**DEMOGRAPHICS, CLINICAL MEASUREMENTS, AND BEHAVIORAL PREDICTORS OF TYPE 1 DIABETES MORTALITY IN RWANDAN ADULTS**

by

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**ABSTRACT**

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**DEMOGRAPHICS, CLINICAL MEASUREMENTS, AND BEHAVIORAL PREDICTORS OF TYPE 1 DIABETES MORTALITY IN RWANDAN ADULTS**

Heather M. Phelos, MPH

University of Pittsburgh, 2017

**Background/Objective**: Life for a Child (LFAC) is an international program that provides care and education to needing youth with Type 1 Diabetes in over 42 countries. The program’s approach is to work with local partners, providing necessary insulin, blood glucose testing supplies, and education to all youth (age ≤26) in need. In Rwanda, LFAC works primarily through the Rwanda Diabetes Association (RDA). The current study is being conducted to serve the need of LFAC to evaluate long-term outcomes, including mortality, and uses a retrospective cohort design to survey 84 participants who ‘aged out’ of the LFAC program in 2012 or 2013, i.e. 4-5 years prior to being surveyed (2017).

**Methods**: Baseline data were obtained from the 2012/2013 clinical exam records kept by the RDA staff. The mortality status was ascertained in May of 2017, with a censoring date of June 1, 2017, via local hospital consultation. Descriptive statistical evaluation of baseline data and last available LFAC measures was performed by gender and mortality status using Stata. Baseline predictors of mortality status were assessed using logistic regression models.

**Results**: Out of the 84 participants with a mean baseline age of 24.2 years, 51 (60.7%) were women. The vital status was obtained for 46 out of the 84, or 54.7% of the sample. During the 4.3 years of mean follow-up, there were 10 deaths (6 females (60.0%)), giving an incidence density of 5.4 /100 person-years. In the logistic regression models, higher last visit HbA1c levels (OR=2.7, p=0.03) and lower BMI (OR=0.6 p=0.02) were significantly associated with mortality status.

**Conclusion**: The results show an alarmingly high mortality rate for these youth. HbA1c and BMI were the sole significant mortality predictors, though the low sample size and the high degree of missing data do not allow for definitive conclusions. Thus, further risk factors may also be important and merit further study. The burden of high mortality, along with annual increases of the disease, show the public health importance of type 1 diabetes research.

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preface

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# Introduction

 Type 1 Diabetes (T1D) is a chronic disease that has a complex casual web and requires life-long, insulin therapy or treatment [1]. Clinical T1D, usually has sudden disease onset and typically occurs much earlier in life than most chronic diseases [2]. Recognition of the stage in disease progression is extremely important to determine the most beneficial therapeutic approach but current research gaps hinder this process [3]. All of this combined, along with the increasing global incidence rates of about ~3% annually, necessitates additional T1D research and scaling-up for preventative programs [3]. In low- and middle- income countries, chronic diseases, in general, pose an increasing threat as urbanization, globalization, and life expectancies rise [4]. There is a double burden from both infectious and chronic diseases that encumbers the health services of already low resources and many low- resource countries chose to focus on infectious diseases since they are often acute and have a simpler causal web [4].

In Rwanda, the group of experts that focuses on diabetes is very small. This adds to the gap in knowledge and hinders the scope of practice. The Rwanda Diabetes Association (RDA), which is partnered with the international diabetes program, Life for A Child (LFAC), is the only form of continual T1D data collection for many of the youth [5]. This study was made possible by the data obtained by the RDA.

The purpose of this study was thus to assess the vital status and current level of diabetes care that youth who aged out of the LFAC program 4-5 years earlier are experiencing and to identify predictors of mortality. This will hopefully provide data to improve care and reduce mortality. In the upcoming introductory sections, the essay will delve into T1D pathogenesis, theories of causation, management, treatment, the global burden of disease, and an in-depth look at T1D in Rwanda.

## Overview of Diabetes

 Diabetes is a metabolic disease that occurs when the body cannot properly auto-regulate blood glucose and has four primary classifications: type 1, type 2, gestational, and rare other causes [6]. Diabetes classification in diagnosis is extremely important for determining therapy and patient-centered care should be utilized to ensure optimal outcomes [7]. Insulin, a hormone made from the pancreas, transports blood glucose into the cells to be used for energy [6]. Type 2 diabetes results from the progressive loss of beta cell function usually on the setting of insulin resistance and accounts for approximately 90% of all diabetes cases [2]. Both type 1 and type 2 diabetes are associated with risk of severe complications.

## Type 1 Diabetes

The primary focus of this essay and study is on T1D. T1D is an autoimmune disease that destroys the beta cells in the pancreas that make insulin and accounts for approximately 5- 10% of all diabetes cases [6]. People diagnosed with T1D are immediately required to start exogenous insulin therapy in order to maintain glucose homeostasis [6]. T1D is one of the most common chronic diseases in youth [2].

### Pathogenesis

 T1D requires life-long treatment, management, and vigilance for possible complications. The disorder is progressive and attributed to a combination of environmental and genetic risk factors [1]. The average age of onset differs by country, but, globally, it is most likely to present itself before age 40. The peak incidence rate ranges from 10 to 14 years old [8]. T1D onset is typically characterized by the presentation of the following symptoms: polyuria (frequent urination), polydipsia (abnormal thirst), and weight loss [8]. A diagnosis can be made via blood tests to ascertain hyperglycemia and the presence of autoantibodies but the latter one is often only done for research purposes [7]. In the clinical setting, diagnostic tests include: fasting plasma glucose, oral glucose tolerance test, and HbA1c [7]. Newly diagnosed patients have varying degrees of beta cell destruction that are correlated with the stage in disease progression [3]. It has been reported that a level of 40% beta cell destruction is sufficient to precipitate clinical symptomatology [1].

 The definitive cause of T1D is largely unknown but there are compelling studies on the theories of causation. The disease has a genetic component, largely inherited by the HLA complex [9]. Genetics require factor(s) that trigger the onset of T1D. Causative agents are important to research because if known, there would be potential for primary prevention.

 Theories of the causative agent include: viruses, namely coxsackie and congenital rubella, as well as environmental toxins, multiple maternal exposures, early exposure to certain foods, and vitamin D deficiencies [9]. One form of evidence in environmental triggers is that migrating populations rapidly take on the incidence rates of the new country [9]. From analytical epidemiology, researchers have found that T1D incidence is associated with seasonality of birth and seasonality of disease occurrence, which may be evidence that enteroviruses and infectious diseases, respectively, are causative agents [10]. Maternal exposures are also associated with T1D incidence such as: maternal age, preeclampsia, and cesarean section delivery [10]. Through meta-analysis, it has been determined that having been breastfed for less time is linked to T1D in two ways: first, because breastmilk is protective and gives maternal antibodies to the baby and secondly, because replacement with cow’s milk can trigger an immune response to insulin [10]. Lastly, Vitamin D deficiencies are associated with T1D incidence. It also explains the high prevalence of T1D in northern countries, and relatively low prevalence in countries near the equator where cow’s milk is less commonly drunk and sun exposure is more constant throughout the year [10].

