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The Burden of Diabetes and Use of Diabetes Care in Humanitarian Crises in Low- and Middle-Income Countries

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ABSTRACT

Human suffering arising out of disaster or conflict includes death and disability from non-communicable diseases, including diabetes, which have largely been neglected in humanitarian crises. The objectives of this paper were to examine the evidence on the burden of diabetes, utilization of health services, and access to care for people with diabetes among populations affected by humanitarian crises in low- and middle-income countries and identify research gaps for future studies We performed a review of the literature on this topic published between 1992 and 2018. The results highlight that the burden of diabetes in humanitarian settings is not being captured, clinical guidance is lacking, and suggest diabetes is not being adequately addressed. Crisis-affected populations with diabetes face enormous constraints in accessing care, primarily due to high medical costs. Further research is needed to characterize the epidemiology of diabetes in humanitarian settings and develop simplified, cost-effective models of care to improve the delivery of diabetes care in the wake of global disasters.

INTRODUCTION

As a result of humanitarian crises, forced migration due to conflict has reached a record number with 68.5 million people forcibly displaced from their homes by the end of 2017.[4] Of these, 25.4 million refugees have fled across international borders and approximately 40 million internally displaced persons (IDPs) have been forcibly displaced within their own country.[5,6] There are also approximately 100 million people who are affected by conflict, but are not displaced.[7] Natural disasters affect an estimated 175 million people annually.[8] In addition, emergencies are increasingly becoming protracted with the average length of forced displacement being over 20 years.[6] Low- and middle-income countries (LMICs) host around 84% of forced migrants globally and commonly have very limited resources to respond to their health needs.[6] LMICs also carry the largest burden of diabetes.

Individuals with diabetes are particularly vulnerable in humanitarian crises, given disrupted health services and impeded food supplies due to insecurity and population movement.[9] This risks exacerbating medical complications from diabetes, particularly for those with type 1 diabetes (T1D). In addition, crisis-affected populations are at risk of developing or exacerbating diabetes through elevated mental disorders and risky behaviours, such as harmful alcohol use. The increasing trend towards urbanisation of crisis-affected populations may also lead to environmental risk-factors related to diet, physical activity and tobacco use.[10] Moreover, childhood malnutrition and exposure to maternal undernutrition in utero increase the risk of diabetes in adulthood.[11,12]

The problem of diabetes and other non-communicable diseases (NCDs) has largely been neglected in humanitarian settings.[9,13-15] Historically, the main causes of morbidity and mortality in humanitarian settings were infectious diseases and malnutrition, particularly among children.[15] Given global epidemiological changes and that LMICs are now commonly affected by crises (where the underlying burden of NCDs is high), humanitarian agencies and governments are challenged with how to effectively tackle diabetes and other NCDs.[9] While there is a growing literature on the burden of NCDs in LMICs, including diabetes, it is unclear whether these studies can be generalised to humanitarian crisis. It is not known what the burden of diabetes is, which interventions are effective and feasible, and there is a lack of evidence-based guidelines and basic

diagnostic, clinical and preventive resources for the management of diabetes in humanitarian contexts.[13,14]

This Series seeks to outline the evidence on the burden of diabetes among crisis-affected populations and capture contemporary challenges in the management of diabetes in humanitarian crises in LMICs. The aim of this first Series paper is to examine evidence on diabetes among crisis-affected populations in LMICs and propose future research priorities. The specific objectives are to: (1) examine the evidence on the burden of diabetes among populations affected by humanitarian crises in LMICs and (2) describe the evidence on health service utilization and access to care for people with diabetes in these settings in order to identify main research gaps and propose priorities for future research. The search strategy and selection criteria for the review are summarized in Panel 1 and detailed in Online Annex 1. The second Series paper describes the concrete challenges of diabetes care delivery in humanitarian crises.[16]

EXISTING EVIDENCE

We identified evidence from forty-one eligible studies.[17-57] All studies were published between 1992 and 2018, with thirty-three published since 2011. Thirty-eight studies reported on populations affected by armed conflict,[17-25,27-33,35,36,38-57] two reported on populations affected by natural disasters,[34,37]and one on all crisis types.[26] Thirty-four studies were conducted in the protracted crisis phase (crisis duration greater than six months),[17-25,27-33,35,39-48,50,52-57] three in the emergency response phase (immediate aftermath of the event up to six months),[36,49,51] two in the early recovery phase (more stable period of rebuilding up to two years following the crisis),[34,38] and two reported on multiple crises phases.[26,37] Twenty-five studies addressed refugee populations,[17-21,25,26,29-31,33,35,39-43,47,48,50,52-55,57] five addressed IDPs,[22,28,32,46,56] and eleven addressed non-displaced conflict-affected populations.[23,24,27,34,36-38,44,45,49,51] The majority of studies were conducted in the WHO Eastern Mediterranean (N=30),[17-24,28-33,39-44,46-48,50,52-57] followed by Europe (N=6),[25,27,36,45,49,51] Western Pacific (N=2),[34,37] South-East Asia (N=1), Africa (N=1), and one covered refugees bound for the United States.[26] Further details on the studies can be found in Table 1 and Online Annex 2.

Burden of diabetes

The evidence on the burden of diabetes among crisis-affected populations was extremely limited and the overall quality of the studies was poor. Diabetes was most commonly used as a single diagnosis and distinctions between T1D, type 2 (T2D), and gestational diabetes (GDM) were rarely made. Three studies focused exclusively on T1D,[27,49,51] eight categorized patients into T1D and/or T2D,[24,32,33,40,41,47,52,53] and two reported on women with GDM.[21,35] Atypical forms of diabetes were not addressed. Only eighteen studies[17,18,20-23,25,28-31,33,45,46,50,52,55,56] assessed the burden of diabetes at the population level using probabilistic sampling (rather than health-facility level using non-probabilistic sampling) and the majority of these relied on self-report rather than medical diagnosis.

Diabetes prevalence rates varied substantially. Prevalence rates of diabetes in displaced Syrian populations during the crisis ranged from as low as 0.8% in Syria[56] and Iraq[53] to as high as 35% in certain governorates of Iraq.[17] When examining older populations (age >60 years), diabetes prevalence rates ranged from 31.8% in Syria[31] to 47% in Lebanon.[55] An assessment on the healthcare needs of IDPs in Iraq reported a 2.8% prevalence of GDM.[22] However, over half of the pregnant women interviewed had not received a single antenatal visit by their third trimester and therefore not been screened for GDM.

