Fear of hypoglycaemia in paediatric diabetes: a literature review

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Abstract
Background: Type 1 diabetes mellitus is one of the most common chronic childhood illnesses and, despite ongoing technological advances, hypoglycaemia remains an inevitable therapeutic risk. Hypoglycaemia results in unpleasant physiological outcomes, social embarrassment and – in extremis – life-threatening consequences. Overlying this inescapable clinical risk is a fear of this risk, ranging from fleeting to overwhelming, and substantially impacting the trajectory of diabetes.

Aim: The aim of this literature review is to identify, summarise and critically appraise works pertaining to the development, impact and management of paediatric fear of hypoglycaemia (FoH).

Methods: A search was conducted on Embase, MEDLINE and PsycINFO for studies published between 2000 and 2020, with cross-referencing searches for articles not detected in the original keyword search. Study quality was assessed using recognised tools, and relevant data were extracted systematically.

Results: Forty-three studies met the inclusion criteria. FoH was a moderate problem throughout the studies, increased by a history of hypoglycaemia and predisposition to psychological stress. There was conflicting evidence on the influence of age, diabetes duration, technology and parental demographics. Some studies showed a significant impact on glycaemic control and quality of life (QoL), more consistently for the latter. Only 13 intervention trials were included, showing mixed success with cutting-edge technology, and decent gains with psychological interventions.

Conclusions: FoH is clearly a ubiquitous issue among some families with type 1 diabetes. Prospective longitudinal studies are required to assess potential risk factors at diagnosis, monitor for the development of FoH at regular intervals, and enable a more comprehensive assessment of the long-term impact on glycaemic control and QoL. Further randomised controlled trials must demonstrate the value of technological and psychological therapies in order to make such interventions commonplace offerings for families suffering from intractable fear.

Key words: diabetes, hypoglycaemia, fear, HbA1c, quality of life

Introduction
Type 1 diabetes mellitus (T1DM) is one of the most common chronic childhood illnesses, affecting 196 per 100,000 children aged 0–15 years in England and Wales.3 Despite rapid technological advances in diabetes therapy,2 hypoglycaemia remains the commonest acute complication of diabetes care.2 Intensive insulin therapy can increase hypoglycaemic frequency three-fold,4 and individuals with a <5-year T1DM duration experience on average 1.1 severe hypoglycaemic episodes per patient per year.3 Hypoglycaemia can result in unpleasant physiological symptoms, social embarrassment and – in extremis – life-threatening consequences. Overlying this inescapable clinical risk is a fear of this risk. This construct has been labelled a fear of hypoglycaemia (FoH) and can substantially impact the trajectory of diabetes. Individuals with strong FoH indulge in compensatory mechanisms to avoid hypoglycaemia, maintaining a ‘safe’ hyperglycaemia while carrying increased diabetes distress (DD) and poorer quality of life (QoL).

The aim of this literature review is to identify, summarise and critically appraise works pertaining to the development, impact and management of paediatric FoH. This will encompass examining FoH measurement tools, identifying predictive factors, exploring its impact and evaluating minimisation strategies. Prior works include a systematic review in parents of young children (PYC) containing six eligible studies5 and a broader review of children, adolescents and parents, comprising 16 studies.6 Although both highlighted the significance of FoH, its consequences were not fully explored, technology was less abundant, and paediatric behavioural trials non-existent. The current review aims to clearly delineate the impact of FoH on glycated haemoglobin (HbA1c) and QoL, underscoring the need for resource allocation. Moreover, diabetes care has been transformed by a decade of technological innovation, from
continuous subcutaneous insulin infusions (CSII) and continuous glucose monitors (CGM) to sensor-augmented pump therapy (SAPT) and closed-loop systems, and the debate deserves reinvigoration.8-10

Methods
The research question was generated using the Population, Intervention, Comparator and Outcome (PICO) approach.11 The population comprised children and young people (CYP) aged 0–18 years with T1DM or their parents, and whether FoH influenced glycaemic control and QoL. A literature search was conducted on Embase, MEDLINE and PsycINFO. The bibliographies of retrieved papers were also reviewed. Letters to the editor, abstracts and scientific meeting proceedings were excluded. The search was restricted to English language publications from 2000 to 2020, to capture recent changes in technology (see Appendix 1, available online www.bjd-abcd.com, for full search strategy).