Ketoacidosis is a metabolic state characterized by high ketones in the urine and blood, hyperglycemia (high blood sugar levels) and often low blood pH, tested by a urine dipstick test or a blood test [11]. Clinical presentation includes emesis, abdominal pain, rapid dehydration, hypotension, disoriented mental state or coma, usually in combination with a ketotic smell to the breath, as well as the classic symptoms of polyuria, polydipsia and weight loss [11]. The presentation of ketoacidosis is often the first manifestation of the disease and signals the need for insulin to control blood glucose levels [7]. It is a severe and life-threatening complication of T1D that may be prevented by monitoring glycemic and ketone levels, as well as, education on adjusting insulin intake when unwell due to ketoacidosis symptoms [11]. The strongest protective factor against ketoacidosis development is reducing HbA1c levels [8]. The level of cognitive impairment due to ketoacidosis is a clinical marker for the severity, as well as the level of hyperglycemia and ketones. In severe cases, cerebral edema, pulmonary edema, myocardial infarction, or venous thromboembolisms may occur [11]. The presence of diabetic ketoacidosis varies by geography in average frequency and severity [8]. The frequency of diabetes ketoacidosis is inversely correlated with the country incidence rate [8]. That is, countries, such as Rwanda, with low incidence rates have a higher frequency of diabetes ketoacidosis due to variable insulin availability, lack of education and blood glucose testing supplies and nutritional deficits, to name a few reasons [12].

The term hypoglycemia refers to low blood sugar and is the result of excessive insulin dosage, physical exertion, inadequate food intake or any combination of these. [8]. The clinical presentation of a hypoglycemic episode includes lethargy, fainting, and disorientation among other symptoms [8]. Long-term or frequent hypoglycemia may result in cognitive impairment [8]. The threat of hypoglycemia poses a major obstacle to glycemic control. It may defer people with T1D from taking insulin and thus interferes with the ability to control glycemic concentrations [8].

### Complications, comorbidities, and concomitants:

Poor management of blood sugar levels can result in a plethora of complications, including retinopathy (loss of vision), kidney disease, neuropathy, and cardiovascular disease [7]. The presence of microalbuminuria (increased protein in the urine) is highly predictive of advanced stages of neuropathy, nephropathy and retinopathy. Diabetic Nephropathy is the leading cause of renal failure, globally [7]. Diabetic neuropathy can cause carpal tunnel, nerve palsies, cardiac dysfunction, erectile dysfunction, skin ulcerations, gangrene, and amputations [9]. The relative risk of cardiovascular disease is 10-fold greater for a young adult with T1D than someone without the condition [9]. Comorbidities such as autoimmune thyroid disease and celiac disease appear in about 5-10% of children with T1D [9]. Research has shown that children with a single parent and low socioeconomic status are less likely to maintain glycemic control and compliance to their diabetes routine and are more likely to have frequent ketoacidosis episodes [9]. Also, children with T1D have an increased prevalence of depression and eating disorders [9].

A comprehensive medical evaluation should be done after diagnosis and at appropriate follow-up visits to assess comorbidities and to ensure a patient-centered approach to T1D care [7]. Common comorbidities of T1D that should be screened for during medical evaluations include:

Diabetic Kidney Disease: assessed via urinary albumin (e.g. via albumin to creatinine ratio (ACR)) and estimated glomerular filtration rate. ACR is an important marker for renal disease and vascular dysfunction [13]. A high ACR is associated with an increased risk of kidney and heart damage and positively linked with high blood pressure [13]. Normal ACR is defined as <30 mg/g, while kidney damaged is defined by a persistent ACR of >30 mg/g [7].

Cardiovascular disease (CVD): Those with any form of diabetes are at increased risk for CVD. The relative risk for CVD can be as high as 10 times that seen in the general population [14]. The American Diabetes Association recommends blood pressure measurements at all routine visits and treatment of hypertension (blood pressure of >140/90) to lower the risk of cardiovascular disease in people with diabetes [14]. Lastly, a comprehensive skin, eye, sensory, and foot examination is used to assess microvascular complications [7].

In order to prevent complications, early detection and active management through sentinel observations and readjustments to control approaches are critical. There is significant evidence that lowering HbA1c significantly reduces the risk of these micro- and macro-vascular complications [15]. The condition is accentuated by unhealthy lifestyle habits so avoiding risk factors such as: smoking, unhealthy eating, sedentary lifestyle, hypertension, and drug abuse is also important [9].

### Successful Management

 Treatment and management of T1D is essential to lowering the risk of developing complications. Managing T1D takes a multidisciplinary approach and requires continual insulin dose administration and adjustments, blood glucose and urine ketones monitoring, nutritional preparedness (meal timing, carbohydrate counting, and micronutrient, or vitamin therapy), attention to psychosocial wellbeing, vigilance and awareness of hypoglycemia and ketoacidosis, and screening for micro- and macro- vascular complications [9]. Providers should tailor and personalize the treatment regimens to reduce disparities and burdens related to socioeconomic context [7]. This includes addressing barriers to: accessing care, food and financial security, and cultural/ linguistic differences [7]. Both patient self-monitoring and provider vigilance is imperative to successful management of T1D.

 Two types of self-monitoring may be prescribed to those with T1D, as a primary measure of glycemic control [7]:

 Self-Monitoring of Blood Glucose (SMBG) is an individualized approach to monitoring and evaluating response to insulin therapy. These data can then be used to adjust food intake, exercise, or insulin therapy to meet specific goals [7]. SMBG should be done prior to meals and snacks, at bedtime, prior to and during exercise, and when they suspect low blood glucose [7].

 Continuous Glucose Monitoring (CGM) may also be prescribed in patients with T1D [7]. CGM measures interstitial glucose every five minutes, allows patients to view trends in their glucose levels, and alarms the user of hypo- and hyper-glycemic episodes [7].

 HbA1c is a blood test that provides average blood glucose over the past three months and is measured by the percentage of hemoglobin with attached glucose molecules [16]. The glycemic management target is <7% (<53 mmol/mol) for most patients but occasionally a more stringent target of <6.5% (<48 mmol/mol), or higher for children at <7.5% (58 mmol/mol) [7].

The researchers from the Diabetes Control and Complications Trial (DCCT) implemented a randomized clinical trial (RCT) to determine if intensive control over HbA1c values would reduce microvascular complications [15]. The results prove that intensive therapy (maintenance of HbA1c median levels of 7.3% over 7 years) reduces the risk of microvascular complications from 35% to 90% from standard care of HbA1c aim of median 9.1%. [15].