In Europe, two studies reported pre- and post-conflict incidence rates of insulin-dependent diabetes (IDDM) in Croatia using the national diabetes registry.[49,51] One study reported the annual age-adjusted incidence of IDDM in children (ages 0-15) in Zagreb of 7.0 in 1988 before the war and 7.8 in 1992 after the war.[49] The second study reported annual incidence rates of IDDM in Zagreb of 6.6 per 100,000 in 1988 and 5.9 per 100,000 in 1992.[51] In the Tuzla region of Bosnia and Herzegovina, which was heavily affected by war, the incidence rate of NIDDM from 1990-1998 was 3.03 per 100,000 person years.[27] In Turkey, 4.1% of Syrian refugees self-reported a diagnosis of high blood sugar (was not further defined) in the past twelve months.[25]

The only study conducted in South-East Asia reported the prevalence of GDM in a refugee camp at the Thai-Myanmar border, screening pregnant women with a 75mg oral glucose tolerance test (OGTT).[35] Although the sample size was small and the number of all pregnant patients in the catchment area was not recorded, the estimated prevalence rate was 10.1% using HAPO trial cut-off values.[58]

In Africa, the only identified study was a retrospective study evaluating mortality patterns based on chart review at a hospital in Liberia.[38] Two percent of deaths from January through July 2005 were attributed to diabetes.

Glycaemic control and diabetes complications

Seven studies reported on glycaemic control,[24,40,41,45,49,52,53] but how this was assessed varied and often relied on fingerstick glucose readings at different times of day, such as fasting or two hours post-prandial (2hPPG). Hemoglobin A1C (A1C) measures were reported in six studies.[27,24,45,49,52,53]

An analysis of the national diabetes registry in Croatia during the war in 1991 reported an average fasting glucose of 194.4 mg/dl (10.8 mmol/l) in displaced persons (average A1C 9.8% (84 mmol/mol)) and 183.6 mg/dl (10.2 mmol/l) in non-displaced persons (average A1C 9.1% (76 mmol/mol)), which was not significantly different (p=0.38).[49] In Bosnia and Herzegovina a study assessed the impact of three years of war on glycaemic control using hospital data from Sarajevo. Between 1992 and 1994/1995 there was a mean weight-loss of 11.7 kg with a reduction in mean fasting glucose from 207.0 mg/dl (11.5 mmol/l) pre-war to 176.4 mg/dl (9.7 mmol/l) post-war, and A1C reduction from 10.3% (89 mmol/mol) to 9.0% (75 mmol/mol) ($p<0.01$).[45] This was accompanied by a reduction in blood pressure (BP) and hypoglycaemic medication use.

In the Eastern Mediterranean, a cross-sectional study of Syrian refugees in a camp setting in Iraq reported an average A1C of 9.3% (78 mmol/mol) in individuals with T1D.[53] Of these, 9.1% had A1C values <7.5% (58 mmol/mol) and 82% >8% (64 mmol/mol). Among those with T2D, the average A1C was 8.8% (73 mmol/mol), with 4.7% having an A1C <7.5% (58 mmol/mol) and 62% an A1C >8% (64 mmol/mol). Two studies by the United Nations Relief and Works Agency for Palestine Refugees (UNRWA) assessing Palestinian refugees in Jordan assessed glycaemic control via 2hPPG. In one study, 42% of those with diabetes attending the clinic had their post-prandial glucose measured.[41] Of those, 50% had a 2hPPG of <180 mg/dl (10 mmol/l), which was considered good control. In the other study, done one year later, 99% of those attending the clinic had their post-prandial glucose measured, of which 65% had a reading <180 mg/dl (10 mmol/l).[40] In Yemen, a significant increase in A1C from 7.7% (61 mmol/mol) to 9.4% (80 mmol/mol) was shown when comparing the same individuals before and during the war.[24]

Diabetes complications and surveillance were mentioned in five papers.[33,40,41,52,53] In two studies by UNRWA in Jordan, the most common complications noted were myocardial infarction, congestive heart failure and stroke.[40,41] Another study by UNRWA with Palestine refugees in Gaza, Jordan, Lebanon and the West Bank, reported the most common complications were peripheral neuropathy (52.6%), foot infections (17%), diabetic retinopathy (11%) and myocardial infarction (9.6%).

Among Syrian refugees in a camp setting in Iraq, 63.6% of individuals with T1D self-reported having had episodes of symptomatic hypoglycemia, and 36.6% reported at least one episode of diabetic ketoacidosis.[53] Among those with T2D, 24.3% reported having had at least one episode of hypoglycemia and 0.52% reported having had at least one episode of diabetic ketoacidosis. Hyperosmolar hyperglycaemic syndrome was not reported

Cardiovascular risk

The control of cardiovascular risk factors in populations with diabetes, particularly hypertension and hyperlipidemia, was addressed in six studies.[24,40,41,45,52,53] Two studies compared hypertension control in cohorts of individuals with T2D pre- and post-conflict. In Yemen, BP control in the cohort with diabetes improved during the war.[24] Likewise, in a cohort of fifty-five individuals with IDDM in Sarajevo, twenty-five individuals had BP readings >140/90 mmHg before the war and only twelve after the war ($p<0.01$).[45]

Three studies were surveys of UNRWA programs for Palestine refugees with diabetes: The first was a survey of UNRWA health centers in 2011 and reported the presence of co-morbid hypertension in 68.5% of the population with diabetes. 55% had BP readings ≤140/90 mmHg and 28.2% had readings ≤130/80 mmHg.[52] Cholesterol levels were elevated >200 mg/dl in 39.8% of the population. Only 53.4% of patients with hyperlipidemia were on lipid lowering agents and most were making out-of-pocket payments.

A second study with Palestine refugees in Amman, Jordan, reported 79% of the population had an associated diagnosis of hypertension, of which 63% had their BP measured and 75% had readings <140/90 mmHg.[41] When evaluating the past 12-15 months, all patients with diabetes were reported to have had a total cholesterol level measured and of those, 72% had cholesterol levels <200 mg/dl. The third study evaluated cumulative and quarterly data on diabetes treatment outcomes from primary healthcare clinics across Jordan.[40] They reported that 78% of patients returned for follow-up within the last quarter with >99% having undergone BP and cholesterol measurements. Of these, 82% had BPs <140/90 mmHg and 71% had blood cholesterol levels <200 mg/dl.

Among Syrian refugees with diabetes in a camp in Iraq, 9.1% of those with T1D and 55.4% of those with T2D were on antihypertensive agents (67.3% on ACE inhibitors).[53] Among those with T1D, systolic and diastolic BP were controlled in 81.8% and 72.7% of patients, respectively. Among those with T2D, systolic BP was controlled in 54.9% and diastolic BP in 36.3% of patients. 9.1% of refugees with T1D and 49.7% of those with T2D were treated with statins. However, in both groups cholesterol levels were not significantly different between those on and off statins.

Health service utilization and access to care

Ten studies reported health service utilization (the frequency and type of care consumed) and access to care,[17,18,20-22,28-31,55] of which seven reported data on NCDs as a group (all included diabetes) and three studies reported data on diabetes separately.[22,29,30] All were cross-sectional

household surveys conducted in the Eastern Mediterranean, which limits generalizability of the findings. Care-seeking behaviours, access to care, and health service utilization were generally not defined, making the results difficult to interpret. None of these studies reported data on health service utilization or access to care disaggregated by gender. Although healthcare service utilization was mostly reported for NCDs as a group, the results are described here since they include information on access to care for people with diabetes and the barriers to care for different NCDs are often similar.

