



Supporting Information

Supplementary figures and tables

This appendix was part of the submitted manuscript and has been peer reviewed.
It is posted as supplied by the authors.

Appendix to: Peña A, Curran JA, Fuery M, et al. Screening, assessment and management of type 2 diabetes mellitus in children and adolescents: Australasian Paediatric Endocrine Group guidelines. *Med J Aust* 2019; doi: 10.5694/mja2.50666.

Table 1. Members of Type 2 diabetes mellitus guideline development group

Name of Participant	Conflict of interest	Expertise	Institution	Geographical Location	Member's role	Membership of Australian professional societies
Jacqui Curran MB BCh, FRACP, PhD	None	Paediatric Endocrinologist	Perth Children's Hospital	Perth, Western Australia	Chair of pharmacotherapy section	APEG ANZOS RACP
Rachana Dahiya MBBS, BsC (Hons),FRACP, PhD	None	Paediatric Endocrinologist	Queensland Children's Hospital	Brisbane, Queensland	Co-chair guideline development group and Chair of diabetes education section	APEG RACP
Michelle Fuery BHLthSc (Nutr &Diet), BBus (Mgt)	None	Dietitian	Queensland Children's Hospital	Brisbane, Queensland	Contributor to healthy lifestyle section (Diet)	APEG
Craig Jefferies MBCHB, FRACP, MD	None	Paediatric Endocrinologist	Liggins institute, University of Auckland Starship Children's Health	Auckland New Zealand	Chair of screening and diagnosis section	APEG New Zealand Society for the Study of Diabetes
Catherine George BAppSc (Physiotherapy)	None	Physiotherapist	Perth Children's Hospital	Perth, Western Australia	Contributor to healthy lifestyle section (Physical activity and sedentary behaviour)	Australian Physiotherapy Association
Kristine Lobley BAppSc, GradDipNutr&Diet, MPH	None	Dietitian	The Children's Hospital at Westmead	Sydney, New South Wales	Contributor to healthy lifestyle section (Diet)	APEG
Karissa Ludwig MBBS, BPharma Sci, DCH, Grad Cert (Clin Epid) FRACP	None	Paediatric Endocrinologist	Sydney Children's Hospitals Network	Sydney, New South Wales	Contributor to pharmacotherapy section	APEG RACP
Ann Maguire MB BCh BAO, MRCP (UK), FRACP, Grad Dip Med (Clin Epi), PhD	None	Paediatric Endocrinologist	The Children's Hospital at Westmead, Medical Lead of Diabetes Service at CHW	Sydney, Australia	Chair of healthy lifestyle section	APEG RACP
Emily Papadimos MBBS	None	Advanced Trainee Paediatric Endocrinology	Children's Health Queensland	Brisbane, Australia	Contributor to screening and diagnosis section	APEG RACP
Alexia Peña MD, FRACP, PhD	None	Paediatric Endocrinologist	The University of Adelaide Robinson Research Institute	Adelaide, South Australia	Co-chair guideline development group Chair of complications and comorbidities section	APEG ANZOS RACP
Aimee Peters	None	Dietitian	Health South Western	Sydney, New	Contributor - healthy	APEG

Name of Participant	Conflict of interest	Expertise	Institution	Geographical Location	Member's role	Membership of Australian professional societies
BSci, M Nut &Diet			Sydney	South Wales	lifestyle section (Diet)	Dietitians Association of Australia
Fiona Sellars BN, CDE, G Dip CCN, MN (Clinical)	None	Credentialed Diabetes Educator	Queensland Children's Hospital	Brisbane, Queensland	Contributor to diabetes education section	APEG Australian Diabetes Educators Association
Jane Speight CPsychol, FBPsS, PhD	None	Health Psychologist	The Australian Centre for Behavioural Research in Diabetes (a partnership between Diabetes Victoria and Deakin University)	Melbourne, Victoria	Contributor to psychological care section within complications and comorbidities section	Australian Diabetes Society
Angela Titmuss MBBS (Hons), MPH, FRACP	None	Paediatric Endocrinologist	Royal Darwin Hospital	Darwin, Northern Territory	Chair of considerations for special groups section	APEG Australian Diabetes Society
Dyane Wilson MBChB, FRACP	None	Paediatric Endocrinologist	Cairns Hospital	Cairns, Queensland	Chair of transition section	APEG RACP
Jencia Wong BHB, MBChB, FRACP, PhD	None	Adult Endocrinologist	Royal Prince Alfred Hospital The University of Sydney	Sydney, New South Wales	Contributor to all sections of guidelines adult perspective Chair of Australian young adult T2D group	Australian Diabetes Society The Endocrine Society of Australia
Caroline Worth NZRD, PGDipDiet, BSc	None	Paediatric Diabetes Dietitian	Starship Child Health	Auckland, New Zealand	Contributor to healthy lifestyle section (Diet)	Dietitians New Zealand

APEG Australasian Paediatric Endocrine Group, ANZOS Australian and New Zealand Obesity Society, RACP Royal Australasian College of Physicians
Each member will reinforce implementation of the guidelines in Australasia and among their own professional societies

Section 1. Search strategies

Search strategies used for each section including databases searched are listed below. Searches were done until February 2019 except the pharmacotherapy one that was done until May 2019 to include the following manuscript published in New England Journal of Medicine in April 28th 2019 after the searches were performed (Tamborlane WV et al. Liraglutide in Children and Adolescents with Type 2 Diabetes. N Engl J Med. 2019. 381(7):637-646). This manuscript was considered by the whole group as landmark study that was going to impact on the guidelines and required to be included.

1. Screening and diagnosis

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily – search strategy

- 1 exp Diabetes Mellitus, Type 2/di (9047)
- 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (123911)
- 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (37241)
- 4 or/1-3 (138417)
- 5 exp Mass Screening/ (121639)
- 6 screen*.ti,ab,kw. (691574)
- 7 (diagnos* adj3 (test* or tool* or approach* or accuracy)).ti,ab,kw. (197686)
- 8 or/5-7 (907838)
- 9 Adolescent/ (1942118)
- 10 exp Child/ (1836527)
- 11 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (1805947)
- 12 or/9-11 (3489072)
- 13 4 and 8 and 12 (1168)
- 14 13 not (Animals/ not (Animals/ and Humans/)) (1167)
- 15 limit 14 to yr="2010 -Current" (675)
- 16 limit 15 to english language (641)

Database: Embase - Search Strategy:

- 1 non insulin dependent diabetes mellitus/di [Diagnosis] (9502)
- 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (199956)
- 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (63183)
- 4 or/1-3 (219669)
- 5 exp mass screening/ (226460)
- 6 screen*.ti,ab,kw. (977059)
- 7 (diagnos* adj3 (test* or tool* or approach* or accuracy)).ti,ab,kw. (283268)
- 8 or/5-7 (1308485)
- 9 adolescent/ (1442891)
- 10 exp child/ (2473249)
- 11 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (2244150)
- 12 or/9-11 (3824830)
- 13 4 and 8 and 12 (1650)
- 14 13 not ((exp animal/ or nonhuman/) not exp human/) (1640)
- 15 limit 14 to yr="2010 -Current" (1131)
- 16 limit 15 to english language (1093)

Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews

ID	Search	Hits
#1	MeSH descriptor: [Diabetes Mellitus, Type 2] this term only and with qualifier(s): [diagnosis - DI]	
	673	
#2	(diabetes NEAR/3 (type2 or "type 2" or "type ii")):ti,ab	29870
#3	("non insulin dependent diabetes" or NIDDM or T2DM or T2D):ti,ab	9701
#4	#1 or #2 or #3	32217
#5	MeSH descriptor: [Mass Screening] explode all trees	3619
#6	screen*:ti,ab	59665
#7	(diagnos* NEAR/3 (test* or tool* or approach* or accuracy)):ti,ab	9030
#8	#5 or #6 or #7	68190
#9	MeSH descriptor: [Adolescent] this term only	100107
#10	MeSH descriptor: [Child] explode all trees	1178
#11	(adolescen* or child* or "school-age*" or schoolage* or preschool* or "pre-school*" or youth* or juvenile* or pediatric* or paediatric* or girl* or boy*):ti,ab	142653
#12	#9 or #10 or #11	219691

#13 #4 and #8 and #12 271

2. Diabetes Education

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily - Search Strategy:

- 1 exp Diabetes Mellitus, Type 2/ (123956)
- 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (124493)
- 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (37459)
- 4 or/1-3 (175240)
- 5 Education/ (20296)
- 6 Health Education/ (59123)
- 7 Health Promotion/ (70130)
- 8 Learning/ (61787)
- 9 Counseling/ (34360)
- 10 Patient Education as Topic/ (82428)
- 11 Health Knowledge, Attitudes, Practice/ (104172)
- 12 ((patient* or client* or participant* or individual* or adolescen* or child* or family or families) adj3 (train* or educat* or teach* or learn* or instruct* or inform or counsel* or empower*)).ti,ab,kw. (170480)
- 13 or/5-12 (518489)
- 14 Adolescent/ (1946014)
- 15 exp Child/ (1839554)
- 16 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (1820943)
- 17 or/14-16 (3499866)
- 18 4 and 13 and 17 (1015)
- 19 18 not (Animals/ not (Animals/ and Humans/)) (1014)
- 20 limit 19 to yr="2010 -Current" (598)
- 21 limit 20 to english language (581)

Database: Embase - Search Strategy:

- 1 non insulin dependent diabetes mellitus/ (236598)
- 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (200286)
- 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (63293)
- 4 or/1-3 (284834)
- 5 education/ (387279)
- 6 health education/ (91575)
- 7 health promotion/ (92758)
- 8 learning/ (183233)
- 9 counseling/ (61656)
- 10 patient education/ (108940)
- 11 ((patient* or client* or participant* or individual* or adolescen* or child* or family or families) adj3 (train* or educat* or teach* or instruct* or inform or counsel* or empower*)).ti,ab,kw. (221014)
- 12 or/5-11 (992771)
- 13 adolescent/ (1443562)
- 14 exp child/ (2475187)
- 15 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (2258474)
- 16 or/13-15 (3831864)
- 17 4 and 12 and 16 (1426)
- 18 17 not ((exp animal/ or nonhuman/) not exp human/) (1418)
- 19 limit 18 to yr="2010 -Current" (902)
- 20 limit 19 to english language (885)

Cochrane Library (Wiley) searching: Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials – ID Search Hits

- | | | |
|-----|---|-------|
| #1 | MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees | 15389 |
| #2 | (diabetes NEAR/3 (type2 or "type 2" or "type ii")):ti,ab | 29871 |
| #3 | ("non insulin dependent diabetes" or NIDDM or T2DM or T2D):ti,ab | 9701 |
| #4 | #1 or #2 or #3 | 34957 |
| #5 | MeSH descriptor: [Education] this term only | 558 |
| #6 | MeSH descriptor: [Health Education] this term only | 3669 |
| #7 | MeSH descriptor: [Health Promotion] this term only | 5272 |
| #8 | MeSH descriptor: [Learning] this term only | 2136 |
| #9 | MeSH descriptor: [Counseling] this term only | 3861 |
| #10 | MeSH descriptor: [Patient Education as Topic] this term only | 8279 |
| #11 | MeSH descriptor: [Health Knowledge, Attitudes, Practice] this term only | 5583 |

#12 ((patient* or client* or participant* or individual* or adolescen* or child* or family or families) NEAR/3 (train* or educat* or teach* or learn* or instruct* or inform or counsel* or empower*)):ti,ab 35617
 #13 #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 55058
 #14 MeSH descriptor: [Adolescent] this term only 100107
 #15 MeSH descriptor: [Child] explode all trees 1178
 #16 (adolescen* or child* or "school-age*" or schoolage* or preschool* or "pre-school*" or youth* or juvenile* or teen* or pediatric* or paediatric* or girl* or boy*):ti,ab 143210
 #17 #14 or #15 or #16 220109
 #18 #4 and #13 and #17 184

CINAHL- Search Strategy

S1 (MH "Diabetes Mellitus, Type 2") (52,998)
 S2 TI (diabetes N3 (type2 or type 2 or type ii)) OR AB (diabetes N3 (type2 or type 2 or type ii)) (42,912)
 S3 TI (non insulin dependent diabetes or NIDDM or T2DM or T2M) OR AB (non insulin dependent diabetes or NIDDM or T2DM or T2M) (5,935)
 4 S1 OR S2 OR S3 (65,842)
 S5 (MH "Education") (9,811)
 S6 (MH "Health Education") (24,525)
 S7 (MH "Health Promotion") (56,898)
 S8 (MH "Learning") (22,141)
 S9 (MH "Counseling") (26,236)
 S10 (MH "Patient Education") (60,803)
 S11 TI ((patient* or client* or participant* or individual* or adolescen* or child* or family or families) N3 (train* or educat* or teach* or learn* or instruct* or inform or counsel* or empower*)) OR AB ((patient* or client* or participant* or individual* or adolescen* or child* or family or families) N3 (train* or educat* or teach* or learn* or instruct* or inform or counsel* or empower*)) (103,844)
 S12 S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 (269,542)
 S13 (MH "Adolescence") (462,196)
 S14 (MH "Child+") (582,573)
 S15 TI (adolescen* or child* or school-age* or schoolage* or preschool* OR pre-school* or youth* or teen* or juvenile* or pediatric* or paediatric* or girl* or boy*) OR AB (adolescen* or child* or school-age* or schoolage* or preschool* or pre-school* or youth* or teen* or juvenile* or pediatric* or paediatric* or girl* or boy*) (590,389)
 S16 S13 OR S14 OR S15 (1,026,024)
 S17 S4 AND S12 AND S16 (505)
 S18 S4 AND S12 AND S16 Limiters - Published Date: 20100101-20191231 (318)
 S19 S4 AND S12 AND S16 Limiters - English Language; Published Date: 20100101-20191231 (313)

3. Healthy lifestyle

Diet

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily-Search Strategy:

