Explanation and source of recommendations

The definitions of the levels of evidence and grades of recommendation in this handbook are provided here. Refer to 'How to use this handbook' for further explanation of how to use these recommendations.

National Health and Medical Research Council's levels of evidence and grades of recommendation (2009–16)

Levels of evidence	
Level	**Definition**
I	Evidence obtained from a systematic review of level II studies
II	Evidence obtained from a randomised controlled trial (RCT)
III–1	Evidence obtained from a pseudo-RCT (ie alternate allocation or some other method)
III–2	Evidence obtained from a comparative study with concurrent controls: • non-randomised, experimental trial • cohort study • case-control study • interrupted time series with a control group
III–3	Evidence obtained from a comparative study without concurrent controls: • historical control study • two or more single-arm studies • interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes
Practice Point	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees

Grades of recommendations	
Grade	**Definition**
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation/s, but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

Diabetes Canada criteria for assigning levels of evidence and grades of recommendation

Criteria for assigning levels of evidence	
Level	**Criteria**
Studies of diagnosis	
Level 1	a) Independent interpretation of test results (without knowledge of the result of the diagnostic or gold standard) b) Independent interpretation of the diagnostic standard (without knowledge of the test result) c) Selection of people suspected (but not known) to have the disorder d) Reproducible description of both the test and diagnostic standard e) At least 50 patients with and 50 patients without the disorder
Level 2	Meets four of the level 1 criteria
Level 3	Meets three of the level 1 criteria
Level 4	Meets one or two of the level 1 criteria
Studies of treatment and prevention	
Level 1A	a) Systematic overview or meta-analysis of high-quality RCTs b) Comprehensive search for evidence c) Authors avoided bias in selecting articles for inclusion d) Authors assessed each article for validity e) Reports clear conclusions that are supported by the data and appropriate analyses OR Appropriately designed RCT with adequate power to answer the question posed by the investigators a) Patients were randomly allocated to treatment groups b) Follow up at least 80% complete c) Patients and investigators were blinded to the treatment* d) Patients were analysed in the treatment groups to which they were assigned e) The sample size was large enough to detect the outcome of interest
Level 1B	Non-randomised clinical trial or cohort study with indisputable results
Level 2	RCT or systematic overview that does not meet level 1 criteria
Level 3	Non-randomised clinical trial or cohort study; systematic overview or meta-analysis of level 3 studies
Level 4	Other
Studies of prognosis	
Level 1	a) Inception cohort of patients with the condition of interest, but free of the outcome of interest b) Reproducible inclusion/exclusion criteria c) Follow up of at least 80% of subjects d) Statistical adjustment for extraneous prognostic factors (confounders) e) Reproducible description of outcome measures
Level 2	Meets criterion a) above, plus three of the other four criteria
Level 3	Meets criterion a) above, plus two of the other criteria
Level 4	Meets criterion a) above, plus one of the other criteria

*In cases where such blinding was not possible or was impractical (eg intensive vs conventional insulin therapy), the blinding of individuals who assessed and adjudicated study outcomes was felt to be sufficient.

RCT, randomised controlled trial

Criteria for assigning grades of recommendations for clinical practice	
Grade	**Criteria**
Grade A	The best evidence was at level 1
Grade B	The best evidence was at level 2
Grade C	The best evidence was at level 3
Grade D	The best evidence was at level 4 or consensus
Source: Adapted from Diabetes Canada Clinical Practice Guidelines Expert Committee. Diabetes Canada 2018 clinical practice guidelines for the prevention and management of diabetes in Canada. Can J Diabetes 2018;42(Suppl 1):S1–S325.	

American Diabetes Association levels of evidence	
Levels of evidence	**Explanation**
A	Clear evidence from well-conducted, generalisable RCTs that are adequately powered, including: • evidence from a well-conducted multicentre trial • evidence from a meta-analysis that incorporated quality ratings in the analysis Compelling non-experimental evidence (ie 'all or none' rule developed by the Centre for Evidence-Based Medicine at the University of Oxford) Supportive evidence from well-conducted RCTs that are adequately powered, including: • evidence from a well-conducted trial at one or more institutions • evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Supportive evidence from well-conducted cohort studies: • evidence from a well-conducted prospective cohort study or registry • evidence from a well-conducted meta-analysis of cohort studies Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies: • evidence from randomised clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience
RCT, randomised controlled trial	