

Framework of T1D Care and Outcomes

Introduction:

The T1D Index will provide novel functionality that estimates current standards of care across all countries in the world, with the 'Four Levers' allowing us to estimate the significant gains in both clinical outcomes and life expectancy that can be achieved by improving on prevailing standards of care.

This document outlines the main assumptions and factors that influence the different levels of care for T1D as modelled in the T1D Index.

Background:

This level of care framework is based on the concept developed by [Ogle et al¹](#), in their paper on Levels of type 1 diabetes care in children and adolescents for countries at varying resource levels. This paper outlines three levels of T1D care: "minimal care," "intermediate care," and "comprehensive care." Each level contains levels, which describe insulin and blood glucose monitoring regimens, requirements for haemoglobin A1c (HbA1c) testing, complications screening, diabetes education, and multidisciplinary care.

The literature provides various examples at each level, including from countries where the Life for A Child (LFAC) and the Changing Diabetes In Children (CDIC) programs have assisted local diabetes centres to introduce intermediate care. In our adaptation of the framework (Table 2), we have linked levels of care to mean HbA1c levels range from 9.0% to 14.0% for the most minimal level of care, 7.5% to 9.5% for intermediate care, and 6.5% to 8.7% for comprehensive care.

The levels concept is based on the "minimal," "recommended," and "comprehensive" care levels in the International Diabetes Federation (IDF)'s [Global Guidelines for Type 2 Diabetes²](#).

The T1D Index further proposes that there are four main interventions or 'Four Levers' through which the prevailing levels of care can be improved across different geographies:

- Timely Diagnosis
- Insulin + Strips Self-Management
- Pumps + CGMs Self-Management
- Preventions + Cures

For the purposes of the modelling, each of these interventions is associated with a clinical outcome through HbA1c as well as the standardised mortality rate (SMR), except for the Timely Diagnosis lever (where the modelling assumes a 100% diagnosis rate).

Levels of Care and Outcomes:

The T1D Index models these four levers which are based on a framework that defines what the spectrum of treatment and care options for T1D look like around the globe today. This framework is informed by current experience and research that is predominantly driven by non-governmental interventions such as from Life for a Child in a number of low and low to middle income (LIC and LMIC) settings around the world. It has also been informed by the JDRF-ISPAD survey of global care levels conducted in 2020.

As with most frameworks, not all care modalities will neatly fit into one of the four defined levels of care. Most of the data to informing 'minimal' and 'intermediate' levels of care is from low resource settings and has not been tested robustly in upper middle or high income (UMIC and HIC) settings. The framework also assumes that well-resourced settings can provide the comprehensive levels of care as outlined in the [ISPAD Clinical Practice Consensus Guidelines 2018³](#).

Our framework is also based on three main evidence-based assumptions:

¹ Ogle GD, von Oettingen JE, Middlehurst AC, Hanas R, Orchard TJ. Levels of type 1 diabetes care in children and adolescents for countries at varying resource levels. *Pediatr Diabetes*. 2019 Feb;20(1):93-98. doi: 10.1111/pedi.12801. Epub 2018 Dec 10. PMID: 30471084.

² International Diabetes Federation Guideline Development Group. Global guideline for type 2 diabetes. *Diabetes Res Clin Pract*. 2014 Apr;104(1):1-52. doi: 10.1016/j.diabres.2012.10.001. Epub 2014 Feb 5. PMID: 24508150.

³ Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong CX, Aschner P, Craig ME. *ISPAD Clinical Practice Consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents*. *Pediatr Diabetes*. 2018 Oct;19 Suppl 27(Suppl 27):7-19. doi: 10.1111/pedi.12773. PMID: 30226024; PMCID: PMC7521365.

- Each extra self-monitoring of blood glucose (SMBG) test per day provides a benefit of 0.5% HbA1c⁴
- Improving education around T1D self-management from limited/minimal levels to 'full service' definition described under Intermediate care settings results in a reduction of 0.5% HbA1c^{5,6,7}
- The framework also makes assumptions around patient compliance within each level of care

As Table 1 below shows, the T1D Index takes as inputs standardised mortality rates (SMR) from various studies based in countries around the world. Using the Pittsburgh EDC data, pseudo HbA1c (pHbA1c) values are assigned to each country, for each broad level of care (minimal or non-minimal). The Index assumes that all HIC and UMIC countries have 100% diagnosis rates, and everyone receives a level of care that is higher than minimal. These SMR and HbA1c levels are then mapped to the framework, which results in the implied levels of care as outlined below.