## Global Burden of Disease

 T1D has had a long history of innovative care approaches since the first human insulin treatment in 1922 [17]. Currently, there is a large global disparity in survival rates due to differences in the access to insulin therapy, as access in some countries may be limited to near non-existent [18]. In remote areas of Sub-Saharan Africa, a six- year survival may be as low as 1%, while this rate is 98% in the United States [18]. For over 25 years now, multi-country collaborated registries have made it easier to assess the global burden of disease. In 1990, the DIAMOND project was initiated by the World Health Organization (WHO) in order to address the public health implications of T1D with a main objective to describe the incidence of T1D in children [8]. In 1999, the WHO initiated StepWise, a country wide, validated surveillance system for low resource countries [19].

 There is extreme global variation in the incidence and severity of T1D. In general, incidence rates increase greatly the further the country is from the equator [8]. Annual incidence ranges from 0.1/100,000 in China to 37/100,000 in Finland [8]. Globally, males and females are equally affected, although gender differences in the incidence of T1D have been reported in high versus low incident regions [8]. For instance, there is a male excess in incidence rates in individuals of European descent, among whom, incidence rates of T1D are generally high, whereas data from cohorts of non-European descent report a female excess in incidence rates [8]. Through descriptive epidemiology, trends in incidence give a better view into the driving factors behind T1D. In the past two decades, the incidence rate for T1D has been increasing and expected to continue climbing. In 2010, the number of people living with T1D was 0.5 million globally but this is expected to double by 2030 [20].

Incidence disparities between countries and ethnic groups could be explained by the difference in the distribution of genetic susceptibility markers and ecological determinants, such as nutrition, economic status, and geographical location [10]. Individuals of European descent have the highest incidence rates compared with any other race. The highest being in Nordic countries: Finland, Sweden, and Norway, in order of the first to the third highest global incidence rates [10].

The financial burden of T1D also varies according to country income level. According to a study by Ogle et al., even minimal costs of T1D care are beyond the means of families in low- resource countries [21]. In this study, total yearly T1D cost was estimated by the direct costs of 18 × 10 ml 100 IU/ml insulin, 1/3 cost of a blood glucose meter, two blood glucose test strips/day, two syringes/week, four HbA1c tests/year and the indirect costs of consultation and travel [21].

### Within country variation of incidence

Within country differences in T1D incidence could be explained by access-to-care and nutritional disparities due to rural and urban access differences, exposure to infectious diseases, and density or make-up of the population (i.e. proportions of migrants, racial background) [10]. Current research studies suggest that the gut microbiome may play a role in the pathogenesis of T1D, perhaps also affecting within country variation in the incidence of this chronic disease [22]. According to Paun et al., the rapid rise of T1D incidence in the past 50 years suggests environmental factors and consequently changes in microbiota composition that contribute to pancreatic autoimmunity [22].

### Burden in Africa

Data on T1D and its complications are scarce in most Sub- Saharan Africa countries. There is a high degree of missing data and most available studies comprise small sample sizes. The true burden of T1D thus remains unknown and is likely to be grossly underestimated. Nevertheless, malnutrition has been associated with the incidence of T1D in Africa [10]. Moreover, although Africa as a whole has lower T1D incidence rates than western continents, the annual increase is much higher for these low incidence countries [9]. Despite a rapidly increasing incidence, however, the national health sectors in this region have largely neglected the risk diabetes poses to public health [18].

Also discordant from western countries, death from ketoacidosis is a major threat to children with T1D in low resource countries [12]. This is partly due to insulin availability being highly variable. A meta-analysis on insulin availability in low to middle-income countries shows the lowest availability reported in Mali, at 20%, and the highest, at 100%, in Nicaragua, which shows the extreme variation as a result of discrepant governmental priorites [23]. In some low resource countries, insulin is not on the formularies of essential drugs, which makes insulin availability patchy to nearly non-existent [23].

Even essential medicines, as a whole, are guaranteed to only half of the population in some of the low resource countries in Africa [24]. Economically speaking, insulin is an off-patent medication and differential pricing adds to the problem of access in low resource countries and remains a barrier to countries with low healthcare expenditure [24]. In fact, the most common cause of death for children with T1D is insufficient access to insulin [24], without which, life expectancy for a newly diagnosed child could be between one to three years [25]. Insulin distribution is also a problem in low resource countries. In multiple African countries, over 3/4 of the national insulin stores stay in the capital city [18]. Thus in developing countries, a child with diabetes implies a great financial burden on the family. In conclusion, as insulin availability continues to be a problem, urgent international financial support is needed.

## Rwanda

 Rwanda is a landlocked country in East Africa that is second in African population density only to Mauritius, and has about 12 million people for 26,338 square kilometers [26]. It has five provinces: North, South, East, West, and the capital, Kigali City [26]. In 2012, the general census provided evidence that the country is disproportionately female by about 4% [26]. Life expectancy is at 64.5 years with the crude death rate at 7.7/1000 people [27]. The crude birth rate is at 30.9/ 1000 with a fertility rate of 4 children per woman [27]. The fertility rate has decreased by over 50% since 1960, where Rwanda once had the highest fertility rate in the world at 8.2 children per woman [28]. This shows that Rwanda is making progress in its demographic transition, as people are living longer.

 According to the World Health Organization, Rwanda is in the low-income economic category and the poverty rate for rural residents is at approximately 50% [27]. Rural persons are a vulnerable population in Rwanda because essential services are limited in these regions [27]. As for the epidemiological transition, infectious diseases still take precedence over all other health crises at 52% proportional morality [27]. With 13% attributed to injury, non-communicable diseases (NDCs) account for only 36% of total deaths [27]. As NCDs increase, so does public and governmental interest but it is not yet enough for a large systems response [27]. Currently, Rwanda lacks NCD surveillance and monitoring systems, evidence-based guideline/protocol/standards on the management of major NCDs, national registries, and operational policies on reducing known risk factors [27], though the recent establishment of NCD clinics and associated registers provide evidence this is being addressed.

 As for funding the health sector, only 11% of government funds are allocated toward health [27]. The rest of the Rwandan healthcare system is funded by foreign aid at 53% [29]. Approximately 80% of Rwandans have some form of health insurance due mainly to the national health insurance program: The Mutuelle de la Sante. [29].

### History of T1D in Rwanda

Rwanda has been rebuilding their health sector for over two decades now. During the 1994 genocide, the health sector was paralyzed and access to medicine and diabetes care was virtually non-existent [5]. During this time, the health sector only had the capacity to focus on emergency services [5]. While Rwanda’s health care was once completely destroyed, it is now becoming a leading pacesetter for health reform in Sub-Saharan Africa. In the past 20 years, the life expectancy rose from 40 to 64.5, the current life expectancy being seven years higher than the average life expectancy for the WHO Africa region. [27]. Throughout the 1990’s, Rwanda was worse than the average for their WHO region in maternal mortality, under-five mortality, and immunization rates but is currently superior in each category [27].