Titles and abstracts were examined for inclusion. All study designs meeting PICO parameters were eligible. Exclusion criteria included primarily adult-based studies, a failure to quantitatively assess FoH or either primary outcome. Included studies were critically appraised using recognised tools: the Centre for Evidence Based Medicine criteria for cross-sectional studies,12 the National Heart, Lung, Blood Institute checklist for pre-post prospective studies,13 and the Critical Appraisal Skills Programme checklist for randomised controlled trials (RCTs)14 and systematic reviews15 (Appendix 2 available online www.bjd-abcd.com).

Data extracted included study design, demographics, diabetes duration, insulin mode, HbA1c, FoH and QoL assessments, hypoglycaemia prevalence, pertinent results, strengths and limitations (Appendix 3 available online www.bjd-abcd.com). Due to differences in populations, treatment regimens and outcome measures, a meta-analysis was not conducted. Instead, a narrative synthesis is presented.

Results
Search results
Of the 395 abstracts screened, 43 papers were included in the final analysis (see Figure 1).

The majority were cross-sectional studies (n=28), of which two datasets were used twice17-20 and three papers aggregated several studies.21-23 There were two literature reviews,6,7 five pre-post prospective studies and eight RCTs. Sample size ranged from 16 to 549 (mean 142) and 90% were of Western origin (Figure 2).

Eleven studies investigated parent-child dyads. Nineteen explored parental FoH, with 11 focusing on PYC, facing specific challenges of irregular eating and activities, difficulty matching insulin, greater aberrant glycaemia and subtleties in detection. Seven of 11 studies examining children’s FoH explored adolescents, confronting the complexities of puberty, subversion and peer influences.

Figure 1. PRISMA flow diagram of study selection process.16

Figure 2. Geographical distribution of selected studies.
Measurement of fear of hypoglycaemia

The Hypoglycaemia Fear Survey (HFS) is the most well-established measure assessing FoH, using a worry (HFS-W) and behaviour (HFS-B) subscale with 33 items graded from never to always on a Likert scale.24 The tool was modified to 25 items for parents (HFS-P)25 and revised for PYC (HFS-PYC).26 An adaptation for 6–18-year-olds also exists (HFS-C).27

The HFS-P demonstrates acceptable reliability with an internal consistency range of 0.88–0.91 for the HFS-W and 0.72–0.76 for the HFS-B.27 The HFS-B often displays slightly reduced internal consistency, registering appropriate hypoglycaemia avoidance strategies alongside inappropriate FoH-driven actions.27 Modified versions also show sufficient test-retest reliability.21 Although less used, the HFS-C has similarly been shown to have an internal consistency of 0.86 and good convergent validity.28 A key limitation of all HFS versions is the absence of established clinical cut-offs, making clinical interpretability challenging.7

The Children’s Hypoglycaemic Index (CHI) is a contemporary alternative, encompassing a fear, situation and behaviour subscale, demonstrating a good internal consistency of 0.89, decent test-retest reliability with a Pearson’s correlation coefficient of 0.76 and strong convergent validity among its various subscales. It was purposefully developed for children, explores more areas and comprises FoH-specific behaviours.29 However, it is less popular and requires further validation in practice.

Predictors of fear of hypoglycaemia

Hypoglycaemic frequency and severity is a key factor in FoH development.18,28 In a large Australian study of 325 parents of 8–18-year-olds, severe hypoglycaemia (SH) conveyed a 6.3 higher HFS-P score (p=0.004),30 while a Slovenian work linked SH with maternal hypoglycaemia preventative behaviours (r=0.25; p=0.03).31 SH also positively correlated with HFS-C helplessness scores (r=0.19; p=0.01) in an aggregated US study of 259 6–18-year-olds.32 SH clearly has a major role in the construct of FoH, although it can of course flourish irrespective of hypoglycaemic experience: in a large US study of PYC, recent SH was wholly unrelated to 549 HFS-P worry scores.32 Other studies show adolescent emergency glucose carriage (F=6.36; p=0.05)28 or diabetes management confidence (r=0.3; p<0.01) to be more predictive,33 highlighting the ability to deal with SH to be at least as important as experience of SH in the development of FoH.

