The burden of diabetes and use of diabetes care in humanitarian crises in low-income and middle-income countries

Diabetes in humanitarian crises 1

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Human suffering as a result of natural disasters or conflict includes death and disability from non-communicable diseases, including diabetes, which have largely been neglected in humanitarian crises. The objectives of this Series paper were to examine the evidence on the burden of diabetes, use of health services, and access to care for people with diabetes among populations affected by humanitarian crises in low-income and middle-income countries, and to identify research gaps for future studies. We reviewed the scientific literature on this topic published between 1992 and 2018. The results emphasise that the burden of diabetes in humanitarian settings is not being captured, clinical guidance is insufficient, and diabetes is not being adequately addressed. Crisis-affected populations with diabetes face enormous constraints accessing care, mainly because of high medical costs. Further research is needed to characterise the epidemiology of diabetes in humanitarian settings and to develop simplified, cost-effective models of care to improve the delivery of diabetes care during humanitarian crises.

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This is the first in a **Series** of two papers about diabetes in humanitarian crises

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Introduction

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.[1] Of these people, 25·4 million refugees have fled across international borders and approximately 40 million people have been forcibly displaced within their own country.[2,3] Approximately 100 million additional people are affected by conflict, but are not displaced.[4] Natural disasters affect an estimated 175 million people annually.[5] Additionally, humanitarian crises are increasingly becoming protracted with an average length of forced displacement of more than 20 years.[3] Low-income and middle-income countries (LMICs) host around 84% of forced migrants globally and commonly have very limited resources to respond to their health needs.[3] LMICs also have the largest burden of diabetes.

Individuals with diabetes are particularly vulnerable in humanitarian crises, given the disruption of health services, impeded access to food supplies because of insecurity, and population movement.[6] These factors increase the risk of exacerbation of medical complications associated with diabetes, particularly for those with type 1 diabetes. Additionally, crisis-affected populations are at risk of diabetes development or exacerbation diabetes secondary to mental disorders and risky behaviours, such as harmful alcohol use. The increasing trend towards the urbanisation of crisis-affected populations might also implicate environmental risk factors associated with diet, physical activity, and tobacco use.[7] Moreover, childhood malnutrition and exposure to maternal undernutrition in utero increase the risk of diabetes in adulthood.[8,9]

The issue of diabetes and other non-communicable diseases (NCDs) has largely been neglected in humanitarian settings.[6,10–12] Historically, the main causes of morbidity and mortality in humanitarian settings were infectious diseases and malnutrition, particularly among children.[12] Given global epidemiological changes and the fact that LMICs (where the underlying burden of NCDs is high) are now commonly affected by crises, humanitarian agencies and governments are challenged with how to effectively address diabetes and other NCDs.[6] Although published literature on the burden of NCDs in LMICs is increasing, including on diabetes, it is unclear whether these studies can be generalised to humanitarian contexts. Although the Global Burden of Disease study 2017[13] provides some background information on disease burden (including diabetes) in crisis-affected countries, the data are not accurately updated to reflect changed disease profiles during crises. Additionally, it does not capture disease burden data specifically among populations affected by humanitarian crises (eg, refugees, internally displaced people, or those entrapped in conflict-affected areas). Moreover, the burden of diabetes and the interventions that are most effective and feasible are unknown, and no evidence-based guidelines or basic diagnostic, clinical, and preventive resources for the management of diabetes in humanitarian contexts are available.[10,11]

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 aims of this first Series paper are to examine the evidence on the burden of diabetes among populations affected by humanitarian crises in LMICs; describe the evidence on health service use and access to care for people with diabetes in these settings, to identify main research gaps; and propose

Panel: **Key study characteristics**

Study population

Refugees (n=25);[15–19,23,24,27–29,31,33,37–41,45,46,48,50–53,55] internally displaced people (n=5);[20,26,30,44,54] other conflict-affected populations (n=11);[21,22,25,32,34–36,42,43,47,49] affected by natural disasters (n=2)[32,35]

Study location

Eastern Mediterranean (n=30);[15–22,26–31,37–42,44–46,48,50–55] Europe (n=6);[23,25,34,43,47,49] western Pacific (n=2);[32,35] southeast Asia (n=1);[33] Africa (n=1);[36] multiple regions (n=1)[24]

Study design

Cross-sectional survey (n=37);[15–24,26–33,36–42,44–55] retrospective cohort study (n=2);[25,43] prospective cohort study (n=2);[34,35] routine clinical or organisational data (n=14)[24,30,36–42,45–47,49,55]

