insulin delivery for appropriate persons with DM. Ideally, these individuals should also use CGM as stated in **R13.6.a**.

Grade B; BEL 1

c. Automated insulin delivery (AID) systems, which include an insulin pump, an integrated CGM, and computer software algorithm, aim to better emulate physiological insulin replacement and achieve glycemic targets. This technology is recommended for many persons with T1D since its use has been shown to increase TIR while often reducing hypoglycemia or at least without causing increased hypoglycemia.

Grade A; BEL 1

d. Open-loop (use of a pump and sensor which do not communicate) and sensor-augmented pump (SAP) systems: (CGM communicates with pump facilitating needed adjustments to basal rate; temporary interruption of insulin delivery when glucose levels are low or forecast to be low within 30 minutes). Insulin pump with a CGM or an SAP is recommended to manage persons with DM treated with intensive insulin management who prefer not to use AID systems or have no access to them.

Grade D; BEL 4

Evidence Base 13: How should insulin therapy be used for management of T1D?

Based on the World Health Organization's Classification of Diabetes 2021,[1112] T1D is defined as β-cell destruction and absolute insulin deficiency. Hence, insulin therapy is necessary for life in all persons with T1D ("all or nothing").[1113] Absolute (or near-absolute) insulin deficiency can result in acute hyperglycemic complications, including DKA, hyperosmolar hyperglycemic state, hypertriglyceridemia, and hypercatabolic state, which can be life-threatening.[1114-1120] All persons with T1D should receive adequate basal insulin replacement, either via frequent injections or CSII, every day to prevent development of life-threating acute hyperglycemic complications.[1117,1121] Inadequate (incomplete) insulin replacement, beyond the use of basal insulin, results in chronic hyperglycemia which is a driver for micro- and macrovascular DM-related complications in T1D. Intensive glycemic control with insulin therapy reduces the risk of these complications.[200,1122,1123]

Since publication of the prior CPG in 2015, there has been extensive development on insulin formulations and delivery, particularly in persons with T1D. Several advantages have been published on newer insulin analogs for both basal and prandial insulin; CSII development with adjunctive use of CGM; and the latest development in the use of nonadjunctive CGM with CSII, also called AID systems, HCL systems, or artificial pancreas device systems (discussed below, in Figure 6, and in 2021 AACE Advanced Diabetes Technology guideline).[153]

Physiologic insulin regimens including both basal and prandial insulin, provided by either MDI or CSII, have not been formally tested in RCTs against nonphysiologic insulin regimens (once or twice daily insulin). Rather, physiologic insulin regimens have been formally studied as one component of a comprehensive treatment strategy for persons with T1D.[1106,1124,1118] In comparisons of regimens of MDI with BGM (without CGM) vs CSII for T1D, there have been small improvements in A1C, but substantial reductions in severe and nocturnal hypoglycemia.[1113,1125-1127] However, in the REPOSE RCT, where all participants received a structured diabetes education program and adjusted insulin based on SBMG, treatment with CSII vs MDI resulted in reduction in severe hypoglycemia after 2 years in both groups, with a nonstatistically significant A1C benefit toward CSII, and better treatment satisfaction and QoL among CSII users.[1128] Regardless of the insulin delivery method (MDI vs CSII), glycemic control metrics, including A1C and CGM TIR, hypoglycemic events, QoL, and patient satisfaction are substantially improved when MDI or CSII is augmented with CGM, with better results when CSII is combined with CGM or integrated into AID systems, compared with using CGM.[158,160,1129-1131]

Basic Principles of Insulin Therapy in Type 1 Diabetes

Several trials have demonstrated that physiologic regimens using basal insulin analogs may reduce hypoglycemia, and bolus insulin analogs may result in better control of PPG excursions for most persons with T1D.[1132-1137] Hence, insulin analogs should be considered first-line choice for most persons with T1D (Table 19).

These effects were demonstrated initially when comparing first-generation insulin analogs to NPH insulin.[1132,1134,1138,1139] Further improvements were confirmed when comparing second generation of ultra-long-acting basal to first-generation insulin analogs,[1135,1137,1140-1145] which may translate into potential cost savings in real-world settings from avoiding severe hypoglycemic and hyperglycemic crises.[1146] There are limited data comparing the latest basal insulin analogs degludec and glargine U300.[1147,1148] The InRange RCT assessed the noninferiority of both basal insulins, as measured by CGM metrics.[1149] Furthermore, a novel ultra-long-acting weekly insulin icodec is under development for persons with T1D.[1150]

Similarly, the use of rapid-acting analogs has resulted in less hypoglycemia, with small reductions in A1C compared to using regular human insulin, including MDI using NPH as basal insulin.[1151-1153] The development of ultrarapid insulin analogs has resulted in better coverage of PPG excursions, compared with rapid-acting insulin analogs, as measured by BGM and CGM, but not all studies have resulted in A1C improvements or hypoglycemia reductions.[1154-1157] Inhaled insulin with a faster peak of action and shorter duration is also available as prandial insulin, with the requirement of using repeated inhaled correctional insulin doses after 1 to 2 hours postmeal.[1158,1159]

The starting dose of insulin is usually estimated based on weight, with doses ranging from 0.4 to 0.5 units/kg/day of total insulin, with higher amounts required for persons who are obese (increasingly common in T1D) or have a sedentary lifestyle, as well as during puberty, pregnancy, and acute medical conditions. Conversely, lower starting insulin doses (0.2 to 0.3 units/kg/day) are recommended for older adults, those with renal failure, malnutrition, or low BMI.[1124,1136]

In general, basal insulin requirements are usually 40% to 50% of TDD insulin. Basal insulin doses are titrated to personalized target fasting glucose. In the ideal prandial/bolus regimen, the dose of prandial insulin is usually determined by estimating the carbohydrate content of the meal. Persons with DM should have formal training on carbohydrate counting as part of a multicomponent DSMES program, provided by professionals (CDCES) if available.[1160-1164] Most would start with 1:15 insulin to carbohydrate (IC) ratio (1 unit for 15 g of consistent carbohydrates) or 450/TDD insulin if using regular insulin; 500/TDD if using rapid-acting IC ratio (eg, for someone using 50 units of insulin/day: 500/50 units = 1:10 IC ratio) as a starting point. The IC ratios can be adjusted based on an individual's response to the calculated boluses of insulin. Insulin sensitivity factor (ISF) approximates the glucose-lowering effect of 1 unit of insulin in a particular individual (1500/TDD units for regular insulin vs 1800/TDD rapid acting insulin). These formulas are just starting points and need to be modified empirically for each person. Numerous mobile applications are also being used to assist with IC ratios and ISF.

IC ratios usually range from 1:20 for the very insulin-sensitive to 1:5 for insulin-resistant persons. Similarly, correction dose insulin for premeal or between-meal hyperglycemia is based on the ISF, also called insulin correctional factor, which is based on the overall insulin sensitivity of a person, loosely estimated by the individual's TDD insulin. Although various formulas have been used to estimate the appropriate ISF, this parameter should only be viewed as an estimation due to numerous factors that can alter BG. The most