Care-seeking behaviours for those with self-reported NCDs who needed care were generally high among displaced populations in urban and camp settings in the Eastern Mediterranean (these were the only studies that included such data).[20,21,30,31] Care was most commonly sought in primary healthcare facilities.[20,21,29] One study reported that refugees with self-reported diabetes had the highest frequency of care-seeking among Syrian refugees with an NCD in Lebanon.[29] Their results describe that 88.2% of Syrian refugees with diabetes had sought care since their arrival and 70% within the three months preceding the survey (of which 60.8% sought care in primary healthcare centres). Among displaced Yazidis in Iraq, 92.9% of those reporting an NCD diagnosis had seen a health provider for their condition during the three months preceding the survey.[28] In Jordan and Syria, 85% of Iraqi refugees indicated that medical attention was sought the last time it was needed.[31]

Despite high care-seeking behaviors, access to health services and medicines for NCDs appeared limited. Among Iraqi refugees with NCDs in Jordan and Syria who reported high care-seeking behaviors (>80%), only 62.5% of those in Jordan and 58.8% of those in Syria could get medical care when necessary.[31] In Lebanon, 56.1% of Syrian refugees reported difficulty accessing care for NCDs.[20] Among older Syrian refugees (>60 years of age) in Lebanon, of whom 47% reported having diabetes, nearly all surveyed reported the inability to obtain adequate medical treatment, primarily due to cost (3% reported having the resources to afford medications).[55]

High costs due to out-of-pocket payments for consultation fees, medication prices, diagnostic tests, and transportation were the most common reason for not being able to access or continue care in all ten studies among all NCDs.[17,18,20-22,30,31,55] The high costs were prohibitive to even seeking care for over half of Syrian refugees with diabetes in Jordan (51.7%).[30] In Lebanon, 91.2% of Syrian refugees reported the expense of medical services being the greatest obstacle while seeking NCD care.[21] In that study, 46.1% of those with chronic conditions reported treatment interruptions, primarily due to medication costs (89.3%), and 6% reported this was due to dangers in the area where medications were disbursed. Among Yazidis with NCDs displaced in Iraq who had reported high care-seeking behaviors, 40.0% were not taking prescribed medications, mainly citing the high costs.[28] In Lebanon, 31.5% of Iraqi refugees with chronic conditions were not taking medications due to cost (78.9%) or lack of availability (10%).[21]

Approximately 70% of all Syrian refugees in Lebanon paid out-of-pocket for consultant, diagnostic and laboratory fees.[29] They noted that refugee spending on consultation fees was similar among the five NCDs assessed in the study, when measured by the proportion of patients with an out-of-pocket consultation payment.[29] A UNHCR survey estimated the average monthly out-of-pocket general health expenditure was USD$90 per household for Syrian refugees in Lebanon who needed care (the average monthly non-assisted household income was USD$173).[20] Another survey reported a mean monthly expenditure on health for Iraqi refugees of USD$70 in Jordan and USD$91 in Syria.[31] Most of the expenses were at outpatient and inpatient facilities for services and treatment (52.5%) and medicine and treatment supplies (29.0%). To cover these costs, 53.9%

of Syrian refugees in Lebanon borrowed money, 39.4% used household income, and 27.8% relied on relatives or friends.[20]

Aside from the cost of care, the unavailability of services was a barrier to care.[17,21,22,35] In a study of Iraqi IDPs, the lack of medication at health facilities was cited as the most important barrier (23.7%).[22] Only six papers in the literature review mentioned the types of diabetes medications that were prescribed and none reported on their availability.[24,33,43,44,52,53] The next most common barrier to access was a lack of services available (18.4%). A report on Syrian refugees in Iraq cited the unavailability of services and the cost of care as the most common challenges of accessing healthcare.[17] In two districts in Iraq, an estimated 6% of Syrian refugee households reported returning to Syria to seek healthcare.[17]

KEY EVIDENCE GAPS AND NEXT STEPS FOR RESEARCH

Our study demonstrates evidence assessing the burden of diabetes in humanitarian settings is very limited and of generally low quality. The levels of needs are not being adequately captured, particularly in crises beyond the Eastern Mediterranean. The following discussion reflects on the results of the review and proposes key research priorities based on these findings and our experience of working in and researching diabetes care in crisis-affected settings (summarized in Table 2).

Burden of diabetes data

Sampling techniques and outcome measures

There are significant knowledge gaps of the epidemiology of diabetes in humanitarian settings, especially in Africa and South-East Asia. Most studies were conducted in conflict-affected populations in the Eastern Mediterranean, predominantly with refugees in host countries, rather than in areas of conflict. Thus, further research is needed within conflict-affected countries, particularly the acute phase of a crisis, and for natural disasters.

Prevalence estimates were limited and difficult to interpret or generalize since nonprobability sampling techniques were frequently used.[59] Most studies identified in the review did not report criteria used to diagnose or monitor diabetes. Fingerstick glucose and A1C measurements were not available or reported in most studies. Another weakness was reporting deaths due to diabetes, since most individuals die from complications of diabetes rather than acute exacerbations.

Most cross-sectional surveys used self-reported medical diagnoses that were not verified by medical reports, which risks misdiagnoses and prevalence underestimations. For example, in a cross-sectional survey of Palestinian households in the West Bank and Gaza Strip that relied on self-report, 2.8% of adults had diabetes in the West Bank and 1.9% in the Gaza Strip.[23] This contrasts with IDF estimated prevalence rates of 7.0% in Palestine.[60] Among Syrian refugees in Lebanon, a household telephone survey with refugees reported a diabetes prevalence of 18%, whereas a cross-sectional cluster survey reported a prevalence of 9.9%.[20,29] Despite these differences, multiple studies identified in this review reported diabetes as being one of the top three reasons for seeking care in Eastern Mediterranean countries.[17-21,29] However, the value of this data for directing resources is questionable, given the lack of uniform standards for data collection.

Diabetes phenotyping

The evidence identified in the review failed to adequately capture the various phenotypes of diabetes. Across most studies retrieved from our search, diabetes was most often reported as a

single entity and distinctions between even the most common subtypes of diabetes (T1D, T2D, and GDM) were rarely mentioned. Making these distinctions is important in terms of triage, management decisions, and resource allocation. For example, in the acute phase of an emergency, identifying and prioritizing the care of individuals with T1D is crucial to minimize serious complications and death.

Only two studies reported on the burden of GDM.[21,35] However, global estimates from 2017 suggest approximately 16% of total live births were affected by hyperglycemia in pregnancy, of which 88% were in LMICs.[60] GDM increases the maternal risk of developing T2D later in life, is associated with serious adverse pregnancy outcomes, and carries the risk of transgenerational metabolic effects on the fetus which can be reduced through identification of GDM and glucose control in the mother.[60] Considering the volume of obstetric and perinatal care in many humanitarian settings,[6] screening and management of hyperglycemia in pregnancy needs to be integrated into routine perinatal care.