Outcome measure

Diabetes diagnostic criteria: self-reported diagnoses (n=12),[18–21,23,26–29,34,44,53] fasting capillary glucose (n=5),[38–41,52] random capillary glucose (n=1),[48] diabetes criteria not specified (n=15),[15–17,24,25,30,35–37,42,45,46,49,54,55] oral glucose tolerance test (n=1),[33] WHO diagnostic criteria (n=1),[31] American Diabetes Association diagnostic criteria (n=1),[22] HbA_{1c} (n=5);[32,43,47,50,51] diabetes complications (n=5);[28,38,39,50,51] glycaemic control (n=7);[22,38,39,43,47,50,51] cardiovascular risk control (n=6)[22,38,39,43,50,51]

Diabetes type

Type 1 diabetes (n=10);[25,31,38,39,45,47,49–51,55] type 2 diabetes (n=13),[22,30,31,38,39,43–45,47,50–52,55] gestational diabetes (n=2),[20,33] type of diabetes not specified (n=24)[15–19,21,23,24,26–29,32,34–37,40–42,46,48,53,54]

Barriers in non-communicable diseases health-service access

Cost (n=10),[15,16,18–20,26–29,53] lack of available services (n=5),[15,16,19,26,29] geography or did not know where to go (n=6)[15,16,18,20,26,28,29,53]

priorities for future research. The second Series paper describes the concrete challenges of diabetes care delivery in humanitarian crises.[14]

Existing evidence

We identified evidence from 41 eligible studies.[15–55] All studies were published between 1992 and 2018, with 33 published since 2011. 38 studies reported on populations affected by armed conflict,[15–23,25–31,33,34,36–55] two on populations affected by natural disasters,[32,35] and one on all crisis types.[24] 34 studies were done in the protracted crisis phase (crisis duration longer than 6 months),[15–23,25–31,33,37–46,48,50–55] three in the emergency response phase (immediate aftermath of the event up to 6 months),[34,47,49] two in the early recovery phase (more stable period of rebuilding up to 2 years following the crisis),[32,36] and two reported on multiple crises phases.[24,35] 25 studies addressed refugee populations,[15–19,23,24,27–29,31,33,37–41,45,46,48,50–53,55] five addressed internally displaced people,[20,26,30,44,54] and 11 addressed non-displaced conflict-affected populations.[21,22,25,32,34–36,42,43,47,49] The majority of studies were done in the WHO eastern Mediterranean (n=30),[15–22,26–31,37–42,44–46,48,50–55] followed by Europe (n=6),[23,25,34,43,47,49] western Pacific (n=2),[32,35] southeast Asia (n=1), and Africa (n=1), and one study investigated refugees bound for the USA.[24] Further details on the studies can be found in the panel and in the appendix.

See Online for appendix

Burden of diabetes

The evidence on the burden of diabetes among crisis-affected populations was extremely scarce and the overall quality of the studies was poor. Diabetes was most commonly used as a single diagnosis, and distinctions between type 1 diabetes, type 2 diabetes, and gestational diabetes were rarely made. Three studies focused exclusively on type 1 diabetes;[25,47,49] eight categorised patients into type 1 diabetes, type 2 diabetes, or both;[22,30,31,38,39,45,50,51] and two reported on women with gestational diabetes.[19,33] Atypical forms of diabetes were not addressed. Only 18 studies[15,16,18–21,23,26–29,31,43,44,48,50,53,54] assessed the burden of diabetes at the population level by the use of probabilistic sampling (rather than health-facility level with non-probabilistic sampling) and the majority of these studies relied on self-reporting rather than medical diagnosis.

Diabetes prevalence varied substantially between studies examining conflict-affected populations within the same region. Prevalence of diabetes in displaced Syrian populations during the crisis ranged from as low as 0·8% in Syria[54] in 2015 and Iraq[51] in 2016 to as high as 35% in certain governorates of Iraq.[15] When examining older populations (age >60 years), diabetes prevalence ranged from 31·8% in Syria[29] to 47% in Lebanon.[53] An assessment on the health-care needs of internally displaced populations in Iraq reported a 2·8% prevalence of gestational diabetes.[20] However, over half of the pregnant women interviewed had not received a single antenatal visit by their third trimester and, therefore, had not been screened for gestational diabetes.