1 exp Diabetes Mellitus, Type 2/ (124274)
 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (125361)
 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (37798)
 4 or/1-3 (176195)
 5 exp Diet/ (265884)
 6 exp Diet Therapy/ (52046)
 7 exp Food/ (1233832)
 8 exp Feeding Behavior/ (162046)
 9 (diet* or food* or nutrition* or (intermittent adj1 fast*) or ((feeding or eating) adj2 behavio?r*)):ti,ab,kw. (1058176)
 10 or/5-9 (2097068)
 11 Adolescent/ (1948607)
 12 exp Child/ (1841780)
 13 (adolescen* or teen* or child* or school-age* or schoolage* or pre?school* or youth* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (1827353)
 14 or/11-13 (3508043)
 15 4 and 10 and 14 (3328)
 16 15 not (Animals/ not (Animals/ and Humans/)) (3277)
 17 limit 16 to yr="2010 -Current" (1788)
 18 limit 17 to english language (1721)

Database: Embase - Search Strategy:

1 non insulin dependent diabetes mellitus/ (237494)

2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (201061)
3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (63559)
4 or/1-3 (285903)
5 exp diet/ (300741)
6 exp diet therapy/ (326827)
7 exp food/ (946054)
8 exp feeding behavior/ (164244)
9 (diet* or food* or nutrition* or (intermittent adj1 fast*) or ((feeding or eating) adj2 behavior?r*)).ti,ab,kw.
(1305297)
10 or/5-9 (2156728)
11 adolescent/ (1447259)
12 exp child/ (2482547)
13 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or
p?ediatric* or girl* or boy*).ti,ab,kw. (2266315)
14 or/11-13 (3842914)
15 4 and 10 and 14 (5338)
16 15 not ((exp animal/ or nonhuman/) not exp human/) (5021)
17 limit 16 to yr="2010 -Current" (3363)
18 limit 17 to english language (3265)

Cochrane Library including: Cochrane Database of Systematic Review and Cochrane Central Register of
Controlled Trials - ID Search Hits

#1	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	15458
#2	(diabetes NEAR/3 (type2 or "type 2" or "type ii")):ti,ab,kw	33887
#3	("non insulin dependent diabetes" or NIDDM or T2DM or T2D):ti,ab,kw	18854
#4	#1 or #2 or #3	36689
#5	MeSH descriptor: [Diet] explode all trees	17252
#6	MeSH descriptor: [Diet Therapy] explode all trees	5487
#7	MeSH descriptor: [Food] explode all trees	31439
#8	MeSH descriptor: [Feeding Behavior] explode all trees	8313
#9	diet* or food* or nutrition* or (intermittent NEAR/1 fast*) or ((feeding or eating) NEAR/2 (behavior* or behaviour*)):ti,ab,kw	133990
#10	#5 or #6 or #7 or #8 or #9	140530
#11	MeSH descriptor: [Adolescent] this term only	100420
#12	MeSH descriptor: [Child] explode all trees	1188
#13	(adolescen* or child* or school-age* or schoolage* or preschool* or pre-school* or youth* or teen* or juvenile* or paediatric* or pediatric* or girl* or boy*):ti,ab,kw	237389
#14	#11 or #12 or #13	237389
#15	#4 and #10 and #14	825

CINAHL – Search Strategy

S1	(MH "Diabetes Mellitus, Type 2")	53,109
S2	TI (diabetes N3 (type2 or "type 2" or "type ii")) OR AB (diabetes N3 (type2 or "type 2" or "type ii"))	42,987
S3	TI ("non insulin dependent diabetes" or NIDDM or T2DM or T2M) OR AB ("non insulin dependent diabetes" or NIDDM or T2DM or T2M)	5,965
S4	S1 OR S2 OR S3	65,954
S5	(MH "Diet+")	102,423
S6	(MH "Diet Therapy+")	27,134
S7	(MH "Food+")	147,118
S8	(MH "Eating Behavior+")	34,430
S9	TI (diet* or food* or nutrition* or (intermittent N1 fast*) or ((feeding or eating) N2 (behavior* or behaviour*))) OR AB (diet* or food* or nutrition* or (intermittent N1 fast*) or ((feeding or eating) N2 (behavior* or behaviour*))))	225,411
S10	S5 OR S6 OR S7 OR S8 OR S9	347,377
S11	(MH "Adolescence")	463,141
S12	(MH "Child+")	583,505
S13	TI (adolescen* or child* or school-age* or schoolage* or preschool* OR pre-school* or youth* or teen* or juvenile* or pediatric* or paediatric* or girl* or boy*) OR AB (adolescen* or child* or school-age* or schoolage* or preschool* or pre-school* or youth* or teen* or juvenile* or pediatric* or paediatric* or girl* or boy*)	591,614
S14	S11 OR S12 OR S13	1,027,971
S15	S4 AND S10 AND S14	1,386
S16	S4 AND S10 AND S14	Limiters - Published Date: 20100101-20191231
S17	S4 AND S10 AND S14	Limiters - English Language; Published Date: 20100101-20191231

Physical Activity

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily - Search Strategy:

1	Diabetes Mellitus, Type 2/ or diabetes Mellitus, type 2.mp.	
	122740	
2	Exercise/ or Exercise.mp.	293508
3	physical activity.mp.	81706
4	2 or 3	334112
5	child\$.mp.	2181207
6	adolesc\$.mp.	1963057
7	5 or 6	3186895
8	1 and 4	8928
9	7 and 8	988
10	High-Intensity Interval Training/	621
11	7 and 10	123
12	1 and 11	0
13	1 and 10	32

4. Considerations for children and adolescents of Indigenous backgrounds in Australasia special groups

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily - Search Strategy:

1	exp Diabetes Mellitus, Type 2/ (123956)
2	(diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (124493)
3	(non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (37459)
4	1 or 2 or 3 (175240)
5	Oceanic Ancestry Group/ and (Australia* or Queensland* or Northern Territory or Victoria* or New South Wales or Tasmania* or Torres Strait Island*).mp. (6163)
6	((Aborigin* or Indigenous) and (Australia* or Queensland* or Northern Territory or Victoria* or New South Wales or Tasmania*)) or Torres Strait Island*).mp. (8997)
7	or/5-6 (9815)
8	Adolescent/ (1946014)
9	exp Child/ (1839554)
10	(adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (1820943)
11	8 or 9 or 10 (3499866)
12	4 and 7 and 11 (81)
13	limit 12 to yr="2010 -Current" (39)
14	limit 13 to english language (39)

Database: Embase - Search Strategy:

1	non insulin dependent diabetes mellitus/di [Diagnosis] (9502)
2	(diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (200286)
3	(non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (63293)
4	or/1-3 (220012)
5	indigenous australian/ (800)
6	((Aborigin* or indigenous) and (Australia* or Queensland* or Northern Territory or Victoria* or New South Wales or Tasmania*)) or Torres Strait Island*).mp. (11480)
7	or/5-6 (11480)
8	adolescent/ (1443562)
9	exp child/ (2475187)
10	(adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (2258474)
11	or/8-10 (3831864)
12	4 and 7 and 11 (85)
13	limit 12 to yr="2010 -Current" (53)
14	limit 13 to english language (53)

