be addressed, such as the appropriateness of applying Western diagnoses, the efficacy of professionally staffed clinical treatments in non-Western cultural contexts, and even the appropriateness of mental health outcomes altogether. We recognize, for example, that many advocates of psychosocial interventions eschew a narrow focus on reducing psychopathology as the desired outcome of their interventions, opting instead to focus on strengthening families and communities and promoting positive outcomes in children (Boothby et al., 2006; Kostelny & Wessells, 2004). It is our hope that in seeking to build a bridge between more clinically focused and psychosocially oriented approaches, we have at least helped initiate a discussion that may lead to further exploration of common ground and collaboration between the advocates of these two influential frameworks.

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Exhibit I

Research letters

Mental health of detained asylum seekers

Allen S Keller, Barry Rosenfeld, Chau Trinh-Shevrin, Chris Meserve, Emily Sachs, Jonathan A Leviss, Elizabeth Singer, Hawthorne Smith, John Wilkinson, Glen Kim, Kathleen Allden, Douglas Ford

Asylum seekers arriving in the USA are likely to be held in detention for months or years pending adjudication of their asylum claims. We interviewed 70 asylum seekers detained in New York, New Jersey, and Pennsylvania. We used self-report questionnaires to assess symptoms of anxiety, depression, and post-traumatic stress disorder. At baseline, 54 (77%) participants had clinically significant symptoms of anxiety, 60 (86%) of depression, and 35 (50%) of post-traumatic stress disorder; all symptoms were significantly correlated with length of detention ($p=0.004$, 0.017 , and 0.019 , respectively). At follow-up, participants who had been released had marked reductions in all psychological symptoms, but those still detained were more distressed than at baseline. Our findings suggest detention of asylum seekers exacerbates psychological symptoms.

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Worldwide, there is a growing trend toward detention of asylum seekers arriving in industrialised countries for months or even years pending adjudication of their asylum claims.¹ In the USA, 5000 asylum seekers are estimated to be held in detention,^{1–3} although reliable statistics on the number of detained asylum seekers are unavailable. Detention of asylum seekers has concerned health professionals and human rights advocates, in part because of the potential detrimental effects on the mental health of detainees.^{1,3} Research on this subject, however, has been limited by difficulties in gaining access to detention centres. The Bellevue New York University (NYU) Program for Survivors of Torture and Physicians for Human Rights have done a systematic and longitudinal study of the effects of postmigration detention on the mental health of asylum seekers.

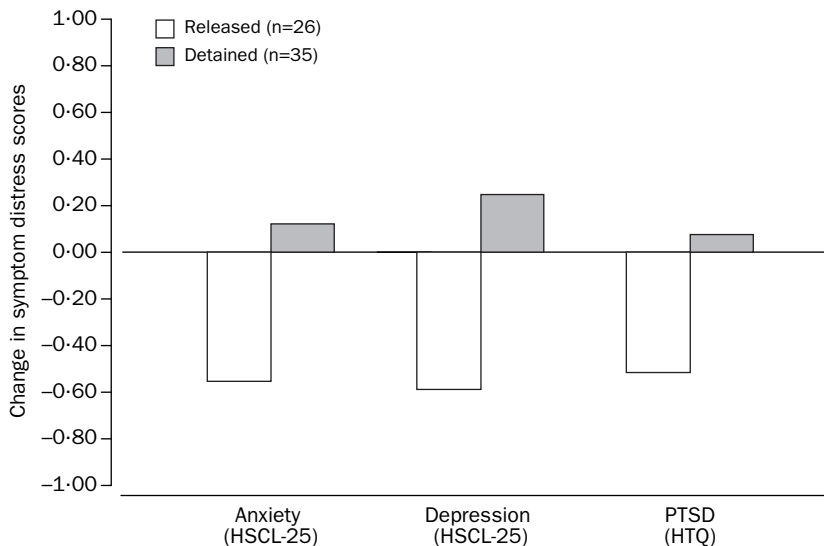
The US Immigration and Naturalization Services (INS) permitted access to detention facilities in New York, New Jersey, and Pennsylvania. These facilities included two INS detention centres run by private contractors. These jails are virtually windowless converted warehouses where only non-criminal INS detainees are incarcerated. Additionally, access was permitted to three local government-run jails in which criminals are also held. In all of these facilities, asylum seekers are heavily guarded, required to wear jail uniforms, and are shackled whenever they are transported outside of the detention facilities. The INS did not allow us access to a random sample of detained asylum seekers at these facilities. Therefore, we asked six local organisations providing pro-bono legal representation to detained asylum seekers to contact clients and ask about their willingness to be interviewed. Detainees were informed by researchers of the voluntary nature of the study and that participation would not affect their asylum applications. We obtained written informed consent from all participants. The study was approved by the Institutional Review Board of New York University School of Medicine and a review committee for Physicians for Human Rights.