A second hypothesis is that predisposition to stress, anxiety and depression contributes to FoH.34 Less mindful parenting was associated with higher HFS-P scores (p=0.006) for 421 Dutch parents,35 and a Norwegian study correlated the Hopkins Symptom Checklist-25 (HSCL-25) for depression and anxiety with HFS-P worry scores among 200 mothers (r=0.04; p=0.001) and fathers (r=0.28; p=0.006).36 Among CYP social anxiety and HFS-C scores positively correlated for North American boys (r=0.45; p<0.01) and girls (r=0.30; p=0.005),36 as did emotional disorders and HFS-B scores among Saudi adolescents.37 Of course, such psychological co-morbidities are also associated with certain sociodemographic factors, compounding vulnerability to FoH. For instance, parenting stress has been linked to having younger children, lower socioeconomic status and a non-Caucasian background, factors all also independently associated with FoH.38

The most noteworthy demographic variable was gender. Several international studies demonstrated significantly higher maternal HFS scores.18,19,26,31 Girls had higher HFS-C helplessness scores (F=4.33; p=0.039) than boys,7 and twice as high FoH scores (p<0.0001) in a 453-strong adolescent Swedish study.39 Few studies depicted no gender disparity.40 Age was also influential: parents of 6–11-year-olds had higher HFS-P scores than parents of children aged 0–5 years (p=0.003) or >12 years (p=0.003), perhaps reflecting care transition from parent to school,40 and adolescent age correlated with higher HFS-C social consequence scores.72 However, associations between age and FoH were inconsistent.31,41 The impact of technology was also indeterminate, ranging from higher HFS-P behaviour scores with multiple daily injections,19 and lower HFS-C worry scores with CSII (p=0.05),42 to no impact28,42 or moderate FoH encouraging CSII use.43

Impact of fear of hypoglycaemia

FoH is postulated to cause hypoglycaemia-avoidant behaviour, prolonged hyperglycaemia, poor glycaemic control and increased HbA1c levels. Hyper-vigilant parents admit to accepting higher target ranges where such vigilance is implausible,44 as do adolescents seeking to avoid humiliating public hypoglycaemia. Several studies confirmed significant associations between FoH scores and HbA1c.19,30,41 Others demonstrated no correlations between HFS-P,18,26,32 HFS-C,17,37 and HbA1c. In some cases, despite high maternal HFS-B,45 or HFS-C maintain high blood glucose factor scales correlating with hyperglycaemia, there was no corresponding rise in Hba1c.45 It is clear that Hba1c is a multi-factorial derivation, often poorly reflective of everyday blood glucose excursions. More detailed glycaemic data are required to truly capture the impact of FoH on glycaemic control. Contrary to the initial hypothesis, FoH can also intensify diabetes control, negating any negative impact on Hba1c, or even improving glycaemic control,71,23 although this was a far less common pattern.

The second key FoH impact is upon QoL, although few studies cite QoL as a primary outcome. It is challenging to deduce whether predisposition to stress, anxiety and depression increases FoH, or if FoH intensifies pre-existing psychological burden. In reality, this relationship is bi-directional and there is likely to be an element of reverse causality.34 Parents and children in the highest fear quartile have been shown to have lower scores on the Paediatric Quality of Life Inventory (PedsQL) by 20–22%,39 and significant associations have been demonstrated between FoH and DD in adolescent girls (p=0.044) and boys (p=0.026).39

Minimisation of fear of hypoglycaemia

The 13 paediatric intervention trials identified highlight the ambiguity of using technology to reduce hypoglycaemia risk and fear. The Juvenile Diabetes Research Foundation CGM RCT failed to exhibit appreciable reductions in HFS-P and HFS-C scores across 10 UK sites,36 while a smaller UK study of 16 adolescents did show HFS-P (98.69 vs 66.69; p=0.0021) and HFS-C (97.38 vs 59.75; p=0.003) reductions with 12 months’ CGM,45 as did an Australian...
crossover RCT evaluating remote monitoring mobile CGM. In a multicentre German observational study, CSII use for 6 months conferred significant reductions in HFS-P worry scores (d=0.4-0.6; p<0.01), with replicable results a decade later, and in Saudi Arabia, flash glucose monitoring improved adolescent HFS-C scores (p=0.0001). A replicate study involving Israel, Slovenia and Germany comparing an artificial pancreas system with SAPT for 4 nights demonstrated significant HFS-C worry reductions (1.04 vs 0.90; p=0.017), whereas a UK crossover RCT comparing closed loop systems with SAPT did not, nor did a multicentre Australian RCT comparing predictive low glucose management versus SAPT.

A comprehensive adult literature review showcased blood glucose awareness training and cognitive behavioural therapy (CBT) as effective interventions. A US multisite RCT involving 258 adolescents evaluated the Flexible Lifestyles Empowering Change (FLEX) programme of motivational interviewing and problem-solving skills. Significant improvements were found in adolescent worry/helplessness criteria (−0.16; p=0.04), adolescent health-related QoL (3.18; p=0.009) and parents’ behaviours to maintain high blood glucose (−0.21; p=0.005). Another American intervention using video-based telehealth (REDCHiP) involved 36 parents of 2–6-year-olds. REDCHiP comprised a 10-week programme applying CBT principles to recognise FoH-related thoughts and behaviours, refining coping strategies and practising exposures to challenging situations. At 3 months there were significant reductions in HFS-PYC and DD scores.