In Europe, two studies reported pre-conflict and post-conflict incidence of insulin-dependent diabetes in Croatia by the use of the national diabetes registry.[47,49] One study reported the annual age-adjusted incidence of this disease in children (ages 0–15 years), in Zagreb, of 7·0 per 100 000 population (95% CI 3·8–11·8) in 1988 (before the war) and 7·8 (4·5–12·5) in 1991 (after the war).[47] The second study reported an annual incidence of insulin-dependent diabetes in Zagreb of 6·6 per 100 000 population (any age) in 1988 and 5·9 per 100 000 population in 1992.[49] In the Tuzla region of Bosnia and Herzegovina, which was severely affected by war (1992–95), the incidence of non-insulin dependent diabetes from 1990 to 1998 was difficult to obtain because of the war and was assumed to be 3·03 per 100 000 person-years, compared with neighbouring Slovenia during that same period, where the incidence was 8·54 per 100 000 population.[25] In Turkey, 4·1% of Syrian refugees self-reported a diagnosis of high blood sugar (not further defined) in the previous 12 months.[23]

The only study done in southeast Asia reported the prevalence of gestational diabetes in a refugee camp at the Thailand–Myanmar border, based on screening pregnant women with a 75 mg oral glucose tolerance test.[33] Although the sample size was small (n=228) and the number of all pregnant patients in the catchment area was not recorded,

the estimated prevalence was 10·1% using Hyperglycaemia and Adverse Pregnancy Outcomes trial cutoff values.[56]

In Africa, the only identified study was a retrospective study evaluating mortality patterns based on chart review at a hospital in Liberia.[36] 2% of deaths from January to July, 2005, were attributed to diabetes.

Glycaemic control and diabetes complications

Seven studies reported on glycaemic control,[22,38,39,43,47,50,51] but how this was assessed varied and often relied on fingerstick glucose readings at different times of day, such as fasting or 2 h postprandial glucose, so study comparison is difficult. HbA_{1c} measurements were reported in six studies.[22,25,43,47,50,51]

An analysis of the national diabetes registry in Croatia during the war in 1991 reported a median fasting glucose of 194·4 mg/dL (IQR 66·7) in displaced people (mean HbA_{1c} 9·8% [SD 8·7–11·5]) and 183·6 mg/dL (52·2 mg/dL) in non-displaced people (9·1% [8·0–10·7]), which was not significantly different (p=0·38).[47] In Bosnia and Herzegovina, a study assessed the effect of 3 years of war on glycaemic control with hospital data from Sarajevo. Between 1992 and 1994–95 a mean weight-loss of 11·7 kg (SD 8·2 kg) was measured with a reduction in mean fasting glucose from 207·0 mg/dL (SD 54·1) pre-war to 176·4 mg/dL (61·3) post-war, and HbA_{1c} reduction from 10·3% (SD 2·4) to 9·0% (2·0; p<0·01).[43] These changes were accompanied by a reduction in blood pressure and hypoglycaemic medication use.

In the eastern Mediterranean, a cross-sectional study of Syrian refugees in a camp setting in Iraq reported a mean HbA_{1c} of 9·3% (SD 1·9) in individuals with type 1 diabetes (16 [5%] of 328 patients).[51] Of these patients, 9·1% had HbA_{1c} of less than 7·5% (<58 mmol/mol) and 81·8% of more than 8·0% (>64 mmol/mol). Among those with type 2 diabetes (312 [95%] of 328 patients), the average HbA_{1c} was 8·8% (SD 1·7%), with 4·7% having an HbA_{1c} of less than 7·5% and 62% more than 8%. Two studies by the UN Relief and Works Agency for Palestine Refugees (UNRWA) assessed glycaemic control with 2 h postprandial glucose test in Palestinian refugees in Jordan.[38,39] In one study, 836 (42%) of 2851 refugees with diabetes attending the clinic had their postprandial glucose measured.[39] Of these patients, 50% had a 2 h postprandial glucose of less than 180 mg/dL, which was considered good control. In the second study, done 1 year later, 99% of those attending the clinic (n=9691) had their postprandial glucose measured, of whom 65% had a reading of less than 180 mg/dL.[38] The authors suggested that their eHealth system, introduced in 2012, might have had incomplete recording and documentation at the time. A year later, the documentation had improved and the eHealth system seemed to be working better, which might explain the differences in the readings between the two studies. In Yemen, a significant increase (p<0·001 in HbA_{1c} from 7·7% (SD 1·9) to 9·4% (2·4) was identified when comparing the same individuals before and during the war.[22]