Furthermore, atypical forms of diabetes have been emerging in recent decades. Ketosis-prone diabetes has become a recognized entity in populations mostly of African descent.[61] These individuals are generally overweight or obese and present with ketoacidosis at diagnosis, but typically do not require long-term insulin therapy. There are also lean phenotypes of diabetes that are reported mostly in LMICs, such as malnutrition-modulated diabetes (MMDM) and fibrocalculous pancreatic diabetes.[62,63] Individuals with these forms of diabetes are extremely lean and require high doses of insulin for good glycaemic control, however ketonuria rarely occurs. Jobanputra et al. recently reported that staff at an MSF-supported hospital in the Democratic Republic of Congo are managing both patients with T2D, as well as those with MMDM who have high insulin requirements and show signs of chronic complications early on.[10] Thus, it is important to recognize that individuals with diabetes may not always present in a typical manner and we need to better characterize the epidemiology of diabetes in low-resource settings to identify individuals with diabetes, particularly in protracted crises, and allocate insulin to those who need it most.

The dearth of baseline epidemiological data hinders appropriate needs-assessments and response-planning which are essential to effectively meet the needs of crisis-affected populations. The development and standardization of epidemiologic tools and methods, particularly digital surveillance systems, are needed to more accurately capture the burden of diabetes (and other NCDs) and related health needs in crisis settings.

Diabetes management and monitoring

This review highlights the differences in treatment targets, standards of care, and monitoring for diabetes in humanitarian crises. Clinical guidance on the management and follow-up of diabetes in humanitarian settings is lacking and the knowledge-base on cost-effective models of care in such environments is very limited.[9,10,13,14] Appropriate diagnostic cut-offs and glycaemic targets for diabetes care in humanitarian crises are unclear. This is particularly relevant in settings where individuals prescribed hypoglycaemic agents are exposed to significant food insecurity, home-based glucose monitoring is unavailable and clinical follow-up is jeopardised due to insecurity. Moreover, optimum glucose testing methods, timing, and location in these settings are unknown.[64] It is also unclear how best to engage in secondary prevention and screening or treatment of diabetes complications in these settings. Importantly, data on monitoring and control of cardiovascular risk factors are lacking and need to be included in routine diabetes care, particularly in protracted crises.

Many of these challenges also affect populations in stable resource-poor settings. Therefore, examining diabetes care and outcomes in crisis-affected populations compared to those in equally resource-poor environments not affected by crisis may provide helpful insights into the unique challenges of each setting.

Current guidelines, such as the Sphere standards (the most widely used guidance in humanitarian crises), provide very limited information on NCDs, including diabetes.[65] The WHO Package of Essential Non-communicable Disease Interventions (PEN guidelines) provides practical resources and information on the delivery of diabetes in LMICs.[66] Although these guidelines are often used in humanitarian crises, their effectiveness and appropriateness in such contexts have not been studied.

The most detailed studies describing the practical management of diabetes in humanitarian crises were published by UNRWA.[40,41,52] Screening methods, diagnostic criteria, medications, glycaemic and cardiovascular control parameters, complications and patient follow-up data were reported. Mobile phone technology was used to contact patients to ensure follow-up and medication adherence. Thus, there is scope to further explore the role of electronic medical records and mobile phone technology to support clinical decision-making, self-management and monitoring in humanitarian settings and develop basic health information systems to track chronic disease patients over time. While UNRWA services for Palestinian refugees are fairly unique in that they serve a very long-term and relatively static population and cannot be generalized to more acute crisis situations, they may provide useful guidance.

Primary preventive and educational activities were not addressed in any of the publications retrieved by our search. Although these activities may not have priority in the acute phase of a humanitarian response, developing and testing cost-effective and sustainable individual or community-based models for promotion of self-care, adherence and health literacy would be valuable in protracted settings.

To tackle these issues, a Working Group on NCD Control by UNHCR is developing an operational guidance document and a minimum set of NCD-specific indicators for the management and monitoring of NCDs across agencies. MSF has drafted and is field-piloting a clinical guideline for NCDs in crisis.

Health service utilization and access to care

Utilization of diabetes care and costs

The results of the literature search described healthcare utilization patterns among displaced populations with diabetes in the Eastern Mediterranean (no reports were available in other global regions). Care seeking behaviors for individuals with diabetes and other NCDs were high overall. However, despite these high rates of healthcare seeking, access to care was significantly limited. The primary reason for this was the high cost of medications and healthcare services at outpatient and inpatient facilities, fees for diagnostic evaluations and transportation. Each study retrieved by our search that examined healthcare access and utilization among displaced populations found that high costs impeded access to care. Medical care in camps is provided by various actors, some may cover all costs, including medications, labs and referrals; others provide a minimum package or rely on unpredictable donations of medications. In non-camp settings, care is usually integrated within the public health system; services are more extensive, requiring co-payments for drugs, tests, and consultations. Thus, it is imperative to examine and implement cost-effective and

sustainable models of care to improve access to care and long-term outcomes. Studies are needed to document current patient, provider and health system costs and determine key cost drivers, which may be addressed through advocacy. Cost analyses would support humanitarian actors and host country systems in planning for the expensive tests and treatments, long disease duration, and specialist referral that may be involved in diabetes care. Since diabetes and its outcome are closely linked with co-morbidities, such as hypertension and hyperlipidaemia, cost-effective models of care need to be addressed together with other NCDs through integrated approaches.

Continuity and integration of diabetes care

Continuity of care is a major challenge in providing care to populations affected by crises.[9,10] None of the studies retrieved by our search discussed ways of dealing with this in unstable settings. For example, how to ensure continuity of care when access or supplies are compromised due to insecurity or high population mobility. However, our search may not have captured these studies as it was limited to quantitative studies and these types of questions are generally explored through qualitative research.

None of the studies described integrating diabetes or NCD care into host country health systems, as has been recommended.[15] Since most displaced persons now live in urban areas, rather than in camps, coordinating and providing healthcare services for these populations is increasingly challenging.[10,67] To ensure successful response planning and delivery, developing close relationships among humanitarian organizations and working with host country systems is important.[68] Building local health system capacity in diabetes management by developing integrated NCD programmes, establishing referral pathways, and strengthening local supply chains, protocols and policies will support delivery of diabetes care to urban-based populations and promote sustainability post-crisis. Moreover, integrating NCD care into host country health services may be one way to address the challenge of financing healthcare in humanitarian crises, using the universal health insurance approach.

NCD care has traditionally been provided in hospitals and by specialists in much of the Eastern Mediterranean, with little involvement of primary care.[69] Decentralizing diabetes care to the primary care level would allow easier access to care and follow-up, although this may require a large cultural shift, even in stable environments. Additionally, given the success of HIV and TB programs using community health workers to deliver care in resource-constrained settings, it is important to examine and identify what routine tasks can be carried out by non-health professionals at the community level.[10,67] For example, task-sharing of medication initiation and titration to nursing cadres, and health education and treatment support to community health workers, can be carried out at the primary care or community level. Moreover, considering the close link between diabetes and infectious diseases, integrating diabetes care into the routine practice of TB and/or HIV programs would likely be beneficial, allowing for the co-management of NCDs and infectious diseases which require long-term management and close surveillance.[70,71] Developing and testing algorithm-driven, task-shared primary care models, building on HIV/TB care experiences, would facilitate diabetes care delivery in humanitarian crises. There is also a need to develop optimal context-adapted training and capacity-building models, for humanitarian workers and host country health system workers in diabetes and NCD care.