Discussion

Main findings

FoH is a pervasive problem, dependent on a range of factors. Negative hypoglycaemic experience is clearly key, with psychological comorbidity serving as both a predictive and confounding factor. Greater female FoH prevalence undoubtedly reflects a higher female psychological burden with double the DD and greater anxiety levels, although paternal FoH is poorly represented with the only dedicated study displaying low FoH and state anxiety. FoH often results in deteriorating glycaemic control, which is sometimes reflected in increased HbA1c levels. The impact of FoH on QoL is also more nuanced, as innumerable variables contribute to QoL, not least of which is chronic illness itself. Technology has a definitive role in minimising FoH, which is most beneficial in conjunction with psychological gains. Successful intervention studies reveal significant reductions in PedsQL, parental health-related QoL, stress and anxiety, alongside FoH reductions. Psychological intervention is clearly vital, but requires significant buy-in. A UK pilot of problem-solving workshops highlighted significant recruitment issues: although over 90% of the 89 families approached had high HFS-P scores, only 25% participated, citing reluctance to miss school, lack of time, interest or travel difficulties. Lessons must be learnt for future directives and further statistically powered RCTs are needed to confirm the validity of this approach.

Strengths and limitations

The majority of papers were cross-sectional studies, relatively quick, low-cost undertakings, useful in displaying prevalence, associations and new hypotheses, but unable to establish causality or temporality. Only seven studies performed power calculations to justify sample size; others were likely woefully underpowered. Inter-study variability also rendered some comparisons or aggregations redundant. For instance, a third of studies lacked a definition for SH, definitions varied widely, and most SH was self-reported. Only four intervention trials listed FoH as a primary outcome, nevertheless 92% provided significant p values with precise confidence intervals. Sadly, all lacked a cost-benefit analysis (Appendix 2).

Although FoH measurement was largely comparable and robust, with 93% of studies using the psychometrically strong HFS, this questionnaire is subject to recall bias, requires literacy, self-assessment and abstract reasoning. Age-specific considerations include the ability of younger children to hypothecate, adolescents to be candid and parental engagement in diabetes care. The impact of FoH was chiefly assessed upon HbA1c and QoL. The validity of the former was marred by historic clinic records, different laboratories, self-report and missing data. It is also likely that time spent in range is a more useful marker than HbA1c. QoL was assessed using an array of established tools, limiting comparability, and was coloured with recall bias.

Selection bias was a fundamental limitation: most recruited opportunistically from diabetes clinics or camps, 22 were restricted to single centres and only a handful accessed national registries. Participants were self-selected by virtue of attending clinic, answering calls or adverts, reflecting a motivated cohort. Further commitment involved questionnaire completion, regular self-monitoring of blood glucose or embracing technology. Response rates across 27 studies ranged from 21% to 96% (mean 61%). Engaged respondents generally revealed better glycaemic control than non-respondents, with a mean study participant HbA1c of 66 mmol/mol and CSII use of 5–86%, often deviating markedly from UK rates of 36.7%. Studying populations with better glycaemic control potentially skews the FoH burden and its confounders.

Reviewing only English language publications delivered populations fairly reflective of the UK. Middle Eastern studies relied on questionnaire translation and back-translation, as did many European studies. This may have introduced inaccuracies and cultural inconsistencies. Study cohorts reflected narrow socioeconomic groups: 20 of 23 studies describing ethnicity were 71–97% Caucasian, 15 had a 69–98% married population and 22 demonstrated higher parental education, employment or income (Appendix 3). This diminishes the wider applicability of the results while highlighting the time, interest and literacy often decisive in study participation. Future studies need selection processes which overcome these biases. Mothers represented 52–98% of parent participants (mean 80%) across 20 studies, excluding exclusively maternal or paternal studies. Achieving gender parity is challenging, as mothers are usually the primary caregivers whereas fathers undertake <20% of diabetes-related tasks. It is nevertheless important that future studies are more representative.