Diabetes complications and surveillance were mentioned in five studies.[31,38,39,50,51] In two studies by UNRWA in Jordan, the most common complications noted were myocardial infarction, congestive heart failure, and stroke.[38,39] Another study by UNRWA of Palestinian refugees in Gaza Strip, Jordan, Lebanon, and the West Bank reported that the most common complications were peripheral neuropathy (52·6%), foot infections (17%), diabetic retinopathy (11%), and myocardial infarction (9·6%).[50]

Among Syrian refugees in a camp setting in Iraq, 63·6% of individuals with type 1 diabetes self-reported episodes of symptomatic hypoglycaemia, and 36·6% reported at least one episode of diabetic ketoacidosis.[51] Among those with type 2 diabetes, 24·3% reported at least one episode of hypoglycaemia and less than 1% reported 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 hyperlipidaemia, was addressed in six studies.[22,38,39,43,50,51] Two studies compared hypertension control in cohorts of individuals with type 2 diabetes before and after the conflict. In Yemen, blood pressure control in the cohort with diabetes improved after the war.[22] Likewise, in a cohort of 55 individuals with insulin-dependent diabetes in Sarajevo, 25 had blood pressure readings of more than 140/90 mm Hg before the war compared with only 14 people after the war (p<0·01).[43]

Three studies that reported on cardiovascular risk in populations with diabetes were based on surveys of UNRWA programmes for Palestine refugees mostly collected via eHealth records. The first study[50] was a survey of UNRWA health centres in 2011 and reported the presence of comorbid hypertension in 68·9% of the population with diabetes. 55·5% of patients had blood pressure readings of 140/90 mm Hg or less and 28·2% had readings of 130/80 mm Hg or less; the remaining patients had blood pressure readings of more than 140/90 mm Hg. Cholesterol was elevated (>200 mg/dL) in 39·8% of the population. Only 53·4% of patients with hyperlipidaemia were on lipid-lowering drugs and most were making out-of-pocket payments.

A second study[39] with Palestine refugees in Amman, Jordan, showed that 79% of the population had an associated diagnosis of hypertension, of whom 63% had their blood pressure measured, with 75% of these patients having readings of less than 140/90 mm Hg. For evaluations during the previous 12–15 months, all patients with diabetes were reported to have had total cholesterol measured and 72% had cholesterol of less than 200 mg/dL. The third study evaluated cumulative and quarterly data on diabetes treatment outcomes from primary health-care clinics across Jordan.[38] The authors reported that 78% of

patients returned to the clinic within the previous quarter with more than 99% having their blood pressure and cholesterol assessed. Of these patients, 82% had a blood pressure of less than 140/90 mm Hg and 71% had blood cholesterol less than 200 mg/dL. These three studies by UNRWA document high prevalence of cardiovascular risk factors among individuals with diabetes and show the ability of eHealth records to track and monitor these comorbidities in protracted refugee situations.

Among Syrian refugees with diabetes in a camp in Iraq, 9·1% with type 1 diabetes and 55·4% with type 2 diabetes were on antihypertensive drugs (67·3% on angiotensin-converting enzyme inhibitors).[51] Systolic blood pressure was controlled in 81·8% of refugees with type 1 diabetes and diastolic blood pressure in 72·6% of these patients. Regarding patients with type 2 diabetes, systolic blood pressure was controlled in 54·9% of patients and diastolic blood pressure in 36·3% of patients. 9·1% of refugees with type 1 diabetes and 49·7% of those with type 2 diabetes were treated with statins. However, in both groups, cholesterol was not significantly different between those on and off statins.

Health service use and access to care

Ten studies reported health service use (the frequency and type of care consumed) and access to care,[15,16,18–20,26–29,53] of which seven reported data on NCDs as a group (all included diabetes) and three studies reported data on diabetes separately.[20,27,28] All were cross-sectional household surveys done in the eastern Mediterranean, which limits the generalisability of the findings. Care-seeking behaviours, access to care, and health service use were generally not defined, making the results difficult to interpret. None of these studies reported data on health service use or access to care disaggregated by gender. Although health-care service use was mostly reported for NCDs as a group, the results are described in this Series paper because 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).[18,19,28,29] Care was most commonly sought in primary health-care facilities.[18,19,27] One study reported that refugees with self-reported diabetes had the highest frequency of care-seeking among Syrian refugees with an NCD in Lebanon;[27] 88·2% of Syrian refugees with diabetes had sought care since their arrival and 70% within the 3 months preceding the survey (of whom 60·8% sought care in primary health-care centres). Among displaced Yazidis in Iraq, 92·9% of those reporting an NCD diagnosis had seen a health provider for their condition during the 3 months preceding the survey.[26] In Jordan and Syria, 85% of Iraqi refugees indicated that medical attention was sought the last time it was needed.[29]