Essential medicines and diagnostics

In many LMICs, the availability and continuous supply of essential medicines is limited for people with diabetes.[72] The barriers to insulin use in LMICs include low insulin availability, high costs, and cold storage.[73,74] These challenges are often magnified in humanitarian crises due to insecurity, interrupted healthcare systems, population mobility, and limited coordination between healthcare providers. Diabetes medications were rarely reported in the studies retrieved and none described the availability or supply of medications or diagnostic materials. Very little appears to be known about the accessibility and affordability of diabetes medications and related equipment in humanitarian crises. Documenting these access issues and developing context-specific solutions to improving access will be important. The use of insulin, and planning for it, in humanitarian crises is especially complicated for the contextual reasons given above.

A positive development from WHO is its piloting a supplemental kit to the Interagency Emergency Health Kit which seeks to provide a temporary ration of medicines in humanitarian crises for a population of 10,000 persons for approximately three months.[75] This kit includes metformin, sulfonylureas, insulin, urine and blood test strips.[76] Since they are intended as temporary supplies, it is critical to build the capacity and resilience of local health systems to ensure the establishment of longer-term, robust medication supply chains.[77] It is also essential to include a rapid training package to support humanitarian workers in its implementation.

CONCLUSION

Our review highlights that the burden of diabetes in humanitarian crises is poorly understood and so likely poorly addressed. Crisis-affected populations with diabetes face enormous constraints in accessing and receiving care, primarily due to the high costs of care. Further research is needed to develop standardized epidemiologic tools to better measure the burden and phenotypes of diabetes in crisis-affected populations, understand access and utilization patterns, develop guidelines and models of care, and evaluate their effectiveness and cost-effectiveness in meeting the needs of people living with diabetes in humanitarian crises.

CONTRIBUTORS

BR led the study and study design, consolidated a final Endnote file and Excel data extraction sheet, completed data screening and extraction for Quarters 1 [A to E] and 2 [F to K], and was responsible for quality control of overall review. SK finalized the published literature search terms, retrieved the citations, performed data screening and extraction for Quarters 1 [A to E] and 4 [S to Z], and wrote the initial draft of the manuscript. JS participated in data screening and extraction of Quarters 2 [F to K] and 3 [L to R]. DF and AC performed the double data extraction of Quarters 3 [L to R] and 4 [S to Z]. RR, PB, and KJ completed the grey literature search, screening and data extraction. EA created Table 2 and participated in manuscript writing and editing. PP participated in checking and reconciling data differences, as well as quality control of overall review. All authors participated in manuscript review and editing.

DECLARATION OF INTERESTS

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REFERENCES

1. The Double Burden of Malbutrition - Policy Brief. Geneva: World Health Organization (WHO), 2017.
2. Double Burden of Malnutrition. 2018. http://www.who.int/nutrition/double-burden-malnutrition/en/ (accessed 2/6/2018).
3. Delisle H BH. The double burden of malnutrition associated with poverty. *Lancet* 2016; **387**.
4. UNHCR: Figures at a Glance. 2018. https://www.unhcr.org/en-us/figures-at-a-glance.html (accessed 12/07/2018).
5. Global Internal Displacement Database. 2018. http://www.internal-displacement.org/database (accessed 12/07/2018).
6. UNHCR Global Trends Forced Displacement in 2016: United Nations High Commissioner for Refugees, 2017.
7. People affected by conflict - humanitarian needs in numbers. Brussels: Centre for Research on the Epidemiology of Disasters (CRED), 2013.
8. The human cost of natural disasters 2015: A global perspective.: Centre for Research on the Epidemiology of Disasters (CRED), 2015.
9. Slama S, Kim HJ, Roglic G, et al. Care of non-communicable diseases in emergencies. *Lancet* 2017; **389**(10066): 326-30.
10. Jobanputra K, Boulle P, Roberts B, Perel P. Three Steps to Improve Management of Noncommunicable Diseases in Humanitarian Crises. *PLoS Medicine* 2016; **13**(11): e1002180.
11. Ravelli ACJ, van der Meulen JHP, Michels RPJ, et al. Glucose tolerance in adults after prenatal exposure to famine. *Lancet* 1998; **351**(9097): 173-7.
12. Li Y, He Y, Qi L, et al. Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood. *Diabetes* 2010; **59**(10): 2400-6.
13. Ruby A, Knight A, Perel P, Blanchet K, Roberts B. The effectiveness of interventions for non-communicable diseases in humanitarian crises: a systematic review. *PLoS One* 2015; **10**(9): e0138303.
14. Demaio A, Jamieson J, Horn R, de Courten M, Tellier S. Non-communicable diseases in emergencies: a call to action. *PLoS Curr* 2013; **5**.
15. Spiegel PB, Checchi F, Colombo S, Paik E. Health-care needs of people affected by conflict: future trends and changing frameworks. *Lancet* 2010; **375**(9711): 341-5.
16. Boulle P, Smith J, Kehlenbrink S, Jobanputra K. Challenges associated with providing diabetes care in humanitarian settings. *Lancet Diabetes Endocrinol* 2018. [Manuscript under revision].
17. Multi-sector needs assessment of Syrian refugees residing in host communities: preliminary findings. REACH Initiative. 2014.
18. Multi-sector needs assessment of Syrian refugees residing in camps: preliminary findings. REACH Initiative. 2014.
19. Inter-agency regional response for Syrian refugees: health and nutrition bulletin; Egypt, Iraq, Jordan, and Lebanon: United Nations High Commissioner for Refugees (UNHCR), 2013.
20. Health access and utilisation survey among non-camp Syrian refugees. Lebanon: United Nations High Commissioner for Refugees (UNHCR), 2014.