Diabetes care has also been on the upsurge. In 1997, the Rwanda Diabetes Association, which was the first dedicated clinic to diabetes care in Rwanda, was founded by Francois Gishoma [5]. In 2002, the country’s focus was still on HIV/AIDS but non-communicable diseases, such as T1D and Type 2 Diabetes, gained interest [29]. Over the past decade, the Rwanda Diabetes Association has partnered with at least eight international diabetes programs: The International Diabetes Federation (IDF), Insulin for Life, Life for a Child Programme, World Diabetes Foundation, Insulin Zum Leben, Team Type 1, Marjorie’s Fund and the University of Pittsburgh, USA [5].

### Scale of problem

The scope of the problem was captured in 2012 with the World Health Organizations STEPWISE survey and clinical measurements study. The STEPWISE study was a well-conducted study, with a larger sample size (n=7240), and representative sample (i.e. the study population included individuals of a wide age range, demographics, and various regions in Rwanda) [19].

 The study found that raised blood glucose defined as fasting blood glucose greater or equal to 6.1 mmol/L is uncommon, affecting just 3.06% of the sampled population [19]. The portion of the population with high ACR was lowest in the capital at 4% and highest in the northern province at 14.9% [19]. The average portion of the population with high ACRs across all provinces was 10% [19]. The study also found that blood pressure and glucose are infrequently measured in Rwanda and consequently, a high proportion of individuals with hypertension or diabetes remain undiagnosed [19]. Approximately 98% of both males and females have reported never having their blood sugar measured [19]. This suggests that the current prevalence of both type 1 and type 2 diabetes is underestimated.

## Public Health Significance

T1D is ubiquitously a financial burden on affected families and country economies. Poorly managed T1D can lead to severe complications and premature death. The disease is a public health crisis in low resource areas, where six-year survival rates can be as low as 1%, which is a 9700% less chance of survival than those with T1D living in the United States [18]. It is also the fastest growing disease amongst all NCDs. Worldwide, the incidence of T1D has been increasing 3% annually [4]. The World Health Organization states “despite enormous achievements in the area of care for T1D, an estimated 4 million years of life were lost for people with the disease in the year 2000” [18].

Also, the causal web is not completely identified, which hinders preventative measures, commanding the need for research. Vulnerable populations are affected disproportionately; since the disease is mainly diagnosed in youth and, in lower-income countries, associated with malnutrition. The incidence rates are highly variable due to genetic and environmental predisposition. The burden imposed by the disease cannot be accurately estimated due to extreme lags in diagnosis in low resource areas. In addition, diabetes inflicts a large financial burden on patients due to the cost of insulin and other “tools” essential for disease management. The cost of T1D may disproportionately affect rural and/or impoverished populations with limited access to the necessary care, thus increasing their risk for severe complications and premature death.

# Study Objective

The aim of the study was to determine the current state of health and diabetes care for adults with T1D who aged out of the LFAC program in Rwanda 4-5 years prior to follow up. This essay is a sub analysis of these data with two primary aims: a) to determine the 4 to 5-year mortality rate of these youth; and b) to determine predictors of mortality in this young population.

## Background

Life for a Child (LFAC) is an international program that provides care and education to needing youth with T1D in over 42 countries. The program’s approach is to work with local partners, providing necessary insulin, blood glucose testing supplies, and education to all youth (age <26) in need. LFAC partnered in Rwanda in 2003. Since then, LFAC works primarily through the Rwanda Diabetes Association (RDA) [5]. The duties of the RDA are in incongruence with LFAC: educate and mobilize the people of Rwanda on diabetes and distribute treatments and glucose monitors [5]. Nevertheless, they also incorporate research and maintenance of governmental and international partnerships [5]. The RDA clinic is based in the capital, Kigali. The staff currently consists of a small group of nurses who aim to visit each of the 44 district hospitals every quarter annually [5], however, limited resources for the last two years have restricted these visits to one to two annually.

### Hypotheses from literature

Measurements of HbA1c are used as a marker of diabetes control. HbA1c is a risk factor for the subsequent development of adverse health outcomes; and, in people with diabetes, increased HbA1c concentrations are associated with micro- and macro-vascular complications, as well as with mortality. Also, Rwanda is a low incidence rate country so death from ketoacidosis may be more common (these measures are inversely related). Since Rwanda has a higher female population, incidence rates may be disproportionately higher in females.

## Methods

The current study is being conducted to serve the need of LFAC to evaluate long-term outcomes, including mortality, and uses a retrospective cohort design to survey 84 participants who ‘aged out’ of the LFAC program in 2012 or 2013, i.e. 4-5 years prior to being surveyed.

### Study population

This analysis is based on all identified youth registered in the Life for a Child (LFAC) program from 2008 to 2012 and aged out of the program in 2012- 2013 (n=84). The LFAC program assists Rwanda citizens <26 years old. The inclusion criterion for this study was that youth had to have been examined by RDA at least once, as indicated by the presence of a clinical record. Since uncertainty surrounds an individual’s birth date, participants were allowed to continue in the LFAC program until the end of their 26th year. Two sets of data were obtained for 81 of the 84 subjects, based on the first and last clinic visits with the LFAC program. In three cases, only one set of data were obtained, at the individual’s first visit.

### Measurements

Data were collected by RDA staff at district hospital visits and at their Kigali clinic as appropriate. Measurements were obtained by interview, anthropometric measures, or laboratory testing. Anthropometric measures of height (cm) and weight (kg) were assessed using a stadiometer and floor scale. ACR and HbA1c were assessed using the Siemens DCA Vantage. Systolic and diastolic blood pressure were assessed via automatic blood pressure cuff (Omrom Healthcare, Inc.).

### Risk factors assessed

 Self-report through interview: date of birth, date of diagnosis, gender, possession of meter (yes or no), insulin types (NPH/REG, Mixture 70/30, Oral agents, or Diet), number of times patient checks glucose per day, amount of injections per day, insulin units per day, total clinic visits per year, and past year: number of hypoglycemic episodes, number of ketoacidosis episodes, number of hospital admissions.

Measured upon arrival: weight (kg), height (cm), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), HbA1c (%),ACR (mg/g).

#### Ascertainment of mortality

 There is a low rate of death registration in Rwanda. The exact percentage is unknown but it is estimated to be much lower than the 63% of births registered [29]. In order to ascertain mortality, the study relied on consultation with hospitals, families, and peers. Follow-up was censored June 1, 2017. When an exact date of death was not available and only the year of death was known, deaths were assumed to have occurred on June 1st of that year. If an individual was known to have died yet the date of death was unknown, the censor date (June 1, 2017) was used as the death date.

## Statistical Analysis

The statistical analysis was performed using STATA version 14.0 (StataCorp LP, College Station, TX). Reported *P*‐values were 2‐tailed, and a p-value <0.05 was considered statistically significant. Descriptive statistical evaluations of baseline data and last available LFAC measures were performed by gender (Table 2 and 3) and mortality status (Table 4 and 5). All continuous values were tested for normality using Q-Q plots and Shapiro-Wilks tests. T-tests were used to assess between group differences for normally distributed continuous variables, whereas the Wilcoxon rank-sum test was used for non-normally distributed continuous variables. Chi-square tests were utilized to assess associations between categorical variables. Logistic regression analysis was performed to assess baseline and last clinic visit predictors of mortality status.