Despite high proportions of care-seeking behaviour, access to health services and medicines for NCDs appeared limited. Among Iraqi refugees with NCDs in Jordan and Syria who reported a high proportion of care-seeking behaviour (>80%), only 62·5% of those in Jordan and 58·8% of those in Syria could access medical care when necessary.[29] In Lebanon, 56·1% of Syrian refugees reported difficulty accessing care for NCDs.[18] Among older Syrian refugees (>60 years of age) in Lebanon, of whom 47% reported having diabetes, nearly all surveyed reported an inability to obtain adequate medical treatment, primarily because of cost (3% reported having the resources to afford medications).[53]

High costs because of 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 among all NCDs in all ten studies.[15,16,18–20,26–29,53] High costs were prohibitive to care-seeking for over half of Syrian refugees with diabetes in Jordan (51·7%).[28] In Lebanon, 91·2% of Syrian refugees reported the expense of medical services as the greatest obstacle when seeking care for NCDs.[19] In the same study, 46·1% of people with chronic conditions reported treatment interruptions, primarily because of medication costs (89·3%), whereas 6% interrupted treatment because of danger in the area where medications were disbursed. Among Yazidis with NCDs displaced in Iraq who had reported high proportions of care-seeking behaviour, 40·0% were not taking prescribed medications, mainly citing the high costs.[26] In Lebanon, 31·5% of Iraqi refugees with chronic conditions were not taking medications because of the cost (78·9%) or lack of availability (10%).[19]

Approximately 70% of all Syrian refugees in Lebanon paid out-of-pocket for consultant, diagnostic, and laboratory fees.[27] The authors of the study 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.[27] A UN High Commissioner for Refugees (UNHCR) survey estimated that the average monthly out-of-pocket general health expenditure was US$90 per household for Syrian refugees in Lebanon who needed care (the average monthly non-assisted household income was $173).[18] Another survey reported a mean monthly expenditure on health for Iraqi refugees of $70 in Jordan and $91 in Syria.[29] 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.[18]

Aside from the cost of care, the unavailability of health services, and diabetes care specifically, were barriers to care.[15,19,20,33] In a study of Iraqi internally displaced people, the lack of medication at health facilities was cited as the most important barrier (23·7%).[20] Only six papers in the

literature review mentioned the types of diabetes medications that were prescribed and none reported on their availability.[22,31,41,42,50,51] The next most common barrier to access was a lack of services (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 health care.[15] In two districts in Iraq, an estimated 6% of Syrian refugee households reported returning to Syria to seek care.[15]

Key evidence gaps and next steps for research

Our study shows that evidence assessing the burden of diabetes in humanitarian settings is very limited and generally of a low quality. Levels of need have not been 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 (table).

Epidemiology of diabetes in humanitarian settings

There are significant knowledge gaps in the epidemiology of diabetes in humanitarian settings, especially in Africa and southeast Asia. Most studies were done 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 in conflict-affected countries, particularly during the acute phase of a crisis, and for natural disasters.

Prevalence estimates were scarce and difficult to interpret or generalise since non-probability sampling techniques were frequently used.[57] Most studies that we identified did not report the criteria used to diagnose or monitor diabetes. Fingerstick glucose and HbA_{1c} measurements were not available or reported in most studies. Another weakness was reporting deaths due to diabetes, because 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 under-estimations. 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.[21] By contrast, the International Diabetes Federation estimated a prevalence of 7·0% in Palestine.[58] 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%.[18,27] Despite these differences, multiple studies identified in this Series paper reported diabetes as one of the top three reasons for seeking care in eastern Mediterranean countries.[15–19,27] However, the value of these data for directing resources is questionable, given the absence of uniform standards for data collection.