Cochrane Library (Wiley) which covers: Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials ID Search Hits

#1	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	15389
#2	(diabetes NEAR/3 (type2 or "type 2" or "type ii")):ti,ab	29871
#3	("non insulin dependent diabetes" or NIDDM or T2DM or T2D):ti,ab	9701
#4	#1 or #2 or #3	34957
#5	MeSH descriptor: [Oceanic Ancestry Group] this term only	163
#6	(Australia* or Queensland* or Northern Territory or Victoria* or New South Wales or Tasmania*)	47992
#7	#5 and #6	115

#8 ((Aborigin* or Indigenous) and (Australia* or Queensland* or Northern Territory or Victoria* or New South Wales or Tasmania*) or Torres Strait Island*) 555
 #9 #7 or #8 563
 #10 MeSH descriptor: [Adolescent] this term only 100107
 #11 MeSH descriptor: [Child] explode all trees 1178
 #12 (adolescen* or child* or "school-age*" or schoolage* or preschool* or "pre-school*" or youth* or juvenile* or teen* or pediatric* or paediatric* or girl* or boy*):ti,ab 143210
 #13 #10 or #11 or #12 220109
 #14 #4 and #9 and #13 12

5. Pharmacotherapy

Database(s): Ovid MEDLINE(R) 1946 to May 03, 2019 - Search Strategy:

#	Searches	Results
1	Biguanides/	(3140)
2	limit 1 to (yr="2000 - 2019" and "all child (0 to 18 years)")	(55)
3	Metformin/	(12002)
4	limit 3 to (yr="2000 - 2019" and "all child (0 to 18 years)")	(902)
5	Insulin/	(179527)
6	limit 5 to (yr="2000 - 2019" and "all child (0 to 18 years)")	(8876)
7	2 or 4 or 6	(9610)
8	Diabetes Mellitus, Type 2/	(121929)
9	limit 8 to (yr="2000 - 2019" and "all child (0 to 18 years)")	(7557)
10	2 or 4 or 6	(9610)
11	9 and 10	(1315)

Database(s): Ovid MEDLINE(R) 1946 to May 03, 2019 - Search Strategy:

#	Searches	Results
1	Diabetes Mellitus, Type 2/	(121929)
2	limit 1 to (yr="2010 -Current" and "all child (0 to 18 years)")	(4498)
3	Guideline/ or Practice Guideline/	(31332)
4	limit 3 to (yr="2010 -Current" and "all child (0 to 18 years)")	(1994)
5	Consensus/	(10390)
6	limit 5 to (yr="2010 -Current" and "all child (0 to 18 years)")	(886)
7	4 or 6	(2786)
8	1 and 7	(44)

Search strategy for additional medications (not including metformin and insulin):

Database: Ovid MEDLINE(R) <1996 to May 03, 2019> Search Strategy:

1	exp Child/	(1012625)
2	exp Sulfonylurea Compounds/	(9902)
3	exp Thiazolidinediones/	(11091)
4	glitazone.mp.	(175)
5	glucagon-like peptide 1/ or liraglutide/	(7590)
6	Exenatide/	(2223)
7	dulaglutide.mp.	(173)
8	lixisenatide.mp.	(268)
9	exp Dipeptidyl-Peptidase IV Inhibitors/	(4244)
10	Sitagliptin Phosphate/	(1252)
11	alogliptin.mp.	(358)
12	saxagliptin.mp.	(520)
13	exp Linagliptin/	(354)
14	exp Sodium-Glucose Transporter 2 Inhibitors/	(1607)
15	*gliflozin/	(1048)
16	dapagliflozin.mp.	(544)
17	empagliflozin.mp.	(666)
18	exp Canagliflozin/	(473)
19	ertugliflozin.mp.	(24)
20	exp Glycoside Hydrolase Inhibitors/	(2908)
21	exp Rosiglitazone/	(4120)
22	exp Pioglitazone/	(3530)
23	glimiperide.mp.	(3)
24	exp Glyburide/	(4170)
25	exp Glipizide/	(437)
26	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25	(36202)
27	exp Diabetes Mellitus, Type 2/	(110770)

28 1 and 26 and 27 (91)

Search strategy for additional medications (not including metformin and insulin):

Database: Ovid MEDLINE(R) <1996 to May 03, 2019> Search Strategy:

- 1 exp Diabetes Mellitus, Type 2/ (129450)
- 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (132099)
- 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (40335)
- 4 or/1-3 (184311)
- 5 Acarbose/ (1329)
- 6 acarbose.mp. (2758)
- 7 5 or 6 (2758)
- 8 Adolescent/ (1994782)
- 9 exp Child/ (1881362)
- 10 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (1883427)
- 11 or/8-10 (3594867)
- 12 4 and 7 and 11 (18)
- 13 12 not (Animals/ not (Animals/ and Humans/)) (18)
- 14 limit 13 to english language (16)

Search strategy also involved search the reference lists of articles for relevant studies, searching for publications reporting on the TODAY study data and searching clinicaltrials.gov for studies currently underway.

6. Complications and comorbidities

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily-
Search Strategy:

- 1 exp Diabetes Mellitus, Type 2/ (123956)
- 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (124493)
- 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (37459)
- 4 1 or 2 or 3 (175240)
- 5 exp Comorbidity/ (101021)
- 6 (comorbid* or co-morbid* or co-occur* or concurren*).ti,ab,kw. (322537)
- 7 5 or 6 (382579)
- 8 Adolescent/ (1946014)
- 9 exp Child/ (1839554)
- 10 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (1820943)
- 11 8 or 9 or 10 (3499866)
- 12 4 and 7 and 11 (1069)
- 13 12 not (Animals/ not (Animals/ and Humans/)) (1064)
- 14 limit 13 to yr="2000 -Current" (1033)

Database: Embase - Search Strategy:

- 1 non insulin dependent diabetes mellitus/ (236598)
- 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (200286)
- 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (63293)
- 4 or/1-3 (284834)
- 5 exp comorbidity/ (240420)
- 6 (comorbid* or co-morbid* or co-occur* or concurren*).ti,ab,kw. (506839)
- 7 or/5-6 (594512)
- 8 adolescent/ (1443562)
- 9 exp child/ (2475187)
- 10 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*).ti,ab,kw. (2258474)
- 11 or/8-10 (3831864)
- 12 4 and 7 and 11 (1413)
- 13 12 not ((exp animal/ or nonhuman/) not exp human/) (1390)
- 14 limit 13 to yr="2000 -Current" (1369)

Cochrane Library including: Cochrane Database of Systematic Reviews and Cochrane Central Register of
Controlled Trials ID Search Hits

- | | | |
|----|---|-------|
| #1 | MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees | 15389 |
| #2 | (diabetes NEAR/3 (type2 or "type 2" or "type ii")):ti,ab,kw | 33686 |
| #3 | ("non insulin dependent diabetes" or NIDDM or T2DM or T2D):ti,ab,kw | 18816 |
| #4 | #1 or #2 or #3 | 36486 |
| #5 | MeSH descriptor: [Comorbidity] explode all trees | 3484 |