Implications for future research and practice

There has been a substantial body of work evaluating the scope of
paediatric FoH, but to truly capture the natural history of an often transient phenomenon, large-scale prospective longitudinal studies are required. An assessment of FoH should include the validated HFS and an objective psychological evaluation. The outcome of glycaemic control should be broadened to include CGM data, acute and secondary complications. QoL should be assessed by both subjective questionnaires and objective psychological appraisal. To limit selection bias, studies must aim to include both parents of all patients within a named diabetes centre, with efforts to minimise language and travel barriers. Further statistically powered RCTs must confirm the validity and applicability of interventions. Awareness of FoH should be raised among local paediatric diabetes multidisciplinary teams, CYP and their parents, with a view to including HFS-P, HFS-PYC and HFS-C surveys within the annual diabetes review so at-risk families can be offered appropriate interventions.

Conclusions

This review indicates that FoH is an important issue among CYP with T1DM and their parents. There are several factors involved in the development of FoH. Personal experience of hypoglycaemia and psychological vulnerability are core features in the construct, but the weight of these factors depends on a host of other sociodemographic variables. The true causality and burden of FoH can be better established in prospective longitudinal studies, assessing these potential risk factors at diagnosis and monitoring for the development of FoH at regular intervals. Significant FoH can invariably impact diabetes management and glycaemic control; longitudinal results with CGM data will enable a subtler evaluation of this relationship. Study spans over decades can also assess the psychological burden of FoH more comprehensively than snapshot cross-sectional data. Although such studies are costly and susceptible to high dropout rates, they are necessary to accurately define the long-term impact of FoH. This enables at-risk individuals to be identified more readily, and intervention measures to be better tailored. Despite a recent expansion in paediatric FoH intervention trials, numbers are still small. A greater volume of such trials, with larger study numbers, are desperately needed to demonstrate the value of technological and psychological therapies in order to make such interventions commonplace offerings for families suffering from intractable fear.

Conflict of interest None.

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Testosterone and Type 2 Diabetes Worldwide Audit

ABCD has launched a Worldwide Audit of Testosterone and Diabetes in the UK and Internationally to assess real clinical efficacy and safety & inform future practice and guidelines

Symptomatic Testosterone Deficiency is present in approximately 40% of men with Type 2 diabetes. Data from patients who are testosterone deficient and not treated can also be entered.

**Does your centre diagnose Testosterone Deficiency?**

If yes, **REGISTER YOUR CENTRE!**

at https://abcd.care/application-join-abcd-worldwide-testosterone-and-diabetes-audit

- you are invited to enter your patients’ data into the bespoke online tool
- you will be able to analyse your local data easily
- the data will be automatically added to the national data in anonymised form
- we can provide easy-to-complete paper proformas for use in clinic if preferred

Please remember:

- the more data, the more complete our understanding of Testosterone in real clinical practice
- all contributors will be listed in publications arising from data submission
Appendix 1. Search Strategies

A. Embase
1. type 1 diabetes mellitus.mp. or insulin dependent diabetes mellitus/ (117090)
2. (T1DM or T1D or IDDM).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (30663)
3. 1 or 2 (122864)
4. hypoglycemia/ or fear of hypoglycaemia.mp. or fear/ (150043)
5. hypoglycemia/ or FoH.mp. or fear/ (150230)
6. 4 or 5 (150251)
7. HbA1c.mp. or hemoglobin A1c/ (113493)
8. glycosylated hemoglobin/ or glycemic control.mp. or glycemic control/ or glucose blood level/ (323176)
9. 7 or 8 (376656)
10. (depression or anxiety).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (566645)
11. 10 or 11 (879500)
12. 3 and 6 and 9 and 12 (1501)
13. limit 13 to (english language and yr="2000 - 2020" and child <unspecified age>) (286)

B. Medline
1. type 1 diabetes mellitus.mp or Diabetes Mellitus, Type 1/ (77260)
2. (T1DM or T1D or IDDM).mp (16468).
3. 1 or 2 (80748)
4. Hypoglycaemia/ or fear of hypoglycaemia.mp (27064)
5. Fear/ or FoH.mp. or Hypoglycemia/ (57847)
6. 4 or 5 (57902)
7. HbA1c.mp. or Glycated Hemoglobin A/ (51919)
8. Glycated Hemoglobin A/ or Blood Glucose/ or glycemic control.mp. (190137)
9. 7 or 8 (202638)
10. “quality of life.mp. or “Quality of Life”/ (317349)
11. Depression/ or Anxiety/ (525114)
12. 10 or 11 (803362)
13. 3 and 6 and 9 and 12 (303)
14. Limit 13 to (English language and yr="2000-2020" and “all child (0 to 18 years)” and last 20 years) (120)