Diabetes phenotyping

The evidence we identified did not 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 (type 1, type 2, and gestational diabetes) were rarely mentioned. Making these distinctions is important in terms of triage,

	Next steps
Burden of diabetes	
Sampling techniques and outcome measures: limited use of probabilistic sampling methods; no uniform standards for data collection; self-reported diagnoses not confirmed with biochemical measurement	Develop standardised epidemiological tools and methods, using probabilistic sampling to capture the burden of diabetes and other NCDs during humanitarian crises; confirm diabetes diagnoses, ideally using HbA_{1c} point-of-care testing
Diabetes phenotyping: prevalence and characterisation of local diabetes epidemiology; effective methods to rapidly identify known cases of diabetes and other NCDs during humanitarian crises	Strengthen surveillance and health information systems in LMICs to improve baseline epidemiological data on diabetes prevalence; adapt and test rapid assessment tools, which distinguish types 1, 2, and gestational diabetes (as well as tools for other NCDs), to map needs and available services and to triage response in acute emergencies
Diabetes management and monitoring	
Evidence-based clinical guidance on diabetes management during crises; optimum glucose testing method, timing, and setting; glycaemic targets that balance safety and effectiveness; control of cardiovascular risk factors; role of EMRs and mHealth in clinical decision making, self-management, and monitoring; validated audit systems and indicators	Develop evidence-based clinical guidance on diabetes care and cardiovascular risk reduction in crises; explore appropriate, safe, and effective diagnostic cutoffs and treatment targets; develop novel cost-effective technologies for standardised glucose and cardiovascular risk monitoring; evaluate cost-effective community or facility-based models of diabetes care; validate indicators and targets with a prospective study; operational research to evaluate use of EMRs and mHealth in clinical decision making, self-management, and monitoring
Health service use and access to care	
Use of diabetes care and costs: use, access, and coverage data for diabetes care in regions other than the eastern Mediterranean; access to and use of diabetes care in the acute phase of a crisis and in natural disasters; available patient, programmatic, and health-system costs and cost-effective models of diabetes care in humanitarian crises	Survey household use and access in regions other than the eastern Mediterranean; evaluate diabetes care delivery in the acute phase of a crisis and in natural disasters; do descriptive studies of costs of diabetes care in humanitarian settings from the patient and provider perspectives; do cost-effectiveness 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 (potentially involving fixed-dose combination medications); explore models of care that maximise continuity of care and integration with other NCDs and between different health-system levels, including secondary prevention screening
Essential medicines and diagnostics: diabetes essential medications and diagnostics access, availability, and affordability; best practice and barriers regarding insulin use in humanitarian settings, including cold storage; role of field-adapted point-of-care tests and technology for diagnosis and monitoring of diabetes 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 humanitarian settings, and develop context-specific solutions, including cold storage; field test point-of-care devices and testing algorithms; explore novel approaches to identify and monitor diabetes complications; evaluate Interagency Emergency Health Kit

NCDs=non-communicable diseases. LMICs=low-income and middle-income countries. EMRs=electronic medical records. mHealth=mobile Health.

Table: **Major research gaps and proposed next steps**

management decisions, and resource allocation. For example, in the acute phase of an emergency, identifying and prioritising the care of individuals with type 1 diabetes is crucial to minimise serious complications and death.

Only two studies reported on the burden of gestational diabetes.[19,33] However, global estimates from 2017 suggest that approximately 16% of total livebirths were affected by hyperglycaemia in pregnancy, of which 88% of cases were in LMICs.[58] Gestational diabetes, which increases the maternal risk of developing type 2 diabetes later in life, is associated with serious adverse pregnancy outcomes, and carries the risk of transgenerational metabolic effects on the fetus that can be reduced through identification of gestational diabetes and glucose control in the mother.[58] Considering the volume of obstetric and perinatal care in many humanitarian settings,[3] screening and management of hyperglycaemia in pregnancy needs to be integrated into routine perinatal care.

Furthermore, atypical forms of diabetes have been increasingly recognised since the 1980s. Ketosis-prone diabetes has been recognised, mainly in populations of African descent.[59] These individuals are generally overweight or obese and present with ketoacidosis at diagnosis, but typically do not require long-term insulin therapy. Lean phenotypes of diabetes, such as malnutrition-modulated diabetes and fibrocalculous pancreatic diabetes, are also reported mostly in LMICs.[60,61] Individuals with these forms of diabetes are extremely lean and require high doses of insulin for good glycaemic control; however, ketonuria rarely occurs. Jobanputra and colleagues[7] reported that staff at a Médecins Sans Frontières-supported hospital in the Democratic Republic of the Congo have managed patients with type 2 diabetes, as well as those with malnutrition-modulated diabetes who have high insulin requirements and show signs of chronic complications at an early stage. Thus, it is important to recognise that individuals with diabetes might not always present in a typical manner and, therefore, we need to improve the characterisation of 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 the 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 standardisation of epidemiological 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 humanitarian settings.