#6 (comorbid* or co-morbid* or co-occur* or concurren*) 40255
 #7 #5 or #6 40270
 #8 MeSH descriptor: [Adolescent] this term only 100107
 #9 MeSH descriptor: [Child] explode all trees 1178
 #10 (adolescen* or child* or school-age* or schoolage* or pre?school* or youth* or teen* or juvenile* or p?ediatric* or girl* or boy*):ti,ab,kw 236155
 #11 #8 or #9 or #10 236155
 #12 #4 and #7 and #11 100
 Limited to 2000 onwards 94

7. Transition to adult services

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily Search Strategy:

1 exp Diabetes Mellitus, Type 2/ (123956)
 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (124493)
 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (37459)
 4 or/1-3 (175240)
 5 Transition to Adult Care/ (1179)
 6 Transitional Care/ (541)
 7 (transition* adj2 (care or health?care or practice* or policy or policies or plan*)).mp. (6766)
 8 or/5-6 (1691)
 9 Adolescent/ (1946014)
 10 Young Adult/ (757593)
 11 (adolescen* or young people or young person* or young adult* or young men or young women or young male* or young female* or youth* or teen*).ti,ab,kw. (464891)
 12 or/9-11 (2462822)
 13 4 and 8 and 12 (13)
 14 13 not (Animals/ not (Animals/ and Humans/)) (13)
 15 limit 14 to yr="2010 -Current" (13)
 16 limit 15 to english language (13)

Database: Embase - Search Strategy:

1 non insulin dependent diabetes mellitus/ (236598)
 2 (diabetes adj3 (type2 or type 2 or type ii)).ti,ab,kw. (200286)
 3 (non insulin dependent diabetes or NIDDM or T2DM or T2D).ti,ab,kw. (63293)
 4 or/1-3 (284834)
 5 transition to adult care/ (1646)
 6 transitional care/ (2238)
 7 (transition* adj2 (care or health?care or practice* or policy or policies or plan*)).mp. (11066)
 8 or/5-7 (12144)
 9 adolescent/ (1443562)
 10 young adult/ (301296)
 11 (adolescen* or young people or young person* or young adult* or young men or young women or young male* or young female* or youth* or teen*).ti,ab,kw. (585621)
 12 or/9-11 (1875066)
 13 4 and 8 and 12 (36)
 14 13 not ((exp animal/ or nonhuman/) not exp human/) (36)
 15 limit 14 to yr="2010 -Current" (32)
 16 limit 15 to english language (32)

Cochrane Library including: Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials ID Search Hits

#1 MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees 15389
 #2 (diabetes NEAR/3 (type2 or "type 2" or "type ii")):ti,ab 29871
 #3 ("non insulin dependent diabetes" or NIDDM or T2DM or T2D):ti,ab 9701
 #4 #1 or #2 or #3 34957
 #5 MeSH descriptor: [Transition to Adult Care] this term only 16
 #6 MeSH descriptor: [Transitional Care] this term only 38
 #7 transition* NEAR/2 (care or healthcare or "health care" or practice* or policy or policies or plan*) 716
 #8 #5 or #6 or #7 724
 #9 MeSH descriptor: [Adolescent] this term only 100107
 #10 MeSH descriptor: [Young Adult] this term only 226
 #11 adolescen* or young people or young person* or young adult* or young men or young women or young male* or young female* or youth* or teen* 194219
 #12 #9 or #10 or #11 194219

#13 #4 and #8 and #12 0

CINAHL –Search Strategy

- S1 (MH "Diabetes Mellitus, Type 2") (52,965)
- S2 TI (diabetes N3 (type2 or type 2 or type ii)) OR AB (diabetes N3 (type2 or type 2 or type ii)) (42,855)
- S3 TI (non insulin dependent diabetes or NIDDM or T2DM or T2M) OR AB (non insulin dependent diabetes or NIDDM or T2DM or T2M) (5,917)
- S4 S1 OR S2 OR S3 (65,781)
- S5 (MH "Transitional Care") (1,159)
- S6 TI (transition* N2 (care or healthcare or "health care" or practice* or policy or policies or plan*) OR AB (transition* N2 (care or healthcare or "health care" or practice* or policy or policies or plan*) (6,352)
- S7 S5 OR S6 (6,880)
- S8 (MH "Adolescence") (461,917)
- S9 (MH "Young Adult") (211,485)
- S10 TI (adolescen* or young people or young person* or young adult* or young men or young women or young male* or young female* or youth* or teen*) OR AB (adolescen* or young people or young person* or young adult* or young men or young women or young male* or young female* or youth* or teen*) (194,193)
- S11 S8 OR S9 OR S10 (615,167)
- S12 S4 AND S7 AND S11 (9)

Table 2. Risk factors for type 2 diabetes

Type of risk factor	Risk factors	Presence of risk factors in children and adolescents with type 2 diabetes
Non Modifiable risk factors Genetics/Epigenetics	First or second degree relative with type 2 diabetes (1-3)	In 75 to 100% of cases
	Minority race/ethnicity (3 -5)	66% among Australian Indigenous Youth
	Gestational diabetes offspring (6)	Odds ratio 5.7 to develop type 2 diabetes
	Single nucleotide polymorphisms (7)	Genetic risk score for β -cell dysfunction
	Specific genetic variants (8)	10% of heritability
Modifiable risk factors	Birth weight (9)	Intrauterine growth retardation, small for gestational age, large for gestational age
	Overweight and Obesity (1-3) – BMI $\geq$ 85 th centile – BMI $\geq$ 95 th centile	Close to 100% of youth with type 2 diabetes had BMI $>$ 85% with 50% reduction in peripheral and hepatic insulin sensitivity
	Waist circumference (10)	
	Sedentary lifestyle (1)	
Other	Maternal obesity (2,11)	Odds Ratio 2.8 to develop type 2 diabetes
	Insulin resistance - physiological insulin resistance of puberty (12)	Reduction in insulin sensitivity by ~30%
	Chronic stress, low mood (13)	
	Socioeconomic and educational status (5,14)	Higher risk of type 2 diabetes in lower socio-economic status
	Population density (5,15)	Increased risk of type 2 diabetes in youth living in less densely populated residential areas (<500 residents/square mile)
	Use of psychotropic medications (16-18)	Children and adolescents are more vulnerable to metabolic effects compared to adults