Table 1: Levels of Care and Index modelling

		France	United States	Brazil	India	DRC
Diagnosis rate		100%	100%	100%	84%	66%
Minimal care	Share of cases	0%	0%	0%	50%	65%
	index paper SMR	-	-	-	30.5	40.1
	pHbA1c	-	-	-	14.0	14.7
	Implied care level				Premix, no strips	Rationed premix
		-	-	-	-	-
Non-minimal care	Share of cases	100%	100%	100%	50%	35%
	index paper SMR	2.7	3.9	5.5	8.0	18.4
	pHbA1c	7.3	8.3	9.1	10.2	12.5
	Implied care level	Pumps/CGMs + analogs/strips	Analog + 3 strips	Human + 1-2 strips	Premix + 1-2 strips	Premix, no strips

Through validation work with in-country experts, we know that these assumptions around all HIC and UMIC countries receiving non-minimal care do not translate well on the ground. For example, the ISPAD 2020 survey of experts as well as anecdotal evidence from key stakeholders indicate that Brazil has 30% of its T1D population on a care regime that is 'minimal' as per the Levels of Care framework. Similarly, in the US we know that affordability issues and subsequent rationing of insulin has resulted in many people living with T1D experiencing outcomes which are equivalent to those achieved through 'minimal' levels of care. The T1D Index dashboard includes a simulation feature that allows users to alter these assumptions for each country and vary inputs to reflect real world situations.

The framework of Levels of Care is as outlined in Table 2. The details of each Level of Care are as below.

Minimal Care:

This level of care describes the regime that is available across most low-income countries and in poorly resourced settings. In many countries, only human pre-mixed insulin is used as it is the only insulin provided in

⁴ Miller KM, Beck RW, Bergenstal RM, Goland RS, Haller MJ, McGill JB, Rodriguez H, Simmons JH, Hirsch IB; T1D Exchange Clinic Network. Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c levels in T1D exchange clinic registry participants. *Diabetes Care*. 2013 Jul;36(7):2009-14. doi: 10.2337/dc12-1770. Epub 2013 Feb 1. PMID: 23378621; PMCID: PMC3687326.

⁵ Hampson SE, Skinner TC, Hart J, et al. Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review. *Health Technol Assess*. 2001;5:1-79

⁶ Grey M, Boland EA, Davidson M, Li J, Tamborlane WV. Coping skills training for youth with diabetes mellitus has long-lasting effects on metabolic control and quality of life. *J Pediatr* 2000; 137: 107-113.

⁷ Montanari VA, Gabbay MAL, Dib SA. Comparison of three insulin bolus calculators to increase time in range of glycemia in a group of poorly controlled adults Type 1 diabetes in a Brazilian public health service. *Diabetol Metab Syndr*. 2022 Sep 13;14(1):129. doi: 10.1186/s13098-022-00903-z. PMID: 36100854; PMCID: PMC9469814.

the public health system. There is little to no point of care testing as health facilities may frequently lack any capacity to measure blood glucose. Self-Management of Blood Glucose (SMBG) is rarely carried out because of financial barriers, so much so that in some settings the cost of two test strips per day is reported to be higher than the cost of insulin. Blood glucose tests are carried out during clinic visits if the measurement is available. HbA1c testing is not likely to be available in any level of the government health system.

Screening for complications is not provided and even basic information around height and blood pressure may not be measured at this level of care. There is minimal or no diabetes education, with care generally provided by an adult physician or a paediatrician inexperienced in the management of T1D. This level of care has devastating outcomes. There is a high early mortality from ketoacidosis at onset, because of misdiagnosis or late diagnosis, and later from early onset of serious complications.

Within Minimal care itself, there are many variations of treatment and management:

0A: Rationed premix

This level of care describes situations in countries where access and supply of even a rationed human premixed insulin regime is unstable. Issues such as unavailability of cold chain supply and storage options may result in limited or poor access to insulin. Such an unstable regime will result in extremely poor glycaemic control (HbA1c higher than 14%) and frequent early complications and mortality (SMR > 30).