## Results

During the period between 2014 and 2017, 42% of study participants (n=36) were known to be alive, 12% were known to have died (n=10), while vital status remained unknown for 46% (n=38). Person years were calculated as time in years from a participant’s last clinic visit to the time of death or end of follow-up (i.e. June 1, 2017) for all with known vital status.

Table 1 shows the demographic characteristics of the 84 participants identified from the master registry as having aged out of the LFAC program in 2012-2013. Eighty-one of these participants had two or more clinic visits, while three had only an initial visit. Overall, the average time spent within the program was two years, with a standard deviation of 1.2 years (range of 0 to 4.2 years). Of 84 participants, mean baseline age was 24.1 years and 60.7% (51) were women. During 4.30 years of follow-up (184.8 person years), there were 10 deaths (6 female (60.0%)), giving an incidence density of 5.4 /100 person-years.

Table 1. Descriptive Characteristics of Rwandese Youth with Type 1 Diabetes (n=84)

|  |  |  |
| --- | --- | --- |
| **Participant Characteristics** | **Mean (SD)** | **Range** |
| Age at baseline (years) | 24.1 (1.4) | 21.3-27.0 |
| Length in program (years) | 2.0 (1.2) | 0-4.2 |
| Follow up time (years) | 4.3 (0.4) | 3.6-6.3 |
| **Variable** | **N** | **Percentage** |
| Gender*Female**Male* | 51 | 60.7 |
| 33 | 39.3 |
| Mortality\**Yes* | 10 | 22 |

\*Mortality only assessed on those with known vital status (n=46)

Differences in baseline characteristics by gender are shown in Table 2. Generally, no differences were observed between men and women with the exception of BMI, being higher among women compared with men (21.9 vs. 19.9 kg/m2, p-value=0.05), and years since diagnosis, with women having been diagnosed on average 2.8 years earlier than men (p-value=0.05). No study participant reported ketoacidosis or episodes of hypoglycemia (not shown).

Table 2. Baseline Characteristics by Gender

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **All(n=84)** | **Women(n=51)** | **Men(n=33)** | **P-Value** |
| Age (years) | 24.2 (1.4) | 24.0 (1.4) | 24.43(1.3) |  0.13 |
| Height (cm) | 160.5 (10.1) | 156.6 (9.6) | 166.2 (8.2) | <0.001 |
| Weight (kg) | 54.2 (9.7) | 53.6 (10.9) | 55.2 (7.5) | 0.48 |
| BMI (Kg/m2) | 21.1 (3.2) | 21.9 (3.7) | 19.9 (1.7) | 0.05 |
| A1c (%) | 9.9 (7.3,12.3) |  9.7 (7.5,11.5) | 10.8(7.3,13.2) | 0.48 |
| SBP (mmHg) | 119.7(16.8) | 118.7(16.7) | 121.3(17.2) | 0.49 |
| DBP (mmHg) | 78.4(11.6) | 79.5(11.8) | 76.7(11.3) | 0.29 |
| ACR (mg/g) | 11.5 (9.3,19.1) | 14(9.5,19.1) | 10.3(5.9,19.6) | 0.45 |
| Insulin dose/ kg | 0.6(0.3) | 0.6(0.3) | 0.6(0.3) | 0.48 |
| Possesses meter (%, n) | 25%(21) | 27%(14) | 22%(7) | 0.57 |
| Number of clinic visits/ year  | 12(12,12) | 12(12,12) | 12(12,12) | 0.90 |
| Treatment Type (%, n) | 0.50 |
| N/R | 50(9) | 58(7) | 22(2) |  |
| Mixture 70/30 | 39(7)  | 25(3) | 67(4) |  |
| Oral agent | 5.5(1) | 8(1) | 0.0 (0) |  |
| Diet | 5.5(1) | 8(1) | 0.0 (0) |  |
| Duration since diagnosis (years) | 2.8(1.3,3.8) | 3.5(1.9,7.5) | 0.7(0.4,0.7) | 0.05 |

\*Numbers reported are means (standard deviation) for normally distributed variables, medians (25th percentile, 75th percentile) for non-normally distributed variables, and % (N) for categorical variables.

Table 3 depicts participant characteristics at their last clinic visit, approximately four years following their initial assessment, by gender. BMI continued to be increased in women compared with men, however, additional differences by gender were now evident. Thus, HbA1c was higher in men compared with women (p=0.02), despite a higher daily insulin dose per kilogram (p=0.03). On the contrary diastolic blood pressure was higher in women than in men (p=0.02).

Table 3. Characteristics at the Last Visit by Gender

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **All (n= 84)** | **Women (n= 51)** | **Men (n=33)** | **P-Value** |
| Age (years) | 26.2(0.9) | 26.0 (0.8) | 26.4(1.1) | 0.09 |
| Height (cm) | 160.9 (9.9) | 156.5 (8.5) | 167.6 (8.1) | <0.0001 |
| Weight (kg) | 57.7 (9.5) | 57.1 (10.4) | 58.7(8.1) | 0.48 |
| BMI (Kg/m2) | 22.3 (3.0) | 23.2(3.1) | 20.9(2.3) | 0.005 |
| A1C (%) | 8.2 (6.8,10.3) | 8.1(6.5, 9) | 8.4(7.4, 12.2) | 0.02 |
| SBP (mmHg) | 125.8 (19.4) | 128.4(21.8) | 121.7(14.4) | 0.13 |
| DBP (mmHg) | 81.8(11.8) | 84.2(11.4) | 78.1(11.5) | 0.02 |
| ACR(mg/g) | 11.2(7.3, 15.2) | 11.2(7.5, 15.2) | 11.4(6.9,48.8) | 0.56 |
| Insulin dose/ kg | 0.8(0.3) | 0.7(0.3) | 0.8(0.3) | 0.03 |
| In Possession of Meter (%, n) | 59(46) | 65(31) | 50(15) | 0.20 |
| Number of Clinic Visits per year | 12(12,12) | 12(12,12) | 12(12,12) | 0.30 |
| Treatment Type (%, n) | 1.0 |
| N/R | 45(10) | 46(6) | 44(4) |  |
| Mixture 70/30 | 45(10) | 38(5) | 55.5(5) |  |
| Oral agents | 4.5(1) | 8(1) | 0.0 (0) |  |
| Diet | 4.5(1) | 8(1) | 0.0 (0) |  |

\*Numbers reported are means (standard deviation) for normally distributed variables, medians (25th percentile, 75th percentile) for non-normally distributed variables, and % (N) for categorical variables.

In univariate analyses assessing baseline characteristics associated with mortality within a four-year period (Table 4), significant associations were noted for height (161.9 vs. 152.7, p=0.02) and weight (56.8 vs. 46.4, p=0.006) whereas borderline associations were observed for age (24.6 vs 23.8, p=0.07) and HbA1c (9.4 vs. 11.1, p=0.09).