BMI=Body mass index

References

1. Arslanian S, Bacha F, Grey M et al. Evaluation and management of youth-onset type 2 diabetes: A Position Statement by the American Diabetes Association. *Diabetes Care* 2018;41:2648-68.
2. Chernausk SD AS, Caprio S, Copeland KC et al. Relationship between parental diabetes and presentation of metabolic and glycemic function in youth with type 2 diabetes: Baseline findings from the TODAY Trial. *Diabetes Care* 2016;39:110-7.
3. Klingensmith GJ, Connor CG, Ruedy KJ et al. Presentation of youth with type 2 diabetes in the Pediatric Diabetes Consortium. *Pediatr Diabetes* 2016;17:266-273
4. Haynes A, Kalic R, Cooper M et al. Increasing incidence of type 2 diabetes in Indigenous and non-Indigenous children in Western Australia, 1990-2012. *Med J Aust* 2016;204:303.
5. Copeland KC, Zeitler P, Geffner M et al. Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. *J Clin Endocrinol Metab* 2011;96:159-67.
6. Dabelea D. The Predisposition to obesity and diabetes in offspring of diabetic mothers. *Diabetes Care* 2007;30:S169-74.
7. Giannini C DMC, Groop L, Cobelli C et al. Co-occurrence of risk alleles in or near genes modulating insulin secretion predisposes obese youth to prediabetes. *Diabetes Care* 2014;37:475-82
8. Billings LK, Florez JC. The genetics of type 2 diabetes: what have we learned from GWAS? *Ann N Y Acad Sci* 2010;1212:59-77.
9. Wei J, Sung, Fc, Li Cy. Low birth weight and high birth infants are both at an increased risk to have type 2 diabetes among schoolchildren in Taiwan. *Diabetes Care* 2003;26:343-8.
10. Franks PW, Hanson RL, Knowler WC et al. Childhood predictors of young-onset type 2 diabetes. *Diabetes* 2007;56:2964-72.
11. Dabelea D, Mayer-Davis EJ, Lamichhane AP et al. Associations of intrauterine exposure to maternal diabetes and obesity with type 2 diabetes in youth. The SEARCH case-control study. *Diabetes Care* 2008;31:1422-6.
12. Hannon TS, Janosky J, Arslanian SA. Longitudinal study of physiologic insulin resistance and metabolic changes of puberty. *Pediatr Res* 2006;60:759-63.
13. Hannon TS, Rofey DL, Lee S, Arslanian SA. Depressive symptoms and metabolic markers of risk for type 2 diabetes in obese adolescents. *Pediatr Diabetes* 2013;14:497-503.
14. McGavock J, Wicklow B, Dart AB. Type 2 diabetes in youth is a disease of poverty. *Lancet* 2017;390:1829.
15. Liese AD, Lamichhane AP, Garzia SCA et al. Neighborhood characteristics, food deserts, rurality, and type 2 diabetes in youth: Findings from a case-control study. *Health Place* 2018;50:81-8.

16. Burcu M, Zito JM, Safer DJ et al. Association of antidepressant medications with incident type 2 diabetes among medicaid-insured youths. *JAMA Pediatrics* 2017;171:1200-7.
17. Bobo WV, Cooper WO, Stein CM et al. Antipsychotics and the risk of type 2 diabetes mellitus in children and youth. *JAMA Psychiatry*. 2013;70:1067-75.
18. Gallin B, Roldan A, Nielsen RE et al. Type 2 diabetes mellitus in youth exposed to antipsychotics: A systematic review and meta-analysis. *JAMA Psychiatry* 2016;73:247-259.

Table 3. Diabetes self-management education content

Education - at diagnosis and ongoing	Continuing curriculum
Simple explanation of how the diagnosis was made and the cause of symptoms. Reassure that treatment will help the child regain health and energy quickly	Pathophysiology, epidemiology and classification
Explore feelings of guilt, shame or blame and discuss the uncertain cause of diabetes	Explore children/adolescents understanding as they mature
Normalise grief and loss reaction to the diagnosis	Address psychological health and diabetes burnout/distress
Discuss risk for siblings and other family members; and interventions available to minimise risk	Revise as needed
Simple explanation of glucose and the relationship between food, blood glucose, metformin and insulin	Explain other sources of glucose, that is, liver glucose
Simple explanation of the effect of metformin and insulin (long and short acting) on blood glucose levels	Metformin action and profile Insulin action and profiles Adjustment of insulin If applicable, simple explanation of other available oral or injectable hypoglycaemic agents
Discuss the role and responsibility of family in the delivery and supervision of self-management tasks and expectation for frequency of follow-up	Review individual roles at each visit and encourage active parental involvement Explore barriers to clinic attendance if missed appointments
Establish clear blood glucose levels and HbA1c targets; and goals of treatment	Self-monitoring blood glucose - monitoring frequency HbA1c Weight loss Balanced diet Exercise/screen time/sleep Goal-setting focus on goals that are SMART: Specific, measurable, achievable, realistic, and time-based Micro- and macro-vascular complications, screening protocol, and prevention
Focus on basic “survival” skills needed to manage the diabetes from day one Accomplishment of these skills will increase the carers/child's confidence in their ability to manage Assess competence in • Self blood glucose monitoring and ketone monitoring • Taking metformin • Insulin devices: injection, pen • Insulin injection sites/techniques • Diabetes diary: what to record and how often • Insulin bolus calculator • Carbohydrate counting tools and glycaemic index • Insulin storage	Revise these skills • As new devices or technologies are introduced • As child/adolescent takes on self-management tasks • If diabetes needs stabilization • In response to episodes of ketosis or severe hypoglycaemia • When new carers are introduced to the family • When child/adolescent is planning school camp/excursion • During transition to adult services • Whenever there are admissions other than due to diabetes
Basic dietetic advice including importance of healthy eating, and meal-time routines Promotion of healthy body weight Link between food and diabetes Carbohydrate counting and glycaemic index if on prandial insulin	Explain effects on blood glucose levels of different food components including proteins, fats, fibre, and glycaemic index; and discuss management strategies to optimise postprandial blood glucose levels Revise nutritional skills as the child grows and develops Adapt nutritional interventions in response to new diagnoses Screen for disordered eating
Explanation of hyperglycaemia and diabetes ketoacidosis (symptoms, prevention, management) If on insulin, explanation of hypoglycaemia (symptoms, prevention, management), identity cards, necklets, bracelets, and other equipment	Revise with introduction of new activities and new carers Practice reconstitution of glucagon Precautions with alcohol, precautions, recognising and treating hypoglycaemia when driving
Diabetes during illnesses	Effects of intercurrent illness, hyperglycaemia,

Advice not to omit insulin and to call the diabetes team for advice May need to stop metformin if dehydrated, ill or require surgery	ketosis, and prevention and identification of diabetes ketoacidosis Diet and fluids on sick days Sick day management plan
Integration of diabetes self-management tasks into family life, social activities, sporting activities, and school	Problem-solving and adjustments to treatment in everyday life, motivation, and coping with unexpected glucose fluctuations Review and revise school management plan annually Exercise, holiday planning and travel, including educational holidays and camps
Address questions about impact on future aspirations for child, that is, career, having children	Sexuality, pregnancy planning, contraception, employment Teratogenic effects of oral/injectable agents, especially newer medications for management of type 2 diabetes
Membership of a diabetes association, joining National Diabetes Service Scheme, medic alert bracelet	Explore opportunities for peer support and family support
Details of emergency telephone contacts and follow-up arrangements	Update as required

Adapted from ISPAD Clinical Practice Consensus Guidelines 2018 (ISPAD Clinical Practice Consensus Guidelines 2018: Diabetes education in children and adolescents. Phelan H, Lange K, Cengiz E, Gallego P, Majaliwa E, Pelicand J, Smart C et al. *Pediatr Diabetes*. 2018; 19 Suppl 27:75-83)

Section 2. Available resources for children and adolescents and/or for type 2 diabetes mellitus

Education materials and a lifestyle program used in Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study: <https://portal.bsc.gwu.edu/web/today/tsdematerials>

Be Healthy TODAY; Be Healthy for Life <http://www.diabetes.org/living-with-diabetes/parents-and-kids/childrenand-type-2/>.