C. PsycINFO
1. (type 1 diabetes mellitus or diabetes mellitus).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (11675)
2. (T1DM or T1D or IDDM).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (785)
3. 1 or 2 (11928)
4. exp Hypoglycemia/ or exp Fear/ or hypoglycaemia.mp. (21131)
5. exp Fear/ or exp Hypoglycemia/ or FoH.mp. (20993)
6. 4 or 5 (21147)
7. HbA1c.mp. (1750)
8. exp Glucose/ or exp Blood Sugar/ or glycemic control.mp. (5846)
9. 7 or 8 (7008)
10. quality of life.mp. or exp “Quality of Life”/ or QoL.mp. (45348)
11. 10 or 11 or 12 (519192)
12. (depression or anxiety).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (456241)
13. 10 or 11 or 12 (519192)
14. 9 or 13 (524970)
15. 3 and 6 and 14 (89)
16. limit 15 to (english language and (childhood <birth to 12 years> or adolescence <13 to 17 years>) and last 20 years) (17)
Appendix 2. Quality Assessment Tables

A. Cross-Sectional Studies (n = 28)
CEBM Critical Appraisal of a Cross-Sectional Study (CEBM, 2014)

| Question                                                                 |
|--------------------------------------------------------------------------|
| 1. Did the study address a clearly focused question/issue?               |
| 2. Is the research method (study design) appropriate for answering the research question? |
| 3. Is the method of selection of the subjects (employees, teams, divisions, organizations) clearly described? |
| 4. Could the way the sample was obtained introduce (selection) bias?      |
| 5. Was the sample of subjects representative with regard to the population to which the findings will be referred? |
| 6. Was the sample size based on pre-study considerations of statistical power? |
| 7. Was a satisfactory response rate achieved?                            |
| 8. Are the measurements (questionnaires) likely to be valid and reliable? |
| 9. Was the statistical significance assessed?                            |
| 10. Are confidence intervals given for the main results?                 |
| 11. Could there be confounding factors that haven’t been accounted for?   |
| 12. Can the results be applied to your organization?                    |
Appendix 2. Quality Assessment Tables (continued)

| Study | 1 | 2 | 3 | 4 | 5 | 6 |
|-------|---|---|---|---|---|---|
| First Author | Publication Year | Clearly focused question | Appropriate research method | Clear study design | Selection bias | Representative sample characteristics | Power calculation |
| 1. | 2018 | Yes | Mindfulness and parental FoH | Yes | Yes | Partially: locally based population 3% non-Dutch; 85% married 83% paid job | No |
| 2. | 2015 | Yes | FoH and anxiety | Yes | Yes | Randomized controlled trial with a follow-up of 1 year | No |
| 3. | 2014 | Yes | FoH, self-efficacy and HbA1c | Yes | Yes | Reflective of local population 100% Iranian | No |
| 4. | 2018 | Yes | FoH, self-efficacy and parenting stress | Yes | Yes | Reflective of local population 100% Iranian | No |
| 5. | 2009 | Yes | Effect of FoH on social anxiety, adherence and QoL | Yes | Yes | Representative of clinic population 82% white; 12% African-American but higher SEE | No |
| 6. | 2016 | Yes | Gender and DD, including FoH | Yes | Yes | Qualitatively-rational database 68% married; 90% economic status above average; more girls | No |
| 7. | 2014 | Yes | Maximised FoH and adherence | Yes | Yes | Yes | No |
| 8. | 2011 | Yes | FoH and diabetes self-management | Yes | Yes | Yes | No |
| 9. | 2006 | Yes | Influence of trait anxiety and hypoglycaemic history on FoH | Yes | Yes | Yes | No |
| 10. | 2011 | Yes | FoH and diabetes control | Yes | Yes | Unclear 88% Caucasian | No |
| 11. | 2009 | Yes | Anxiety & depression in mothers related to FoH, coping and metabolic control | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 12. | 2019 | Yes | FoH, hypoglycaemia and parental emotional distress | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 13. | 2015 | Yes | Examine psychometric properties of HFS-IP | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 14. | 2014 | Yes | Parental FoH and glycaemic control | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 15. | 2014 | Yes | Relationship of sleep, FoH and diabetes self-efficacy | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 16. | 2013 | Yes | Evaluate FoH, hypoglycaemia and quality of life | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 17. | 2005 | Yes | Provision of preliminary psychometric data on CHI | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 18. | 2012 | Yes | Comparison of psychological characteristics: CGM v. SMBG | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 19. | 2009 | Yes | Correlates of fathers parenting stress including FoH | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 20. | 2019 | Yes | Parental FoH, anxiety and well-being | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 21. | 2007 | Yes | Parental FoH & BG levels | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 22. | 2008 | Yes | Development of HFS-PYC | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 23. | 2011 | Yes | Parenting stress & FoH depression | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 24. | 2017 | Yes | Update psychometric properties of HFS-PYC | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 25. | 2016 | Yes | Exploring constructs of HFS-P and HFS-C | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 26. | 2006 | Yes | Parenting stress and its correlates (including FoH) | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 27. | 2017 | Yes | FoH in parents of young children | Yes | Yes | Baseline data from an RCT on coping skills training | No |
| 28. | 2017 | Yes | Parenting stress, FoH and metabolic control | Yes | Yes | Baseline data from an RCT on coping skills training | No |
### Appendix 2. Quality Assessment Tables (continued)