1A: Human premix only

At this level of minimal care, human insulin (if available), is given through two injections daily, with little or no SMBG testing at all. As a result of poor glycaemic control (HbA1c of 12-14%) there are also high rates of early complications, with serious long-term complications in some.

1B: Human premix + 1-2 tests strips/day

At this level, people living with T1D may be able to access human premixed insulin and 1-2 test strips per day. There may be some basic education around T1D provided, and care maybe delivered by an adult diabetologist or a paediatrician. Basic complications screening (usually limited to weight, height, blood pressure, visual acuity, and light touch) is conducted. Glycaemic control remains poor (9.5-12%). This level of care still results in serious early onset of long-term complications as well as substantial mortality.

1C: Human basal bolus + 2 test strips/day

At this level, human short- and long-acting insulins are given through two injections per day. A basal-bolus regime should be complemented by testing and education around insulin dose adjustment, which is crucial in optimising use of these insulins. At this level of care, this may be provided sporadically or unaffordable without financial support from government or NGO's. As above, care in large clinics is usually provided by an adult diabetologist or paediatrician, or a paediatric endocrinologist if available. Mortality rates fall sharply as glycaemic control (9-10.5%) and care (including management of diabetic ketoacidosis) begins to improve, and thus prevalence increases.

Intermediate Care:

The key feature of Intermediate care is multiple daily injections ("basal bolus regimen"), accompanied by SMBG and point-of-care HbA1c testing, basic complications screening and diabetes education provided by a paediatric or adult endocrinologist and/or a diabetes nurse educator.

Our framework outlines 4 sub-levels of care within this level (2A1, 2A2, 2B1, 2B2) all differentiated by incremental changes to number of SMBG tests per day at each level of care. It is assumed that each extra SMBG test per day reduces around 0.5% from average HbA1c.⁸

A human insulin basal bolus regime of multiple daily injections, accompanied by frequent testing to monitor blood glucose level and education to support self-management is the cornerstone of Intermediate care. Human insulin is still recommended in this level as it is substantially less expensive than analog insulin. While many LICs and LMIC's are able to provide access to a basal bolus regime of human insulin, access to subsidised SMBG essentials, like test strips and glucometers, remains variable and is often the main barrier for many countries towards moving to an intermediate level of care provision.

Intermediate care is also generally supported by access to point of care HbA1c testing. Complications screening is expanded to include more thorough assessment of eyes and feet, measurement of urinary albumin, serum creatinine, and lipids, with treatment as indicated. Appropriate diabetes education with respect to age, language, culture, and literacy level is provided, and diabetes camps maybe held. A 24-hour emergency support call service may also be available, as well as initiatives in peer and school support.

⁸ Op cit. Miller et al.

Expected mean clinic HbA1c levels, once intermediate care is fully implemented across clinical settings, are 7.5% to 9%. Glucagon would also be available under this level of care; however, it is rarely provided by government health services in less-resourced countries, and the out-of-pocket cost, if it can be purchased at all in these countries, is unaffordable for many. Mortality in this level of care is substantially lower (SMR 3.1-6.3) and long-term complications are also much reduced.

For the purposes of modelling the 'Insulin + Strips Self-Management' intervention, the T1D Index assumes this level of care to include Human basal bolus regime, 4 test strips per day and education and complications screening as outlined above. The T1D Index lever calculations estimate an HbA1c of 8.25% and an SMR of 4.06 for this level of care.

Comprehensive Care:

This level of care is as detailed in the [ISPAD 2018 guidelines](#). The insulin regimen is either basal-bolus or, if possible, by continuous subcutaneous infusion with an insulin pump. The type of insulin provided is analog.

Our framework outlines 4 sub-levels of care within this level (3A1, 3A2, 3A3, 3C) all differentiated by incremental changes to number of tests per day under each level and the move to insulin pumps and continuous glucose monitoring in the last sub-level.