21. Syrian Refugee Access to Care Study Lebanon: Medical service needs among post-emergency Syrian refugees in Bekaa Valley, Lebanon: Médecins Sans Frontières, Switzerland, 2014.
22. MSF health surveillance program: Mid-Euphrates region follow-up assessment: Médecins Sans Frontières, 2016.
23. Abukhdeir HF, Caplan LS, Reese L, Alema-Mensah E. Factors affecting the prevalence of chronic diseases in Palestinian people: an analysis of data from the Palestinian Central Bureau of Statistics. *East Mediterr Health J* 2013; **19**(4): 307-13.
24. Al-Sharafi BA, Al-Tahami BA. The effect of war on the control of diabetes in patients with type 2 diabetes mellitus in Yemen: a cross-sectional study. *Endocrinology & Metabolic Syndrome* 2017; **6**(4).
25. Balcilar M. Health status survey of Syrian refugees in Turkey: non-communicable disease risk factors surveillance among Syrian refugees living in Turkey. Health Status Survey of Syrian Refugees in Turkey. Ankara, Turkey, 2016.
26. Benoit SR, Gregg EW, Zhou W, Painter JA. Diabetes among United States-bound adult refugees, 2009-2014. *J Immigr Minor Health* 2016; **18**(6): 1357-64.
27. Bratina NU, Tahirovic H, Battelino T, Krzisnik C. Incidence of childhood-onset type I diabetes in Slovenia and the Tuzia region (Bosnia and Herzegovina) in the period 1990-1998. *Diabetologia* 2001; **44 Suppl 3**: B27-31.
28. Cetorelli V, Burnham G, Shabila N. Prevalence of non-communicable diseases and access to healthcare and medications among Yazidis and other minority groups displaced by ISIS into the Kurdistan Region of Iraq. *Confl Health* 2017; **11**(4).
29. Doocy S, Lyles E, Hanquart B, Team LS, Woodman M. Prevalence, care-seeking, and health service utilization for non-communicable diseases among Syrian refugees and host communities in Lebanon. *Confl Health* 2016; **10**: 21.
30. Doocy S, Lyles E, Roberton T, Akhu-Zaheya L, Oweis A, Burnham G. Prevalence and care-seeking for chronic diseases among Syrian refugees in Jordan. *BMC Public Health* 2015; **15**: 1097.
31. Doocy S, Sirois A, Tileva M, Storey JD, Burnham G. Chronic disease and disability among Iraqi populations displaced in Jordan and Syria. *Int J Health Plann Manage* 2013; **28**(1): e1-e12.
32. Dudova Z KI, Ulman P, Krcmery V, Pyšný L, Majer-Müller L, Slezakova Z, Jankechova M, Elkova L, Gburik V, Hajj Ali P. Commonest diseases amongst Iraqi internally displaced after Islamic State expansion. *Clinical Social Work and Health Intervention* 2015.
33. Eljedi A, Mikolajczyk RT, Kraemer A, Laaser U. Health-related quality of life in diabetic patients and controls without diabetes in refugee camps in the Gaza strip: a cross-sectional study. *BMC Public Health* 2006; **6**: 268.
34. Furusawa T, Furusawa H, Eddie R, Tuni M, Pitakaka F, Aswani S. Communicable and non-communicable diseases in the Solomon Islands villages during recovery from a massive earthquake in April 2007. *N Z Med J* 2011; **124**(1333): 17-28.
35. Gilder ME, Zin TW, Wai NS, et al. Gestational diabetes mellitus prevalence in Maela refugee camp on the Thai-Myanmar border: a clinical report. *Glob Health Action* 2014; **7**: 23887.
36. Hebert K, Quevedo HC, Gogichaishvili I, et al. Feasibility of a heart failure disease management program in eastern Europe: Tbilisi, Georgia. *Circ Heart Fail* 2011; **4**(6): 763-9.
37. Huang K, Deng X, He D, et al. Prognostic implication of earthquake-related loss and depressive symptoms in patients with heart failure following the 2008 earthquake in Sichuan. *Clin Cardiol* 2011; **34**(12): 755-60.

38. Huerga H, Vasset B, Prados E. Adult and paediatric mortality patterns in a referral hospital in Liberia 1 year after the end of the war. *Trans R Soc Trop Med Hyg* 2009; **103**(5): 476-84.
39. Isreb MA, Kaysi S, Rifai AO, et al. The effect of war on Syrian refugees with end-stage renal disease. *Kidney International Reports* 2017; **2**(5): 960-3.
40. Khader A, Ballout G, Shahin Y, et al. Diabetes mellitus and treatment outcomes in Palestine refugees in UNRWA primary healthcare clinics in Jordan. *Public Health Action* 2013; **3**(4): 259-64.
41. Khader A, Farajallah L, Shahin Y, et al. Cohort monitoring of persons with diabetes mellitus in a primary healthcare clinic for Palestine refugees in Jordan. *Trop Med Int Health* 2012; **17**(12): 1569-76.
42. Khader A, Farajallah L, Shahin Y, et al. Cohort monitoring of persons with hypertension: an illustrated example from a primary healthcare clinic for Palestine refugees in Jordan. *Trop Med Int Health* 2012; **17**(9): 1163-70.
43. Khader A, Farajallah L, Shahin Y, et al. Hypertension and treatment outcomes in Palestine refugees in United Nations Relief and Works Agency primary healthcare clinics in Jordan. *Trop Med Int Health* 2014; **19**(10): 1276-83.
44. Khader MI, Snouber S, Alkhatib A, Nazzal Z, Dudin A. Prevalence of patients with end-stage renal disease on dialysis in the West Bank, Palestine. *Saudi J Kidney Dis Transpl* 2013; **24**(4): 832-7.
45. Kulenovic I RA, Grujic M, Suljevic E, and Smajkic A. The impact of war on Sarajevans with non-insulin-dependent diabetes mellitus. *European Journal of Public Health* 1996: 252-6.
46. Lafta R, Aflouk NA, Dhiaa S, Lyles E, Burnham G. Needs of Internally Displaced Women and Children in Baghdad, Karbala, and Kirkuk, Iraq. *PLoS Curr* 2016; **8**(Disasters).
47. Mateen FJ, Carone M, Al-Saedy H, et al. Medical conditions among Iraqi refugees in Jordan: Data from the United Nations refugee assistance information system. *Bulletin of the World Health Organization* 2012; **90**(6): 444-51.
48. Meiqari L, Hoetjes M, Baxter L, Lenglet A. Impact of war on child health in northern Syria: the experience of Medecins Sans Frontieres. *Eur J Pediatr* 2018; **177**(3): 371-80.
49. Metelko Z, Roglic G, Skrabalo Z. Diabetes in time of armed conflict: the Croatian experience. *World Health Stat Q* 1992; **45**(4): 328-33.
50. Mousa H YS, Riccardo F, Zeidan W, and Sabatinelli G. Hyperglycaemia, hypertension and their risk factors among Palestine refugees served by UNRWA. *East Mediterr Health J* 2010; **16**(6): 460-5.
51. Roglic G, Pavlic-Renar I, Sestan-Crnek S, et al. Incidence of IDDM during 1988-1992 in Zagreb, Croatia. *Diabetologia* 1995; **38**(5): 550-4.
52. Shahin Y KA, Khader A, Zeidan W, Harries AD, Nerup J, Seita A. Clinical Audit on the Provision of Diabetes Care in the Primary Care Setting by United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA). *Journal of Diabetes Mellitus* 2015; **5**: 12-20.
53. Shamsi HGH. Prevalence, management and control of diabetes mellitus among Syrian refugees in Duhok governorate, Kurdistan Region of Iraq – a cross sectional study in the camp of Domiz 1. Kaunas: Lithuanian University of Health Sciences; 2017.
54. Sofeh ASA, Khan AS, Khan MA. Diabetes mellitus and its concomitant disorders in Afghan Refugees residing in Peshawar, Pakistan. *Journal of Postgraduate Medical Institute* 2004; **18**(3): 359-67.