Resources for Maori/Pacific Islander obese children may help promote lifestyle changes in type 2 diabetes: (<https://www.childrens.health.qld.gov.au/service-good-start-resources/>).

Resources for Aboriginal/Torres Strait Islanders adults with type 2 diabetes: (<https://healthinonet.ecu.edu.au/learn/health-topics/diabetes/resources/>)

Table 4. Studies of pharmacotherapeutic agents for treatment of children and adolescents with type 2 diabetes

Pharmacotherapeutic agent class	Route of administration	Mechanism of action	Side effects Safety in pregnancy	Evidence for use in children	Trials currently underway †
Biguanides Metformin [1-13] *	Oral	Decreases gluconeogenesis in the liver and hence glucose release by the liver, increases insulin stimulated glucose uptake by muscle and fat. Renally excreted (unchanged)	Gastrointestinal (GI) side effects (abdominal pain, nausea, diarrhoea), headache, lactic acidosis (rare), lowering of Vitamin B12 levels causing anaemia Consider safe to use in pregnancy	RCT (n=82) showed superior effect of metformin over placebo reducing HbA1c, fasting glucose and cholesterol in metformin group. No weight gain or safety issues with metformin. [4] NHMRC Level II evidence Observational study Pre-randomization (n=927) 90% of youth able to achieve HbA1c <8%, 8.5% intolerant of metformin. [13] NHMRC Level IV Grade A recommendation for its use	-
Insulins Glargine * [3] Detemir * [14] Pre-mix 30/70 * [15] Aspart * Isophane * Degludec 70/ aspart 30	Subcutaneous injection, Continuous subcutaneous insulin infusion	Binds to insulin receptors to increase glucose uptake and to inhibit hepatic glucose output	Hypoglycaemia, weight gain, oedema, hypersensitivity at injection site and generalised hypersensitivity to insulin Consider safe to use in pregnancy but there is no data on Degludec	RCT (n=91) of glargine (3mths) followed by metformin (9mths) versus metformin (12mths). Neither treatment halted the deterioration of β -cell decline [3]. NHMRC Level II Grade B recommendation (Glargine) for its use	-
Sulfonylureas Glimepiride [5] Glyburide [16] Glipizide	Oral	Closes K-ATP channel to stimulate insulin release from beta cells Increases insulin sensitivity in peripheral tissues	Hypoglycaemia, weight gain and possible acceleration of beta-cell loss Limited information in relation to pregnancy, alternative agents are preferred Glyburide may be used but metformin/insulin are preferred	RCT (n=285) of glimepiride vs metformin showed similar reduction in HbA1c, similar safety profile but significant weight gain in glimepiride group [5]. NHMRC level III-1 evidence RCT (n=167) of glyburide alone or in combination with metformin showed combination therapy was not superior to monotherapy with either agent [16]. Grade B recommendation against its use as causes significant weight gain and not superior to metformin alone or in combination	-
Thiazolidinediones (glitazones) Rosiglitazone [6-12] Pioglitazone	Oral	Improves insulin sensitivity in adipose tissue, muscle and liver via activation of the Peroxisome	Weight gain, fluid retention, anaemia, possible reduction in bone mineral density	RCT (n=699) found metformin plus rosiglitazone resulted in better durability of glycaemic control compared with metformin alone or metformin plus lifestyle change. Similar safety profile but	-

		proliferator-activated receptor gamma receptor	and increased risk of heart failure Limited information in relation to pregnancy, alternative agents preferred	small increase in BMI in patients taking rosiglitazone [12, 17] NHMRC level II evidence Rosiglitazone is not used in adults due to cardiovascular side effects with no data about these side effects in children. Grade D recommendation against its use due to potential side effects	
Glucagon-like peptide 1 (GLP-1) receptor agonists [18-23] Exenatide [19, 23] Liraglutide [20 -22] ** Dulaglutide Lixisenatide	Subcutaneous injection	Incretin effects: increases insulin secretion, suppresses glucagon, prolongs gastric emptying, increases satiety	Acute pancreatitis, GI side effects (nausea, vomiting, diarrhoea) and potential increased risk of medullary cell carcinoma Limited information in relation to safety in pregnancy for liraglutide (no information for other agents in this class) alternative agents preferred	RCT (n=134) found liraglutide plus metformin resulted in improvement in HbA1c and fasting glucose at 26 and 52 weeks compared with placebo plus metformin [21]. NHMRC level II evidence RCT (n=19) reported greater decline in HbA1c over 5 weeks in patients treated with liraglutide compared with placebo. No major side effects [22]. NHMRC level III-1 evidence RCT (n=13) reported lower post-prandial glucose after a single dose of exenatide compared with placebo [23]. NHMRC level III-2 evidence Grade C recommendation for its use	Phase III trial of exenatide (monotherapy or combination therapy) vs placebo. Estimated completion 2023. (clinicaltrials.gov NCT01554618) Phase III trial of once weekly dulaglutide vs placebo over 60 weeks Estimated completion Jan 2022 (ClinicalTrials.gov Identifier: NCT02963766)
Dipeptidyl peptidase-IV (DPP-IV) inhibitors Sitagliptin [24] Alogliptin [25] Saxagliptin Linagliptin [26]	Oral	Inhibition of DPP-IV which reduces breakdown of incretins including GLP-1. Do not have the same effect on satiety, gastric emptying and weight loss as GLP-1 agonists.	Acute pancreatitis GI side effects Limited information in relation to pregnancy for Sitagliptin (no information for other agents in this class) alternative agents preferred	Only single dose pharmacokinetics studies available on sitagliptin [24] and alogliptin [25] showing similar doses can be used in children and adults RCT of linagliptin (n=39) over 12 weeks improve HbA1c [26] NHMRC Level II No serious adverse events. Grade D recommendation for its use	
SGLT-2 inhibitors Dapagliflozin [28, 29] Empagliflozin [30] Canagliflozin Ertugliflozin	Oral	Inhibits renal tubular reabsorption of glucose causing glycosuria and reducing plasma glucose. Promotes weight loss.	Urinary tract infection, euglycaemic diabetic ketoacidosis and vulvovaginal candidiasis No published information in pregnancy alternative agents preferred	Only single dose pharmacokinetics studies available on empagliflozin [29] and dapagliflozin [27] showing similar doses can be used in children and adults. No serious adverse events. Very limited data (pharmacokinetics studies) to be able to make a GRADE recommendation	Phase III trial of empagliflozin, linagliptin or placebo. Expected completion Jan 2022. (clinicaltrials.gov NCT03429543) Phase III trial of canagliflozin vs placebo for 26 weeks. Expected completion July 2022) (ClinicalTrials.gov Identifier:NCT03170518)
Alpha-glucosidase inhibitors Acarbose	Oral	Inhibits breakdown of oligosaccharides delaying absorption of carbohydrates	GI (flatulence, abdominal pain, diarrhoea)	No trials in children and adolescents Unable to GRADE as no evidence available in children	-

		and reduces post-prandial hyperglycaemia	Limited information in pregnancy alternative agents preferred		
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* Therapeutics Goods administration (TGA) approved for children

** Recent Foods and Drugs Administration (FDA) approval for children (June 2019)

† As the majority of the trials underway will be available in 5 years and update of the guidelines will be required then using the similar process.