Diabetes management and monitoring

This Series paper highlights differences in treatment targets, standards of care, and monitoring for diabetes in humanitarian crises. Evidence-based clinical guidance on the management and follow-up of diabetes in humanitarian settings is not available and the knowledge-base on cost-effective models of care in such environments is very limited.[6,7,10,11] Appropriate diagnostic cutoffs and glycaemic targets for diabetes care in humanitarian crises are unclear. These parameters are particularly relevant in settings where individuals prescribed hypoglycaemic drugs are exposed to substantial food insecurity, home-based glucose monitoring is unavailable, and clinical follow-up is jeopardised because of insecurity. Moreover, optimal glucose testing methods, timing, and location in these settings are unknown.[62] 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 in individuals with diabetes are insufficient 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 with those in equally resource-poor environments not affected by a humanitarian crisis might provide helpful insights into the unique challenges of each setting.

Available guidelines, such as the Sphere standards[63] (the most widely used guidance in humanitarian crises), provide very limited information on NCDs, including diabetes. The WHO PEN guidelines[64] provide practical resources and information on the delivery of diabetes care in LMICs. 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.[38,39,50] 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 patients with chronic disease over time. Although UNRWA services for Palestinian refugees are unique in that they serve a very long-term and relatively static population, and cannot be generalised to more acute crisis situations, they might provide useful guidance.

Primary preventive and educational activities were not addressed in any of the publications retrieved by our search. Although these activities might not be a 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 crisis settings.

To tackle these issues, a Working Group on NCD control, led 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. Médecins Sans Frontières has drafted and is field-piloting a clinical guideline for NCDs during humanitarian crisis.

Use of diabetes care and costs

This Series paper described health-care use patterns among displaced populations with diabetes in the eastern Mediterranean (no reports were available in other global regions). Overall, care-seeking behaviours for individuals with diabetes and other NCDs were high. However, access to care was substantially limited. The primary reason for this limited access to care was the high cost of medication and health-care services at outpatient and inpatient facilities, fees for diagnostic evaluations, and transportation. Each study retrieved by our search that examined health-care access and use among displaced populations found that high costs impeded access to care. Medical care in camps is provided by various actors; some might cover all costs, including medications, laboratory tests, 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 copayments 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 patient, provider, and health system costs, and determine key cost drivers, which might be addressed through advocacy. Cost analyses would support humanitarian actors and host country systems in planning for the long-term provision of expensive tests and treatments, and specialist referral that might be required in diabetes care. Since diabetes and its outcome are closely linked with comorbidities, such as hypertension and hyperlipidaemia, cost-effective models of care need to be addressed together with other NCDs using integrated approaches.

Continuity and integration of diabetes care

Continuity of care is a major challenge in providing care to populations affected by humanitarian crises.[6,7] None of the studies retrieved by our search discussed ways of dealing with this issue in unstable settings (eg, how to ensure continuity of care when access or supplies are compromised because of insecurity or high population mobility). However, our search might not have captured these studies because it was limited to quantitative studies and these types of questions are generally explored through qualitative research.

None of the studies described the integration of diabetes or NCD care into host country health systems, as has been recommended.[13] Since most displaced people now live in urban areas, rather than in camps, coordinating and providing health-care services for these populations is increasingly challenging.[7,65] To ensure successful response planning and delivery, developing close relationships among humanitarian organisations and working with host country systems are important.[66] 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 the delivery of diabetes care to urban-based populations and promote sustainability post crisis. Moreover, integrating NCD care into host country health services might be one way to address the challenge of financing health care 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 minimal involvement of primary care.[67] Decentralising diabetes care to the primary care level would allow easier access to care and follow-up, although this decentralisation might require a substantial cultural shift, even in stable environments. Additionally, given the success of HIV and tuberculosis programmes that use community health workers to deliver care in resource-constrained settings, it is important to examine and identify what routine tasks can be done by non-health professionals at the community level (eg, task sharing of medication initiation and titration to nursing cadres, and health education and treatment support to community health workers).[7,65] Moreover, in view of the associations between diabetes and infectious diseases, integrating diabetes care into the routine practice of tuberculosis and HIV programmes would probably be beneficial, allowing for the comanagement of NCDs and infectious diseases that require long-term management and close surveillance.[68,69] Developing and testing algorithm-driven, task-shared primary care models, building on HIV and tuberculosis care experiences, would facilitate diabetes care delivery in humanitarian crises. Development of optimal context-adapted training and capacity-building models in diabetes and NCD care for humanitarian and host country health-care workers are also needed.