55. Strong J, Varady C, Chahda N, Doocy S, Burnham G. Health status and health needs of older refugees from Syria in Lebanon. *Confl Health* 2015; **9**: 12.
56. van Berlaer G, Elsafti AM, Al Safadi M, et al. Diagnoses, infections and injuries in Northern Syrian children during the civil war: A cross-sectional study. *PLoS One* 2017; **12**(9): e0182770.
57. Yanni EA, Naoum M, Odeh N, Han P, Coleman M, Burke H. The health profile and chronic diseases comorbidities of US-bound Iraqi refugees screened by the International Organization for Migration in Jordan: 2007-2009. *J Immigr Minor Health* 2013; **15**(1): 1-9.
58. Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. *NEJM* 2008; **358**(19): 1991-2002.
59. Seage AAaG. Essentials of Epidemiology in Public Health, Third Edition; 2014.
60. IDF Diabetes Atlas Eigth Edition 2017: International Diabetes Federation, 2017.
61. Umpierrez GE. Ketosis-prone type 2 diabetes: time to revise the classification of diabetes. *Diabetes Care* 2006; **29**(12): 2755-7.
62. Unnikrishnan R, Mohan V. Fibrocalculous pancreatic diabetes (FCPD). *Acta Diabetologica* 2015; **52**(1): 1-9.
63. Samal KC, Kanungo A, Sanjeevi CB. Clinicoepidemiological and biochemical profile of malnutrition-modulated diabetes mellitus. *ANN N Y Acad Sci* 2002; **958**: 131-7.
64. Atun R, Davies JI, Gale EAM, et al. Diabetes in sub-Saharan Africa: from clinical care to health policy. *Lancet Diabetes Endocrinol* 2017; **5**(8): 622-67.
65. The Sphere Handbook | Humanitarian Charter and Minimum Standards in Humanitarian Response. 2018 Edition. https://handbook.spherestandards.org (accessed 12/3/2018).
66. Package of Essential Noncommunicable (PEN) Disease Interventiona for Primary Healthcare in Low-Resource Settings. 2010. http://www.who.int/nmh/publications/essential_ncd_interventions_lr_settings.pdf (accessed 3/1/2018).
67. Boyd AT, Cookson ST, Anderson M, et al. Centers for Disease Control and Prevention public health response to humanitarian emergencies, 2007-2016. *Emerg Infect Dis* 2017; **23**(13).
68. Besançon S, Fall I-S, Doré M, et al. Diabetes in an emergency context: the Malian case study. *Confl Health* 2015; **9**(1): 15.
69. Al Hilfi TK, Lafta R, Burnham G. Health services in Iraq. *Lancet* 2013; **381**(9870): 939-48.
70. Lonnroth K, Roglic G, Harries AD. Improving tuberculosis prevention and care through addressing the global diabetes epidemic: from evidence to policy and practice. *Lancet Diabetes Endocrinol* 2014; **2**(9): 730-9.
71. van Crevel R, van de Vijver S, Moore DAJ. The global diabetes epidemic: what does it mean for infectious diseases in tropical countries? *Lancet Diabetes Endocrinol* 2017; **5**(6): 457-68.
72. Beran D, Yudkin JS. Looking beyond the issue of access to insulin: what is needed for proper diabetes care in resource poor settings. *Diabetes Research and Clinical Practice* 2010; **88**(3): 217-21.
73. Beran D, Ewen M, Laing R. Constraints and challenges in access to insulin: a global perspective. *Lancet Diabetes Endocrinol* 2016; **4**(3): 275-85.
74. Beran D EM, Laing R. Access to insulin: Current Challenges and Constraints. Amsterdam: Health Action International, 2015.

75. Interagency Emergency Health Kit 2017. http://www.who.int/emergencies/kits/iehk/en/ (accessed 12/09/2018).
76. Tonelli M, Wiebe N, Nadler B, Darzi A, Rasheed S. Modifying the Interagency Emergency Health Kit to include treatment for non-communicable diseases in natural disasters and complex emergencies. *BMJ Global Health* 2016; **1**(3): e000128.
77. Noncommunicable diseases kit. Cairo, Egypt: WHO Regional Office for the Eastern Mediterranean; 2017. https://www.who.int/emergencies/kits/ncd-information-note.pdf?ua=1 (accessed 12/09/2018).
78. The World Bank Data. 2018. https://data.worldbank.org/income-level/low-and-middle-income (accessed 01/25/2018).
79. (UNHCR) UNHCfR. Convention relating to the Status of Refugees. 1951. http://www.ohchr.org/EN/ProfessionalInterest/Pages/StatusOfRefugees.aspx (accessed 03/20/2018).
80. Nations U. Guiding principles on internal displacement. 2001. http://www.unhcr.org/en-us/protection/idps/43ce1cff2/guiding-principles-internal-displacement.html (accessed 3/20/2018).
81. Tol WA, Barbui C, Galappatti A, et al. Mental health and psychosocial support in humanitarian settings: linking practice and research. *Lancet (London, England)* 2011; **378**(9802): 1581-91.

Abbreviations

A1C – hemoglobin A1c
ADA – American Diabetes Association
BMI – body mass index
CDC – Center for Disease Control
CHF – Congestive heart failure
CI – confidence interval
DM – diabetes mellitus
EMR – electronic medical record
ESRD – end-stage renal disease
FCPD - fibrocalculous pancreatic diabetes
GDM – gestational diabetes mellitus
GFR – glomerular filtration rate
HAPO - Hyperglycemia and Adverse Pregnancy Outcomes study
HF – heart failure
HRQOL - health-related quality of life
HTN – hypertension
IDDM – insulin-dependent diabetes mellitus
IDP – internally displaced persons
IOM – International Organization for Migration
KPD - ketosis-prone diabetes
LMIC – low and middle-income country
MI – myocardial infarction
MMDM - malnutrition-modulated diabetes
MSF – Médecins Sans Frontières
NCD – non-communicable disease
NGO – non-governmental organisation
NIDDM – non-insulin dependent diabetes mellitus
OGTT – oral glucose tolerance test
PAD – peripheral arterial disease
PHC – primary healthcare center
POC – point of care
PPG – post-prandial glucose
PTSD – post-traumatic stress disorder
QRC – Qatar Red Crescent
T1D – Type 1 Diabetes
T2D – Type 2 Diabetes
TB – tuberculosis
UNHCR – United Nations High Commissioner for Refugees
UNRWA - United Nations Relief and Works Agency for Palestine Refugees
USD – United States dollar
WHO – World Health Organization
WHOQOL-BREF - World Health Organization Quality of Life questionnaire

Panel 1: Search strategy and selection criteria for literature review

Eligibility: The population of interest was civilians (all ages) affected by complex humanitarian crises and natural disasters in LMICs, as defined by the World Bank.[78,79] This included refugees and IDPs based upon standard definitions[79,80] and those remaining in areas affected by crises. Refugees from LMICs living in high-income countries were excluded. The search was limited to LMICs since the majority of humanitarian crises occur in LMICs and the resources available to cope with them are different compared to those in high income countries. Humanitarian crises were defined as events stemming from armed conflicts, natural disasters, food insecurity and persecution that threaten the health and safety of a community. The time periods of humanitarian crises included emergency (immediate aftermath of the event up to six months), protracted (crisis duration greater than six months), and early recovery time periods (more stable period of rebuilding up to two years following the crisis). For studies that include both crisis-affected and non-crisis affected populations, only studies that provided separate data for crisis and non-crisis affected populations were included.