| Study | 7 | 8 | 9 | 10 | 11 | 12 |
|-------|---|---|---|----|----|----|
| **Authors** | **Year** | **Satisfactory response rate** | **Valid & reliable measures (Cronbach’s alpha)** | **Statistical significance assessed** | **Confidence intervals given** | **Confounders accounted for** | **Results applicable locally** |
| 1. Ausbun | 2013 | Yes - 75% | Yes-HFS-P, MISP score (α = 0.88) | Yes | Yes | Partially |
| 2. Al Hayek | 2015 | Unknown | Yes-HFS-P (α = 0.60) Literacy translated | Yes | Yes | Less so - Saudi Arabia based |
| 3. Armit | 2014 | Yes - 81% | Yes-HFS-P (α = 0.85) Persian translated | Yes | Yes | Less so - Iran based |
| 4. Armit | 2015 | Yes - 81% | Yes-HFS-P (α = 0.85) Persian translated | Yes | Yes | Less so - Iran based |
| 5. Di Battista | 2005 | No - 23% US, 45% Canada | Yes-HFS-P (α = 0.87) Self-report demographics | Yes | Yes | Partially |
| 6. Fransesfontein | 2015 | No - 71% | No-scale 0 to 10 to assess FPI | Yes | Yes | Partially |
| 7. Freedenstien | 2015 | Yes - 66% | Yes-HSP (α = 0.85) Illness Perception Questionnaire | Yes | Yes | Partially |
| 8. Friedlander | 2015 | Unknown | Yes-CHI (α = 0.89) Diabetes Behavioural Rating Scale (DBRS) | Yes | Yes | Partially |
| 9. Gonder-Frederick | 2005 | Yes - 63% | Yes-HSP (α = 0.85) & HFS-C (α = 0.86) | Yes | Yes | Partially |
| 10. Gonder-Frederick | 2011 | NA | Yes-HSP (α = 0.86) & HFS-C (α = 0.85) | Yes | No | Yes |
| 11. Iwai | 2015 | No - 40% | Yes-HFS-P, MISP (α = 0.85) | Yes | Yes | Partially |
| 12. Haukswald | 2015 | Yes - 71% | Yes-HSP (α = 0.85) & HFS-C (α = 0.86) | Yes | Yes | Partially |
| 13. Haukswald | 2015 | Same data 2015 | Yes-HSP (α = 0.85) & HFS-C (α = 0.86) | Yes | Yes | Partially |
| 14. Hawkins | 2014 | Unknown | Yes-HPS-PY, Demographic questionnaire & self-report hypoglycaemia | Yes | No | Yes |
| 15. Herbst | 2014 | No - 47% | Yes-HPS-PY (α = 0.92) Pittsburgh Sleep Quality Index (PSQI); Sed-P (α = 0.76) | Yes | No | Yes |
| 16. Johnson | 2014 | No - 49% | Yes-HPS-PY, Decisional Conflict Questionnaire | Yes | No | Yes |
| 17. Kampe | 2005 | Yes - 66% | Yes-HPS-PY, Demographic Questionnaire | Yes | No | Yes |
| 18. Markel | 2015 | 16% of participants already recruited to JDRF-CGM trial | Yes-HPS-PY, Pediatric QOL Inventory; Short Form Health Survey Center for Epidemiologic Studies Depression scale (CES-D), BDM Communication Questionnaire, Diabetes Family Conflict Scale (DFCS), STAI & Pain, quality of life | Yes | No | Partially |
| 19. Mitchell | 2009 | Yes - 85% | Yes-HPS-PY (α = 0.85), Demographic questionnaire, self-report interview | Yes | No | Partially |
| 20. Patel | 2019 | Yes - 62% | Yes-HPS-PY (α = 0.85), | Yes | No | Partially |
| 21. Patton | 2007 | Yes - 88% | Yes-HPS-PY (α = 0.85) | Yes | No | Partially |
| 22. Patton | 2008 | Yes - 75% | Yes-HPS-PY (α = 0.91) | Yes | No | Partially |
| 23. Patton | 2011 | Judy - 51% | Yes-HPS-PY, Behavioral Assessment Scale | Yes | No | Partially |
| 24. Patton | 2017 | NA | Yes-HPS-PY | Yes | No | Unclear |
| 25. Shepard | 2014 | NA | 5 studies | Yes-HPS-PY | Yes | No | Partially |
| 26. Sheppard | 2005 | Yes - 70% | Yes-HPS-PY (α = 0.85) | Yes | No | Yes |
| 27. Vani | 2017 | Yes - 71% at site level | Yes-HPS-PY, Demographic Questionnaire, Diabetes Family Responsibility Questionnaire (DFRQ) | Yes | No | Yes |
| 28. Vaune | 2016 | Yes - 74% | Yes-HPS-PY | Yes | No | Yes |