Detainees were interviewed by physicians experienced in caring for refugees; translators assisted if necessary. Standardised psychological symptom measures were used: the Hopkins symptom checklist-25 (HSCL-25)⁴ and the post-traumatic stress disorder subscale of the Harvard trauma questionnaire (HTQ).⁵ Both measures have been used in studies of refugee populations and previously translated and back-translated in several languages, including French, Spanish, and Arabic. For participants who spoke other languages, scales were translated by the interpreter. Demographic information and history of

	Detained (n=35)		Released (n=26)	
	Number (%) above recommended cut-off*	Symptom scores, mean (SD)	Number (%) above recommended cut-off*	Symptom scores, mean (SD)
Baseline				
Anxiety	28 (80%)	2.40 (0.71)	19 (73%)	2.33 (0.72)
Depression	30 (86%)	2.52 (0.69)	22 (85%)	2.45 (0.65)
PTSD	19 (54%)	2.52 (0.62)	10 (39%)	2.45 (0.62)
Follow-up				
Anxiety	30 (86%)	2.58 (0.80)	9 (35%)	1.59 (0.56)
Depression	31 (89%)	2.73 (0.70)	10 (39%)	1.65 (0.59)
PTSD	21 (60%)	2.63 (0.71)	3 (12%)	1.80 (0.56)
Change in symptom scores†				
Anxiety	..	0.17 (0.61)	..	-0.75 (0.84)
Depression	..	0.21 (0.42)	..	-0.80 (0.81)
PTSD	..	0.12 (0.51)	..	-0.64 (0.64)

PTSD=post-traumatic stress disorder. *Cut-offs: 1.75 for HSCL-25 depression and anxiety subscales, 2.5 for HTQ. †p not significant for changes in any symptom score in detained group. $p=0.0001$ for all three symptom score changes in released group. Mean (SD) values are group mean at each assessment. Change=change in mean score from baseline assessment.

Psychological symptoms of asylum seekers still detained and those released at follow-up



Changes in psychological distress at follow-up

PTSD=post-traumatic stress disorder.

traumatic experiences were elicited from participants' asylum applications. Detainees who could be located were followed up 2 months or more after the initial interview to assess psychological changes.

Spearman correlation coefficients were used to analyse the relation between length of detention, which had a skewed distribution, and psychological distress. Independent sample *t* tests were used to assess differences in psychological distress between baseline and follow-up for patients who had been released and those still detained at follow-up.

Between Jan 1, 2001, and June 15, 2002, 87 detainees (73% of the caseload for the six agencies providing referrals) were referred to the study. Of these 87, 17 were excluded from the study: one was deported; ten were released before interview; one had been granted asylum but was still awaiting release; three did not complete the interview questionnaires; one withdrew the asylum claim; and one lost pro-bono legal support. Analyses are based on the remaining 70 participants (56 male, 14 female, mean age 28 years [SD 7.3; range 15–52]). Follow-up interviews were done at a median of 101 days (62–299) with 61 participants; 35 were still in detention and 26 had been released. Of the 26 released, 22 had been granted asylum and four released without asylum for medical or humanitarian reasons. Of the nine participants lost to follow-up: two had been deported; five could not be located; one had been transferred to another facility; and one refused to be interviewed. In April, 2003, 40 (57%) of the 70 participants had been granted asylum in the USA, and 14 individuals (20%) had been denied asylum and deported. Of the 40 individuals granted asylum, the median length of detention had been 7 months (2–42).

61 (87%) participants were detained in two INS detention centres and nine (13%) in three local government-run jails. The median length of detention before initial interview was 5 months (1–54). Most participants were from Africa (n=54), seven were from eastern Europe, four from Asia, two from the Middle East, and three from South America. 28 interviews were done in English, 17 in French, seven in Arabic, and 18 in other languages.

52 (74%) detainees had been tortured before immigration, 47 (67%) had been imprisoned in their native country, 41 (59%) reported the murder of a family member

or friend, and 18 (26%) reported sexual assault. 54 (77%) detainees had clinically significant symptoms of anxiety, 60 (86%) of depression, and 35 (50%) of post-traumatic stress disorder. 18 (26%) participants reported thoughts of suicide while in detention, and two reported having attempted suicide.

49 (70%) participants perceived their mental health as having worsened substantially while in detention, and this perception was supported by Spearman correlations between length of time in detention and baseline levels of anxiety ($r_s=0.34$, $p=0.004$), depression (0.28 , $p=0.017$), and post-traumatic stress disorder (0.28 , $p=0.019$). Baseline mental health scores did not differ significantly between detainees eventually released and those who remained in detention, although differences were significant at follow-up (table). Participants still

detained at follow-up had increased symptom scores for anxiety, depression, and post-traumatic stress disorder, whereas those who had been released had lower scores on all three scales ($p<0.0001$; figure).