Table 4. Baseline Risk Factors by Mortality Status

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable**  | **All (n= 46)** | **Alive (n= 36)** | **Deceased (n=10)** | **P-Value** |
| Age (years) | 24.4(1.3) | 24.6(1.2) | 23.8(1.5) | 0.07 |
| Gender (male) | 48 (22) | 50(18) | 40(4) | 0.59 |
| Height (cm)  | 160.0 (10.5) | 161.9 (10.1) | 152.7 (9.2) | 0.02 |
| Weight (kg) | 53.8 (9.9) | 56.1 (9.52) | 46.4 (8.0) | 0.006 |
| BMI (Kg/m2)  | 21.2(3.0) | 21.5(3.1) | 20.1(2.4) | 0.20 |
| A1C (%) | 10.1(7.3,13) |  9.4(7.1, 11.9) | 11.5(7.3, 13) | 0.09 |
| SBP (mmHg) | 121.3(19.1)) | 120.9(18.9) | 122(20.9) | 0.80 |
| DBP (mmHg) | 80.0(11.8) | 79.0(11.0) | 83.2(14.7) | 0.33 |
| ACR (mg/g) | 11.2(9.5, 16.3) | 11.2(8.3, 15.2) | 307.5(9.6, 16.3) | 0.40 |
| Insulin dose/ kg | 0.6(0.3) | 0.6(0.3) | 0.7(0.3) | 0.33 |
| In Possession of Meter (%, n)  | 28(13) | 30(11) | 20(2) | 0.50 |
| Number of Clinic Visits per year | 12(12,12) | 12(12,12) | 12(12,12) | 1.0 |
| Treatment Type (%, n) | 0.10 |
| N/R | 42(6)  | 33.3(4)  | 100(2)  |  |
| Mixture 70/30 | 50(7)  | 58.3(7) | 0.0 (0) |  |
| Oral agents | 8(1) | 8.3(1)  | 0.0 (0) |  |
| Diet | 0.0 (0) | 0.0 (0) | 0.0 (0) |  |
| Duration since date of Diagnosis (years) | 2.9(0.7, 3.8) | 2.9(0.7, 3.8) | 2.4(1.3,3.5) | 1.0 |

\*Numbers reported are means (standard deviation) for normally distributed variables, medians (25th percentile, 75th percentile) for non-normally distributed variables, and % (N) for categorical variables.

However, when univariate analyses focused on characteristics assessed at the last clinical visit (Table 5), a lower BMI (22.5 vs. 19.7, p=0.01) and higher HbA1c concentrations (8.2 vs. 11.0, p=0.04), in addition to height (161.9 vs. 153.5, p=0.02) and weight (59.0 vs. 46.4, p=0.0005) were associated with mortality.

Table 5. Risk Factors at the Last Visit by Mortality Status

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable**  | **All (n= 46)** | **Alive (n= 36)** | **Deceased (n=10)** | **P-Value** |
| Age (years) | 26.3(0.9) | 26.3(0.6) | 26.3(1.6) | 0.90 |
| Height (cm)  | 159.7 (9.6) | 161.9 (9.4) | 153.5 (8.1) | 0.02 |
| Weight (kg) | 56.1 (10.6) | 59.0 (10.2) | 46.4 (4.3) | 0.0005 |
| BMI (Kg/m2)  | 21.8 (3.2) | 22.5 (3.2) | 19.7 (2.2) | 0.01 |
| A1C (%) | 8.4(6.9,10.9) |  8.2(6.5, 9) | 11(8.8, 11.4) | 0.04 |
| SBP (mmHg) | 123.8(15.7) | 122.0(15.4) | 129.6(16.0) | 0.20 |
| DBP (mmHg) | 81.1(11.3) | 80.4(10.8) | 83.7(12.9) | 0.40 |
| ACR(mg/g) | 13.7 (8.5, 138.4) | 13(7.3, 84.1) |  394.5(394.5, 394.5) | 0.12 |
| Insulin dose/ kg | 0.8(0.3) | 0.7(0.2) | 0.9(0.4) | 0.059 |
| In Possession of Meter (%,n) | 67(28) | 64(21) | 78(7) | 0.40 |
| Number of Clinic Visits per year | 12(12,12) | 12(12,12) | 12(12,12) | 1.0 |
| Treatment Type (%,n) | n/a |
| N/R | 60(6)  | 60(6)  | 0.0 (0) |  |
| Mixture 70/30 | 40(4)  | 40(4) | 0.0 (0) |  |
| Oral agents | 0.0 (0) | 0.0 (0) | 0.0 (0) |  |
| Diet | 0.0 (0) | 0.0 (0) | 0.0 (0) |  |
| Duration since date of Diagnosis (years) | 4.4(3.5, 7.5) | 4.4(3.4, 7.0) | 5.5(3.5, 7.5) | 0.81 |

\*Numbers reported are means (standard deviation) for normally distributed variables, medians (25th percentile, 75th percentile) for non-normally distributed variables, and % (N) for categorical variables.

A multivariable logistic regression model was constructed to assess whether participant characteristics at the last visit predicted mortality status (Table 6). Among last visit risk factors assessed, BMI (OR=0.6, 95% CI=0.3, 0.9) and HbA1c (OR=2.7, 95% CI=1.1, 6.6) independently predicted mortality status.

Table 6. Last Visit Risk Factor Association with Mortality

|  |  |  |
| --- | --- | --- |
| **Variable** | **Odds ratio (95% Confidence Interval)** | **P-value** |
| Sex(referent group= male) | 11.5 (0.5, 24.4) | 0.12 |
| Meter Possession (referent group= no) | 16.7 (0.5, 50.3) | 0.10 |
| SBP | 1.0 (0.9, 1.2) | 0.27 |
| DBP | 1.0 (0.0, 1.2) | 0.67 |
| BMI | 0.6 (0.3, 0.9) | 0.02 |
| A1C | 2.7 (1.0, 6.6) | 0.03 |

Table 7 is a multivariable regression model with the same risk factors as Table 6, but instead, BMI is broken down into its constituent parts: height and weight. In this model, weight is a significant inverse risk factor for mortality (OR=0.7, 95% CI=0.5, 0.9). Meter possession and A1c are borderline significant risk factors associated with mortality (p-value of 0.07 and 0.05, respectively).

Table 7. Last Visit Risk Factor Association with Mortality

|  |  |  |
| --- | --- | --- |
| **Variable** | **Odds ratio (95% Confidence Interval)** | **P-value** |
| Sex(referent group= male) | 1.7 (0.02, 24.4) | 0.80 |
| Meter Possession (referent group= no) | 31.2 (0.6, 40.2) | 0.07 |
| SBP | 1.0 (0.9, 1.2) | 0.41 |
| DBP | 0.9 (0.7, 1.1) | 0.88 |
| Height | 0.9 (0.8, 1.0) | 0.87 |
| Weight | 0.7 (0.5,0.9)  | 0.04 |
| A1C | 2.8 (0.9, 7.9) | 0.05 |

Finally, Table 8 shows the results of the multivariable regression model for the change in BMI and A1C from the first to the last visit, along with the participant length in the program. Neither of these factors was significantly associated with mortality.