The primary outcome of interest was the burden of diabetes mellitus (all types) and its complications (including fatal and non-fatal events). The secondary outcomes of interest were healthcare services and access to care for individuals with diabetes. The initial literature search included all NCDs and from this initial literature search we included the studies that reported data on diabetes. Mental health was not included as it has already been reviewed elsewhere.[81] Studies on organ failure arising from crushes (e.g. natural disasters) were excluded.

Only quantitative studies using cross-sectional or cohort study designs (retrospective or prospective) reporting prevalence or incidence estimates were included. No date restrictions were used. Only papers in English were included. Both published and grey literature were included.

Information Sources: We searched (with a search end date of October 30, 2017): Medline, Embase, IBSS, Web of Science, and Global Health. Grey literature was sought through a combination of web-based searching of the main humanitarian databases and agency websites and contacting the main humanitarian agencies conducting such studies. The search fields were: (i) crisis-related terms; AND (ii) NCD terms; AND (iii) terms related to burden/prevalence/incidence. The full search sources, terms and syntax for the published literature are provided in Online Annex 1.

Study Selection and Data Extraction: Study selection involved a four-stage process: removal of duplicates (stage 1); screening by title (stage 2a) and abstract (stage 2b) and then full text (stage 2c); grey literature screening and review of the reference lists of the final selected studies (stage 3); and final review and analysis of the selected studies (stage 4). All data were double-screened and extracted by six authors (AC, DF, BR, JS, SK, RR) and any variances resolved between them.

Analysis: Descriptive analysis was used given the heterogeneous nature of study context, population exposure, health outcomes, and study methodologies. Findings were organized by the three study objectives, and then into commonly recurring themes.

Table 1: Key study characteristics

Study populations	Refugees (N=25)[17-21,25,26,29-31,33,35,39-43,47,48,50,52-55,57] IDPs (N=5)[22,28,32,46,56] Other conflict-affected populations (N=11)[23,24,27,34,36-38,44,45,49,51] Affected by natural disasters (N=2)[34,37]
Study location	Eastern Mediterranean (N=30)[17-24,28-33,39-44,46-48,50,52-57] Europe (N=6)[25,27,36,45,49,51] Western Pacific (N=2)[34,37] South-East Asia (N=1)[35] Africa (N=1)[38] Multiple regions (N=1)[26]
Study design	Cross-sectional survey (N=37)[17-26,28-35,38-44,46-57] Retrospective cohort study (N=2)[27,45] Prospective cohort study (N=2)[36,37] Routine clinic/organizational data (N=14)[26,32,38-44,47-49,51,57]
Outcome measure	DM diagnostic criteria Self-reported diagnoses (N=12)[20-23,25,28-31,36,46,55] Fasting capillary glucose (N=5)[40-43,54] Random capillary glucose (N=1)[50] DM criteria not specified (N=15)[17-19,26,27,32,37-39,44,47,48,51,56,57] OGTT (N=1)[35] WHO diagnostic criteria (n=1)[33] ADA diagnostic criteria (n=1)[24] A1C (N=5)[34,45,49,52,53] DM Complications (N=5)[30,40,41,52,53] Glycaemic control (N=7)[24,40,41,45,49,52,53] Cardiovascular risk control (N=6)[24,40,41,45,52,53]
Diabetes types	T1D (N=10)[27,33,40,41,47,49,51-53,57] T2D (N=13)[24,32,33,40,41,45-47,49,52-54,57] GDM (N=2)[22,35] Type of DM not specified (N=24)[17-21,23,25,26,28-31,34,36-39,42-44,48,50,55,56]
Barriers in health services access	Cost (N=10)[17,18,20-22,28-31,55] Lack of available services (N=5)[17,18,21,28,31] Geography/did not know where to go (N=6)[17,18,20,22,28,30,31,55]

Table 2: Major research gaps and proposed next steps

Knowledge Gaps	Next Steps
Burden of diabetes data	
Sampling techniques and outcome measures • Limited use of probabilistic sampling methods • Lack of uniform standards for data collection • Self-reported diagnoses not confirmed with biochemical measurement	• Develop standardized epidemiologic tools and methods, using probabilistic sampling, to capture the burden of diabetes and other NCDs in crises • Confirmation of diabetes diagnoses, ideally using HbA1c point of care testing
Diabetes phenotyping • Prevalence and characterisation of local DM epidemiology • Effective methods to rapidly identify known cases of DM and other NCDs in crises	• Strengthen surveillance and health information systems in LMICs to improve baseline epidemiological data on DM • Adapt and test rapid assessment tools, which distinguish DM types 1 and 2, GDM (and other NCDs) to map needs, current services and to triage response in acute emergencies
Diabetes management and monitoring	
• Evidence-based clinical guidance on diabetes management in crises • Optimum glucose testing method, timing and setting • Glycaemic targets which balance safety and effectiveness • Control of cardiovascular risk factors • Role of EMR and mHealth in clinical decision making, self-management and monitoring • Validated audit systems and indicators	• Develop evidence-based clinical guidance on DM care and cardiovascular risk reduction in crises • Explore appropriate, safe and effective diagnostic cut-offs and treatment targets • Develop novel cost-effective technologies for standardized glucose and cardiovascular risk monitoring • Evaluate cost-effective community or facility-based models of DM care • Validate indicators and targets with a prospective study • Operational research to evaluate use of EMR/mHealth in clinical decision making, self-management and monitoring
Health service utilization and access to care	
Utilization of diabetes care and costs • Utilization, access and coverage data for diabetes care in regions other than the Eastern Mediterranean • Access to and utilization of DM care in the acute phase of a crisis and in natural disasters. • Current patient, programmatic, and health system costs and cost-effective models of DM care in crises	• Perform household utilisation and access surveys in regions other than the Eastern Mediterranean • Evaluate DM care delivery in the acute phase of a crisis and in natural disasters • Descriptive studies of costs of diabetes care in humanitarian settings from the patient and provider perspectives • Cost effective studies of models of care, which minimise patient direct and indirect costs
Continuity and integration of diabetes care • Effective strategies to reduce treatment interruption in unstable settings • Evidence-based programmatic guidance on cost effective and sustainable integrated primary level delivery models including essential secondary prevention and referral systems • Cost-effectiveness of decentralised, algorithm-driven care model suited to task-sharing	• Develop and test emergency preparedness plans, emergency packs and patient-held medical records • Develop and test an algorithm-driven care model, integrated with other NCDs, suited to task-sharing, with minimal clinical monitoring and complications screening Explore models of care which maximise continuity of care and integration between different health system levels, including secondary prevention screening
Essential medicines and diagnostics • Current diabetes essential medications and diagnostics access, availability and affordability • Best practice and barriers re insulin use in humanitarian settings, including cold storage • Role of field-adapted POC tests/technology for diagnosis and monitoring DM and complications • Effective implementation and health worker training around use of Interagency Emergency Health Kit	• Document diabetes essential medications and diagnostics access, availability and affordability in crisis settings and develop context- specific solutions, including around cold storage • Field test POC devices and testing algorithms • Explore novel approaches to identify and monitor DM complications • Evaluate Interagency Emergency Health Kit