Analog insulin is almost universally preferred over human insulin by health care professionals and people with type 1 diabetes in well-resourced countries. It is accepted that analog insulin helps to reduce rates of nocturnal hypoglycaemia and is considered to provide better Time in Range (TiR) for glycaemic control. It is important to note that, despite many studies, significant improvements in HbA1c levels have not been demonstrated. While there may be associated improvements to TiR and reduction in nocturnal hypoglycaemia, our framework assumes that moving from human insulin to an analog basal bolus regime is associated with a no improvement in HbA1c.

The frequency of testing remains the main variable amongst the levels of care in this level. Under a comprehensive care regime here is sufficient access to SMBG supplies to permit 4 to 6 or more tests per day, and in many situations, there is access to continuous glucose monitoring (CGM), which has added advantages in many contexts. Most recently, "closed-loop" devices are becoming widely used that link the insulin pump to the CGM device. Automated Insulin Delivery systems and closed-loop devices have not been included in our levels of care framework at this stage.

Under a comprehensive care regime, full complications screening at the frequency stipulated by the ISPAD guidelines should be conducted, including, in addition to those outlined in intermediate care, fundus examination by bio-microscopy or photography, and screening for thyroid and celiac disease. Clinic-based, and if possible national, registries should be instituted as part of comprehensive care, with participation in benchmarking efforts such as SWEET providing further benefits. With such care as the norm, mortality is rare (SMR 2.3-3.3)

The challenge, even in well-resourced settings, is to ensure that comprehensive, guidelines-based care is effectively delivered to all people with T1D, not just those who access the leading clinics or who can afford more comprehensive private health insurance plans, but also to those in regional and rural areas and those from disadvantaged socio-economic situations.

For the purposes of modelling the 'Pumps + CGMs Self-Management' intervention for HIC countries, the T1D Index assumes this level of care to include Analog insulin delivered via an insulin pump, CGM system and complications screening as outlined above. The T1D Index lever calculations estimate an HbA1c of 6.75% and an SMR of 2.48 for this level of care.

Ultimately, people living with T1D need access to cures to ensure that they can live full and healthy lives.

The T1D Index also models a hypothetical level of care for 'Preventions + Cures', where we assume that T1D has been successfully cured to the point that HbA1c returns to within normal range of glycaemic control and SMR returns to 1.

Table 2: Framework of Levels of Care and Outcomes

Level	Insulin	Testing	Education	Assumed HbA1c		Estimated SMR * (Pittsburgh)	
				Low	High	Low	High
<i>Minimal care</i>							
0A	Rationed premix	N/A	None	14.0		31.1	
1A	Human premix	Only at clinic	None	12.0	14.0	15.3	31.1
1B	Human premix	1-2 tests	Limited materials, diabetologist	9.5	12.0	6.3	15.3
1C	Human short +long acting insulin twice daily injections	1-2 tests	Dose adjustment coaching	9.0	10.5	5.3	9.0
<i>Intermediate care</i>							
2A1	Human basal/bolus	2 tests	Camps, peer support, 24/hr emergency call, diabetologist, paediatrician, nurse educator, dietician, social worker	9.0	9.5	5.3	6.3
2A2	Human basal/bolus	3 tests	Camps, peer support, 24/hr emergency call, diabetologist, paediatrician, nurse educator, dietician, social worker	8.5	9.0	4.4	5.3
<i>Insulin + Strips Self-Management lever</i>							
2B1	Human basal/bolus	4 tests	Camps, peer support, 24/hr emergency call, diabetologist, paediatrician, nurse educator, dietician, social worker	8.0	8.5	3.7	4.4
2B2	Human basal/bolus	5+ tests	Camps, peer support, 24/hr emergency call, diabetologist, paediatrician, nurse educator, dietician, social worker	7.5	8.0	3.1	3.7
<i>Comprehensive care</i>							
3A1	Analog basal/bolus	3 tests	+ multidisciplinary care team	8.5	9.0	4.4	5.3
3A2	Analog basal/bolus	4 tests	+ multidisciplinary care team	8.0	8.5	3.7	4.4
3A3	Analog basal/bolus	5+ tests	+ multidisciplinary care team	7.5	8.0	3.1	3.7
<i>Pumps + CGMs Self-Management lever</i>							
3C	Pump	CGM	+ multidisciplinary care team	6.5	7.0	2.2	2.8

* SMRs are adjusted across different age cohorts as per Appendix 4 of the paper