Table 8. Risk Factor Across Program Length Association with Mortality

|  |  |  |
| --- | --- | --- |
| **Variable** | **Odds ratio (Confidence Interval)** | **P-value** |
| Length in Program | 1.0 (1.0, 1.0) | 0.49 |
| Change in BMI | 1.2 (0.8, 1.7) | 0.49 |
| Change in A1C | 1.0 (0.7, 1.5) | 0.99 |

# Discussion

 There were some similarities to the study results and existing findings from the literature, as expected. Interestingly, the study population was similar to other low incidence countries in that the participants were disproportionately female (~61%) [10]. In addition, a greater proportion of deceased participants were female (60%) (shown in table 2). HbA1c is a significant predictor of diabetes complications and, as expected, was significantly associated with mortality status in the present study as well, as shown in Table 6 [15]. Study findings further showed that deceased had shorter mean height lower weight, and BMI (table 4 and 5). This could be due to an inherently better health in living participants than ones who have died, and probably reflects poor nutrition in the deceased. Nutrition should be a major component for preventative measures. Unexpectedly, females have a significantly higher BMI in both first and last visit clinics, although the mean height and weight are lower for females (Tables 2 and 3).

 A major strength of the study is that it sheds light on a vulnerable population that is not usually followed. Since Rwanda does not have a diabetes registry, many of those who age out of the LFAC program are lost to follow up. Another strength is that the RDA staff is the primary data collector so methods of interviewing and interacting with the patients are often consistent over time. Moreover, the RDA staff calibrates the DCA tool used for ACR and HbA1c measurements prior to each quarterly visit.

 A major limitation to this study is the high degree of missing data. The 46% of unknown vital status extremely limits the scope of the mortality analyses. In addition, out of the 36 variables, 10 were missing for over 50% of the study population. The study design also has its limitations, namely the low sample size. A large portion of the data rely on participant self -report. There could be self-reporting bias due to lack of memory on the topic (some of the data rely on participants recalling the exact number of hypoglycemic episodes since the last quarterly visit) or stigma of saying something displeasing. There is a degree of inconsistency in data reporting, for instance there are whole years of gaps in certain variable measurements. Lastly, the timing of quarterly visits was inconsistent which could increase attrition from the LFAC program.

Additionally, since the switch in the national language to English is relatively new (it became an official language in 1994 and took over from French in schools in 2008), there is a mix of languages in reporting [26]. The Rwanda Ministry of Health prefers all quarterly reports to be in English and this is challenging for the staff who speak mainly Kinyarwanda and French.

There are quite a few barriers to care in Rwanda that also increase attrition from the LFAC program and clinic visits. Namely, these barriers are lack of transportation, communication, and knowledge. A cumbersome challenge for patients is to find transportation to the clinic visits. Even though the RDA visit each of the 44 district hospitals, the closest one may require multiple forms of transportation (bus, walking, ride share), can be very costly, and can take several hours. These barriers to care are accentuated in rural areas.

Another challenge in low resource areas is communication and disseminating information. This is extremely critical to the staff of the RDA for clinic visits. The RDA does not have a set date for visits so they rely on time-consuming and often unreliable tools such as calling every patient with a phone (which is not nearly enough) or relaying messages via local hospital staff or other patients. Another barrier to care is the resource consumption of T1D. Due to the nature of diabetes affecting youth, young children often rely on parents for diabetes management. Many parents are too busy to constantly monitor their child or lack education on the disease.

Diabetes complications attributed to socioeconomic status are widespread and difficult to intervene upon. The poverty rate is high in Rwanda, affecting ~40% countrywide and 50% in rural areas [27]. Stunting in children under five is at a rate of 44% in 2011, 17% of those cases are extremely severe, and 78% of infants two and younger receive low nutrient diets [27]. Chronic malnutrition is partly due to inadequate household food security. Nutrition intake and diet reforms are difficult to make in areas of arid soil and poverty.

## Projections on Rwanda

As the typical Rwandan lifestyle changes and obesity rates climb, there is expected to be an increase in NCDs, namely an increase in cardiovascular disease and type 2 diabetes, especially in the capital [30]. In a 2016 report from the Rwandan Ministry of Health, 36% of a Kigali sample was overweight to obese [31]. Nevertheless, the political and social climate looks promising for a positive public health shift on NCDs. Rwanda is a politically stable democracy in which the government is putting more resources, funding, and training into its health sector. Currently the health sector expenditure totals $153 billion per year. Of that, $117 million goes to NCD control (approximately 13% of total expenditure) [32]. In the past decade, 425 staff members from health centers and district hospitals across the country were trained in NCD screening, education, and management [31]. More specifically, from 2006-2012, 57 doctors and 103 nurses trained in diabetes follow-up and care [31]. In June of 2016, an international NCD conference took place in Kigali to plan a multi-disciplinary approach on treatment and management of NCDs [33]. Along with efforts in NCD preparedness, there are efforts in increasing economic development. Vision 2020 is a developmental strategic plan to move from low-income to middle-income country [33]. The focus is to shift toward economic improvement to reduce poverty and geographic inequality. This requires that less than 30% of the population lives in poverty [33]. Currently, the portion of the population living in poverty is ~40% [27].

## Implications

The multitudinous amount of NCD research shows how important it is to surveil the burden to prevent negative health outcomes. In order to have proper surveillance, national disease registries are key and can lead to a better understanding of mortality predictors and causative agents.

 Between 2011 and 2030, it is estimated that NCDs will result in a cumulative loss of $47 trillion, globally [34]. NCDs are especially burdensome in low- to middle-income countries. In these countries, NCDs cause and perpetuate poverty and further disruption to the economy [34]. In Africa, the ‘double burden of disease,’ due to the ongoing challenge of infectious diseases and the staggering increases in NCD incidence, produces a strain on the already low resources [34].

Often, NCD patients are neglected in order to better focus on the communicable diseases at hand.

 Trained health workers, as well as a vigilant surveillance system, are needed to ensure the wellbeing of those diagnosed with a NCD. This is especially the case for those with diabetes, since, in the years to come, the global prevalence rates are expected to dramatically increase. Chronic diseases accounts for more than ¾ of global deaths and diabetes mortality is expected to rise from the 11th leading cause of death to the 6th [35]. It would be wise to be prepared for an already underway diabetes epidemic and start to disseminate symptoms and management information to the population overall. In order to do this, two steps need to occur: research to further assess risk factors, country preparedness/ resources, and global burden of disease (especially in low income regions) and a national disease registry to increase diagnosis and data quality. Both of these steps would also be helpful for health care planning and would possibly bring funding and political will to the topic.