Essential medicines and diagnostics

In many LMICs, the availability and continuous supply of essential medicines is limited for people with diabetes.[70] Barriers to insulin use in LMICs include low insulin availability, high costs, and cold storage.[71,72] These challenges are often magnified in humanitarian crises because of insecurity, interrupted health-care systems, population mobility, and limited coordination between health-care 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

Search strategy and selection criteria

We searched (on Oct 30, 2017) MEDLINE, Embase, International Bibliography of the Social Sciences, Web of Science, and Global Health, for papers published until that date (the studies included, as a result of the search, ranged from 1992 to 2018). The search fields were: crisis-related terms; AND non-communicable disease terms; AND terms related to burden, prevalence, and incidence. The full search sources, terms, and syntax for the published literature are provided in the appendix. Grey literature was sought through a combination of web-based searching of the main humanitarian databases and agency websites and through contacting the main humanitarian agencies doing such studies. Grey literature was updated on Jan 29, 2018.

The population of interest was civilians (all ages) affected by complex humanitarian crises and natural disasters in low-income and middle-income countries (LMICs), as defined by the World Bank. This population included refugees and internally displaced people based on standard definitions and those remaining in areas affected by crises. Refugees from LMICs living in high-income countries were excluded. 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 6 months), protracted (crisis duration >6 months), and early recovery time periods (more stable period of rebuilding up to 2 years following the crisis). For studies that included both crisis-affected and non-crisis-affected populations, only studies that provided separate data for crisis and non-crisis-affected populations were included.

The main outcome of interest was the burden of diabetes (all types) and its complications (including fatal and non-fatal events). The other outcomes of interest were health-care services and access to care for individuals with diabetes. The initial search included all non-communicable diseases (NCDs) and from this initial literature search we included the studies that reported data on diabetes. Mental health was not included because it has already been reviewed elsewhere. Studies on organ failure arising from crushes (eg, natural disasters) were excluded. Only quantitative studies using cross-sectional or cohort study designs (retrospective or prospective) reporting prevalence or incidence estimates were included. Only papers in English were included.

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, DCF, BR, JS, SK, and RR) and any variances resolved between them. Descriptive analysis was used because of the heterogeneous nature of study context, population exposure, health outcomes, and study methods. Findings were organised by the three study objectives, and then into commonly recurring themes.

context-specific solutions to improve access will be important. The use of insulin, and planning for it, in humanitarian crises is especially complicated for the contextual reasons given in this Series paper.

The WHO pilot of 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 people for approximately 3 months, is a positive development.[73] This kit includes metformin, sulfonylureas, insulin, and urine and blood test strips.[74] Because they are intended as temporary supplies, it is crucial to build the capacity and resilience of local health systems to ensure the establishment of long-term, robust medication supply chains.[75] It is also essential to include a rapid training package to support humanitarian workers in its implementation.

Conclusions

Our Series paper highlights that the burden of diabetes in humanitarian crises is poorly understood, and as such, poorly addressed. Crisis-affected populations with diabetes face enormous constraints in accessing and receiving care, primarily because of the high costs of care. Further research is needed to develop standardised epidemiological tools to better measure the burden and phenotypic variation of diabetes in crisis-affected populations, understand access and use 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 work, contributed to the literature search, contributed to data screening and extraction, and was responsible for overall quality control. SK finalised the search terms used, contributed to data screening and extraction, and wrote the initial draft. JS, DCF, AC, RR, PB, and KJ participated in data screening and extraction. EA created the table and participated in the writing and editing of the Series paper. PP contributed to checking and reconciling data differences, as well as overall quality control. All authors participated in the review and editing of the Series paper and approved the final version.

Declaration of interests

SK reports salary support from the US National Institutes of Health and consultancy fees from Medécins Sans Frontières. EA reports grants and non-financial support from Medécins Sans Frontières. PP reports grants from Medécins Sans Frontières. All other authors declare no competing interests.

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