References

1. Laffel, L., et al., Metformin monotherapy in youth with recent onset type 2 diabetes: experience from the prerandomization run-in phase of the TODAY study. *Pediatr Diabetes*, 2012. 13(5): 369-75.
2. Bacha, F., et al., Initial Presentation of Type 2 Diabetes in Adolescents Predicts Durability of Successful Treatment with Metformin Monotherapy: Insights from the Pediatric Diabetes Consortium T2D Registry. *Horm Res Paediatr*, 2018. 89(1): 47-55.
3. Consortium, R., Impact of Insulin and Metformin Versus Metformin Alone on beta-Cell Function in Youth With Impaired Glucose Tolerance or Recently Diagnosed Type 2 Diabetes. *Diabetes Care*, 2018. 41(8):1717-1725.
4. Jones, K.L., et al., Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial. *Diabetes Care*, 2002. 25(1):89-94.
5. Gottschalk, M., et al., Glimepiride versus metformin as monotherapy in pediatric patients with type 2 diabetes: a randomized, single-blind comparative study. *Diabetes Care*, 2007. 30(4): 790-4.
6. Group, T.S., et al., A clinical trial to maintain glycemic control in youth with type 2 diabetes. *N Engl J Med*, 2012. 366(24): 2247-56.
7. Arslanian, S., et al., Effects of metformin, metformin plus rosiglitazone, and metformin plus lifestyle on insulin sensitivity and B-cell function in TODAY. *Diabetes Care*, 2013. 36(6): 1749-57.
8. Marcus, M.D., et al., Weight change in the management of youth-onset type 2 diabetes: the TODAY clinical trial experience. *Pediatr Obes*, 2017. 12(4): 337-345.
9. Group, T.S., Treatment effects on measures of body composition in the TODAY clinical trial. *Diabetes Care*, 2013. 36(6):1742-8.
10. Gandica, R. and P. Zeitler, Update on Youth-Onset Type 2 Diabetes: Lessons Learned from the Treatment Options for Type 2 Diabetes in Adolescents and Youth Clinical Trial. *Adv Pediatr*, 2016. 63(1):195-209.
11. Group, T.S., Safety and tolerability of the treatment of youth-onset type 2 diabetes: the TODAY experience. *Diabetes Care*, 2013. 36(6):1765-71.
12. Narasimhan, S. and R.S. Weinstock, Youth-onset type 2 diabetes mellitus: lessons learned from the TODAY study. *Mayo Clin Proc*, 2014. 89(6):806-16.
13. Laffel, L., et al., Metformin monotherapy in youth with recent onset type 2 diabetes: experience from the prerandomization run-in phase of the TODAY study. *Pediatr Diabetes*, 2012. 13(5): 369-75.
14. Wheeler, M.D., et al., A 26-week, randomized trial of insulin detemir versus NPH insulin in children and adolescents with type 2 diabetes (iDEAt2). *Eur J Pediatr*, 2018. 177(10):1497-1503.
15. Sellers, E.A. and H.J. Dean, Short-term insulin therapy in adolescents with type 2 diabetes mellitus. *J Pediatr Endocrinol Metab*, 2004. 17(11):1561-4.
16. Vaidyanathan, J., S. Choe, and C.G. Sahajwalla, Type 2 diabetes in pediatrics and adults: thoughts from a clinical pharmacology perspective. *J Pharm Sci*, 2012. 101(5):1659-71.
17. Effects of metformin, metformin plus rosiglitazone, and metformin plus lifestyle on insulin sensitivity and beta-cell function in TODAY. *Diabetes Care*, 2013. 36(6):1749-57.
18. Wood, J.R. and J. Silverstein, Incretins and amylin in pediatric diabetes: new tools for management of diabetes in youth. *Curr Opin Pediatr*, 2013. 25(4):502-8.
19. Kelly, A.S., et al., Exenatide as a weight-loss therapy in extreme pediatric obesity: a randomized, controlled pilot study. *Obesity (Silver Spring)*, 2012. 20(2):364-70.
20. Petri, K.C., L.V. Jacobsen, and D.J. Klein, Comparable liraglutide pharmacokinetics in pediatric and adult populations with type 2 diabetes: a population pharmacokinetic analysis. *Clin Pharmacokinet*, 2015. 54(6):663-70.
21. Tamborlane, W.V., et al., Liraglutide in Children and Adolescents with Type 2 Diabetes. *N Engl J Med*, 15;381(7):637-646.
22. Klein, D.J., et al., Liraglutide's safety, tolerability, pharmacokinetics, and pharmacodynamics in pediatric type 2 diabetes: a randomized, double-blind, placebo-controlled trial. *Diabetes Technol Ther*, 2014. 16(10):679-87.
23. Malloy, J., et al., Pharmacology and tolerability of a single dose of exenatide in adolescent patients with type 2 diabetes mellitus being treated with metformin: a randomized, placebo-controlled, single-blind, dose-escalation, crossover study. *Clin Ther*, 2009. 31(4): 806-15.
24. Fraser, I.P., et al., A randomized clinical trial to evaluate the single-dose pharmacokinetics, pharmacodynamics, and safety of sitagliptin in pediatric patients with type 2 diabetes. *Pediatr Diabetes*, 2019. 20(1):48-56.
25. Dudkowsky, C., et al., The pharmacokinetics and pharmacodynamics of alogliptin in children, adolescents, and adults with type 2 diabetes mellitus. *Eur J Clin Pharmacol*, 2017. 73(3):279-288.
26. [Tamborlane WV](#) et al. Randomized, double-blind, placebo-controlled dose-finding study of the dipeptidyl peptidase-4 inhibitor linagliptin in pediatric patients with type 2 diabetes. [Pediatr Diabetes](#), 2018 Jun; 19(4):640-648
27. Tirucherai, G.S., et al., Pharmacokinetics and pharmacodynamics of dapagliflozin in children and adolescents with type 2 diabetes mellitus. *Diabetes Obes Metab*, 2016. 18(7):678-84.
28. Parkinson, J., et al., Comparison of the exposure-response relationship of dapagliflozin in adult and paediatric patients with type 2 diabetes mellitus. *Diabetes Obes Metab*, 2016. 18(7): 685-92.
29. Laffel, L.M.B., et al., Pharmacokinetic and pharmacodynamic profile of the sodium-glucose co-transporter-2 inhibitor empagliflozin in young people with Type 2 diabetes: a randomized trial. *Diabet Med*, 2018. 35(8):1096-1104.