# Conclusions

Our findings suggest an alarmingly high mortality rate for Rwandese youth with T1D, with an incidence density rate of 5.4 /100 person-years. HbA1c and BMI (or weight, when BMI was replaced by weight and height in Table 7) assessed at the most recent clinical visit were significant predictors of mortality. This finding is consistent with the high quality DCCT cohort publication and shows the importance of maintaining HbA1c under control [15]. HbA1c is a modifiable risk factor and control of this measure can prevent complications. Interestingly, there are significant differences in BMI, height, and weight observed between living and deceased participants. This may be due to differences in their overall nutrition and socioeconomic status. Unfortunately, the small sample size and the high degree of missing data do not allow for definitive conclusions. Thus, all assessed risk factors may be important and merit further study. The lack of universal death records in Rwanda hinder this study and any other that incorporate Rwandan death statistics into the analysis. In conclusion, it is imperative to continue and further resources, education, and awareness on diabetes control and healthy lifestyle choices in order to decrease negative health outcomes related to Type 1 Diabetes in Rwanda.

bibliography

1. Klinke DJ. Extent of Beta Cell Destruction Is Important but Insufficient to Predict the Onset of Type 1 Diabetes Mellitus. Vella A, ed. *PLoS ONE*. 2008;3(1):e1374. doi:10.1371/journal.pone.0001374.

2. U.S Department of Health & Human Services, Centers for Disease Control and Prevention. National diabetes statistics report, 2017.

3. Skyler JS, Bakris GL, Bonifacio E, et al. Differentiation of Diabetes by Pathophysiology, Natural History, and Prognosis. *Diabetes*. 2017;66(2):241-255. doi:10.2337/db16-0806.

4. R. Beaglehole, J. Epping-Jordan, V. Patel, et al. Improving the prevention and management of chronic disease in low-income and middle-income countries: a priority for primary health care. Lancet, 372 (2008), pp. 940-949. [https://doi.org/10.1016/S0140-6736(08)61404-X](https://doi.org/10.1016/S0140-6736%2808%2961404-X)

5. Rwanda Diabetes Association Overview. 2017. RDA, Kigali.

6. National Institute of Diabetes and Digestive and Kidney Diseases. 2016. What is Diabetes? Health Information, NIH.

7. American Diabetes Association. *Diabetes Care*. 2017;40(Supplement 1):S11-S24. DOI: 10.2337/dc17-S005.

8. Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ. Chapter 1: Epidemiology of Type 1 Diabetes. *Endocrinology and metabolism clinics of North America*. 2010;39(3):481-497. doi:10.1016/j.ecl.2010.05.011.

9. Jeffcoate, W. 2006. Drive to eliminate the burden of type 1 diabetes. The Lancet. 2006;367(1):795-797. doi:[10.1016/S0140-6736(06)68314-1](http://dx.doi.org/10.1016/S0140-6736%2806%2968314-1)

10. Soltesz, G., Patterson, C., Dahlquist, G. and EURODIAB Study Group, 2007. Worldwide childhood type 1 diabetes incidence – what can we learn from epidemiology?. Pediatric Diabetes, 8: 6–14. doi:10.1111/j.1399-5448.2007.00280.x

11. Tidy, C. 2016. Diabetic Ketoacidosis. Patient 2016;1542 (v25). doctor/diabetic-ketoacidosis

12. Yudkin, S. Insulin for the world's poorest countries. 2000. The Lancet. 2000, 355(9207) 919-921; DOI: [0.1016/S0140-6736(99)09225-9](http://dx.doi.org/10.1016/S0140-6736%2899%2909225-9)

13. Koroshi A. Microalbuminuria, is it so important? *Hippokratia*. 2007;11(3):105-107.

14. De Ferranti et al.Type 1 Diabetes Mellitus and Cardiovascular Disease: A Scientific Statement From the American Heart Association and American Diabetes Association. Diabetes Care Oct 2014, 37 (10) 2843-2863; **doi:** 10.2337/dc14-1720International Insulin Foundation. Diabetes in Sub-Saharan Africa. Access 2 insulin, London.

15. Diabetes Control and Complications Trial Research Group. Effect of intensive therapy on the microvascular complications of Type 1 diabetes mellitus. JAMA. 2002;287:2563–2569.

16. National Institute of Diabetes and Digestive and Kidney Diseases. 2016. The A1C Test and Diabetes. Health Information, NIH.

17. Ragnar, Hanas. Type 1 Diabetes, fourth edition. London: Class Publishing; 2011

18. International Insulin Foundation. Diabetes in Sub-Saharan Africa. Access 2 insulin, London.

19. World Health Organization. 2015. Rwanda Non-communicable Diseases Risk Factors Report. Technical report, World Health Org, Geneva.

20. Roglic, G. World Health Organization. 2016. WHO Global report on diabetes: A summary. Global report, World Health Org, Geneva.

21. Ogle et al. Financial costs for families of children with Type 1 diabetes in lower-income countries. Diabet Med. 2016 Jun;33(6):820-6.

22. Paun, A., Yau, C., Danska, J. The Influence of the Microbiome on Type 1 Diabetes. 2017.The Journal of Immunology January 15, 2017, 198 (2) 590-595; DOI: 10.4049/jimmunol.1601519

23. Bazargani YT, de Boer A, Leufkens HGM, Mantel-Teeuwisse AK (2014) Selection of Essential Medicines for Diabetes in Low and Middle Income Countries: A Survey of 32 National Essential Medicines Lists. PLoS ONE9(9): e106072. https://doi.org/10.1371/journal.pone.0106072

24. Beran, D. World Health Organization. 2011. Improving access to insulin: what can be done? Policy Perspective, World Health Org, Geneva.

25. Distiller LA. Why do some patients with type 1 diabetes live so long? *World Journal of Diabetes*. 2014;5(3):282-287. doi:10.4239/wjd.v5.i3.282.

26. Government of Rwanda. 2015. Rwanda. Geography, Kigali.

27. World Health Organization Regional Office for Africa. 2014. WHO Country Cooperation Strategy Rwanda 2014-2018. Technical report, World Health Org, Geneva.

28 World Bank Group. 2017. Fertility rate total (births per woman). Census report, World Bank.

29. Mbanjumucyo G, DeVos E, Pulfrey S, Epino HM. State of emergency medicine in Rwanda 2015: an innovative trainee and trainer model. *International Journal of Emergency Medicine*. 2015;8:20. doi:10.1186/s12245-015-0067-2.

30. World diabetes foundation. 2012. Global diabetes trends begin to show in Rwanda. News, WDF.

31. Ministry of Health Rwanda. 2016. Health Sector Annual Report. Technical Report, Republic of Rwanda, Kigali.

32.Fortune of Africa. 2015. The Health Sector of Rwanda.

33. International Organization for Migration. 2012. Rwanda. IOM.

34. Kaiser Family Foundation. 2017. The U.S. Government and Global Non-Communicable Disease Efforts. Global Health Policy, US.

35. Mathers CD, Loncar D. Projections of Global Mortality and Burden of Disease from 2002 to 2030. Samet J, ed. *PLoS Medicine*. 2006;3(11):e442. doi:10.1371/journal.pmed.0030442.