Nearly all the detainees in our study had clinically significant symptoms of anxiety, depression, or post-traumatic stress disorder, which worsened with time in detention and improved on release. Our findings support anecdotal observations of other researchers and highlight the concerns raised by health professionals about the adverse effect of detention on asylum seekers.^{1,2}

A limitation of our study is that there was no comparison group of non-detained asylum seekers. Although our sample of released participants was confounded by the fact that most were also granted asylum, the significant correlation between symptom severity at baseline and length of time in detention supports the hypothesis that detention significantly contributed to psychological distress. However, our reliance on self-report questionnaires rather than diagnostic interviews might have increased the proportion of individuals assessed as having clinically significant distress. Additionally, sampling was not random, which might limit the general applicability of our results to the entire population of detained asylum seekers. Furthermore, although we have no reason to think that detained asylum seekers represented by pro-bono legal groups differ from other detained asylum seekers, we cannot be certain.

Some participants could have deliberately exaggerated psychological symptoms, past traumatic experiences, or both, in order to bolster their asylum claims—despite being informed that their asylum application would not be affected by their responses. Nevertheless, the large proportion of participants ultimately granted asylum lends credence to their reports. Furthermore, there was no difference in reported distress at baseline or premigration traumatic experiences between detainees who were or were not granted asylum. Finally, despite a marked reduction in symptoms after release, many participants still had high levels of psychological distress, suggesting that symptom endorsement was not solely motivated by secondary gain.

Despite the limitations of this study, our results suggest that detaining asylum seekers exacerbates symptoms of depression, anxiety, and post-traumatic stress disorder in this vulnerable population. Our findings suggest that

policies concerning detention of asylum seekers should be reviewed, and highlight the need for mental health intervention to address the psychological needs of these individuals.

Contributors

A Keller, D Ford, C Trinh-Shevrin, J Leviss, H Smith, K Allden, and G Kim conceived and designed the study. A Keller, C Meserve, E Sachs, J Leviss, E Singer, H Smith, and J Wilkinson participated in the acquisition of data. E Sachs coordinated data collection. C Trinh-Shevrin and B Rosenfeld did statistical analyses. A Keller, B Rosenfeld, C Trinh-Shevrin, D Ford, C Meserve, J Leviss, E Sachs, and B Rosenfeld participated in analysis and interpretation of data. All authors helped to write the report.

Conflict of interest statement

None declared.

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Association of intercellular adhesion molecule-1 gene with type 1 diabetes

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Intercellular adhesion molecule-1 (ICAM-1) functions via its ligands, the leucocyte integrins, in adhesion of immune cells to endothelial cells and in T cell activation. The third immunoglobulin-like extracellular domain binds integrin Mac-1 and contains a common non-conservative aminoacid polymorphism, G241R. Phenotypically, ICAM-1 has been associated with type 1 diabetes, a T-cell-mediated autoimmune disease. We assessed two independent datasets, and noted that R241 was associated with lower risk of type 1 diabetes than is G241 (3695 families, relative risk 0.91, p=0.03; 446 families, 0.60, p=0.006). Our data indicate an aetiological role for ICAM-1 in type 1 diabetes, which needs to be confirmed in future genetic and functional experiments.

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The molecular mechanisms underlying type 1 diabetes are partly known. Three disease loci have been identified so far: the human leucocyte antigen (HLA) complex, the variable number tandem repeat locus located in the promoter region of the insulin gene (*INS*), and the cytotoxic T lymphocyte-associated antigen-4 gene (*CTLA4*).¹ The known functions of these genes suggest that T-cell activity is an important pathway in development of type 1 diabetes. Results of research in the mouse shows that ICAM-1 function during immune priming is necessary for the generation of effector T cells capable of destroying pancreatic insulin-producing β cells.² Genetic analysis of the ICAM-1 gene in families affected by type 1 diabetes could indicate whether its function has a causal role in the disease.

ICAM1 is located on chromosome 19p13 in a region that has shown some evidence of linkage to type 1 diabetes.¹ Two non-synonymous single nucleotide polymorphisms are known to be frequent in European populations: G→A in exon 4 encoding G241R, and A→G in exon 6 encoding K469E (rs1799969 and rs5030382, respectively; <http://www.ncbi.nlm.nih.gov/SNP/>). The K469E polymorphism has been investigated in type 1 diabetes in small samples, with variable results.³ We assessed association of these two *ICAM1* coding polymorphisms in a sample of 3695 families affected by type 1 diabetes.

All family members were white, from Europe or the USA, with at least one affected child in every family (table). Mean age at onset of the affected offspring was 9.3 years (range 0–50). We obtained approval from the relevant research ethics committees and written informed consent of participants. DNA samples were genotyped with Invader (Third Wave Technologies, Madison, WI, USA) and TaqMan (Perkin Elmer Applied Biosystems, Foster City, CA, USA) assays. We recorded 99.5% concordance between these methods in 1242 samples tested to assess error in genotyping of the G241R polymorphism. Statistical analysis was done with STATA (version 8.1). Calculations of p values and 95% CI of relative risk (RR) were based on robust variance estimates, used to correct for clustering of affected individuals within families.

K469E did not show any association with the disease: K469 was transmitted 1931 times of 3897 (49.6%, p=0.59). By contrast, R241 was transmitted significantly less often: 938 transmissions of 1974 (47.5%, p=0.03; table). To control for the possibility that genotyping error or transmission ratio