Overall, a very nice summary.
Stages 1 and 2 are defined as having 2 or more autoantibodies.
I have a semantic comment. It may not be absolutely clear that multiple means more than one. It is often used to mean several (i.e., more than 2). Therefore, I suggest explicitly stating at least 2 or 2 or more autoantibodies.
Thankyou we have changed “multiple” to “two or more islet autoantibodies” in the text.

Page 4 The terminology used for HLA genotyping is confusing to non-experts. As written, it is not clear whether DQ2/DQ8 is an alternative nomenclature for DR3/DR4. I suggest re-writing this section with the non-expert reader in mind.
The text page para 1 page 4 has been rewritten as follows: The highest-risk haplotypes are DRB1*03:01-DQA1*05:01-DQB1*02:01 and DRB1*04-DQA1*03:01-DQB1*03:02 (also expressed as DR3/DR4 or DQ2/DQ8 which are in strong linkage disequilibrium).
This sentence is confusing: “There are likely other, as yet unknown, islet antigens, as the presence of islet cell antibodies confer added risk for development of T1D in individuals with other antibodies.” What are the other antibodies referred to?

Islet cell antibodies are not completely accounted for by the presence of autoantibodies to GAD, IA2 Insulin and ZnT8 antigens. The sentence above has been removed as islet cell antibodies aren’t measured generally now.

Pages 6 and 7 It is notable that studies with GAD-alum are not mentioned.
Reference to GAD vaccine is reference 76 Wherrett DK, Bundy B, Becker DJ, et al. Antigen-based therapy with glutamic acid decarboxylase (GAD) vaccine in patients with recent-onset type 1 diabetes: a randomised double-blind trial. Lancet. 2011;378(9788):319-327 (as an example of lack of success in antigen therapies). This has been expanded to “Randomised controlled trials of GAD alum vaccine have produced inconsistent results. Bayesian meta-analysis indicated that GAD with alum administered twice in Stage 3 diabetes reduces the loss of C-peptide by 15 – 20% at 1 year after treatment67” page 8 Beam CA, MacCallum C, Herold KC, et al. GAD vaccine reduces insulin loss in recently diagnosed type 1 diabetes: findings from a Bayesian meta-analysis. Diabetologia. 2017;60(1):43-49.
Page 10 “Recent data suggest that most individuals with type 1 diabetes have minimal residual c-peptide secretion by age 7 years (Hattersley). The citation is missing.
This citation has been inserted, Shields BM, McDonald TJ, Oram R, et al. C-Peptide Decline in Type 1 Diabetes Has Two Phases: An Initial Exponential Fall and a Subsequent Stable Phase. Diabetes Care. 2018;41(7):1486-1492. Apologies.
Table 1 Candidiasis may also occur in boys wearing diapers. How about replacing (vulvo)vaginal candidiasis with the gender-neutral term perineal candidiasis?

This has been replaced

3/4/2018 at 5:55:30 AM GMT

Permalink

Stages of diabetes

Thank you to the authors and I agree with Joe's comments.

I suggest that the Title of the Chapter could include "and Prevention studies". The consensus of the authors was not to change the title.

Could the authors please review the references for the statement that "Individuals with a first degree relative with type 1 diabetes have an approximately 15 fold increased relative risk of type 1 diabetes" References date from 1984, 1993 and the most recent reference is 2012 of an Italian twin study. References have been updated to include Harjutsalo V 2006

Could the authors clarify the statement that "IVGTT is not required as a prognostic tool". For the clinician it has little value but may be helpful in a research setting. This has been clarified “IVGTT does not add prognostic information to the risk of progression”. page 5 para 2

Could the authors also clarify on page 8 "Children and adolescents were participants in these trials and in general had a better C peptide response to adults" : is this to the intervention or at baseline? i.e. were they better responders to the intervention or in general? They were better responders to the intervention – this has been added to the text.

"Children and adolescents were participants in these trials and in general had a better C peptide response to the intervention than adults"
Thank you all so much for putting these important guidelines together. I’d like to offer a thought re: [Differentiating between type 1 and type 2 diabetes at diagnosis (pgs. 2 & 10)]

Features suggesting the diagnosis of type 2 diabetes rather than type 1 diabetes at diagnosis include:
- Overweight or obesity
- Age greater than 10 years
- Strong family history of type 2 diabetes
- Acanthosis nigricans
- High-risk racial or ethnic group
- Undetectable islet autoantibodies

The inclusion of high-risk racial or ethnic group here stands out to me as potentially problematic. I understand the impetus, as rates of T2D are higher in African American and Latino populations than NHW, but at the same time, since rates of DKA at diagnosis for youth with T1D are higher in African American and Latino populations as well(1) and rates of obesity/overweight are high in AA youth with T1D and also rising across all ethnic/racial groups,(2,3) I would be concerned that the inclusion of this statement here might inadvertently cause bias, resulting in T1D being overlooked in racial/ethnic minority youth. This is unlikely to happen, but even if it happens once, it could be life-threatening for the individual. Perhaps a caveat something along the following lines:

High-risk racial or ethnic group*

*Youth of high-risk racial or ethnic groups are also at increased risk for DKA at diagnosis of T1D,(1) so it is particularly important that they be screened for antibodies when T1D is suspected.

Thank you. We have removed high-risk racial or ethnic groups from the list of features suggesting the diagnosis of T2D.