**Notes:**
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Appendix 2. Quality Assessment Tables (continued)

B. Randomised Controlled Trials (n = 8)
CASP Randomised Control Trial Checklist (CASP, 2018)

|   |   |
|---|---|
| 1. | Did the trial address a clearly focused issue? |
| 2. | Was the assignment of patients to treatments randomised? |
| 3. | Were all of the patients who entered the trial properly accounted for at its conclusion? |
| 4. | Were patients, health workers and study personnel ‘blind’ to treatment? |
| 5. | Were the groups similar at the start of the trial? |
| 6. | Aside from the experimental intervention, were the groups treated equally? |
| 7. | How large was the treatment effect? |
| 8. | How precise was the estimate of the treatment effect? |
| 9. | Can the results be applied to the local population, or in your context? |
| 10. | Were all clinically important outcomes considered? |
| 11. | Are the benefits worth the harms and costs? |
## Appendix 2. Quality Assessment Tables (continued)

| First Author | Clearly focused issue | Assignment randomised | Patient accountability | Blinded intervention | Similar baseline characteristics | Equal treatment of two groups |
|--------------|-----------------------|-----------------------|------------------------|----------------------|---------------------------------|------------------------------|
| 1. Abraham (2018) | Yes | PGM v. SAPT | Yes | Minimisation at randomisation | Yes | 19% loss (withdrawal deviation) | No | Yes | Yes |
| 2. Barnard (2014) | Yes | CLS v. SAPT | Yes | Permutated block four approach | Yes | 52% recruitment; 1 withdrawal | No | not to patient Allocation concealed to staff | Unclear | Almost CLS- extra supervision |
| 3. Burchardt (2018) | Yes | CGM v. SMBG | Yes | Computer generated | No | No | No | Unclear | Yes |
| 4. JDF CWM (2010) | Yes | CGM v. SMBG | Yes | Permutated block design | Yes | 95-100% completion rate | No | No | Almost CGM- additional direction |
| 5. Mayer-Davis (2018) | Yes | PLEX v. control | Yes | Automated block method | Yes | 18-5% eligible; 51% refused final sample; 93% retention rate | No | not to patient Allocation concealed to staff | Yes | Yes |
| 6. Mueller-Godfrey (2018) | Yes | CGS v. MID | Yes | Software; stratified by centre | Yes | 32% recruitment; 18% excluded final analysis | No | not to patient Allocation concealed to staff | Yes | Yes |
| 7. Patton (2019) | Yes | RECHP v. control | Yes | Block assignment by child sex | No | No | Unclear | Yes |
| 8. Ziegler (2019) | Yes | AP v. SAPT | Yes | Computer software blocked randomisation | No | No | Unclear | Unclear |

### Study

| First Author | Publication Year | Treatment Effect | Precision Estimate | Applicable Results | Significant outcomes explored | Benefits outweigh harms/ costs |
|--------------|------------------|------------------|--------------------|--------------------|-------------------------------|-------------------------------|
| 1. Abraham (2018) | Primary outcome: time spent in hypoglycaemia | Reduction in time spent in hypoglycaemia (mean difference -0.95% CI 1.30 to -0.61) | somewhat | 5 Australian centres Limited demographics | Yes | No adverse events Cost not explored |
| 2. Barnard (2014) | Primary outcome: time spent in target BG range | Time spent in target increased from 47% to 64% with CLS than CGM 10% | Least square mean difference between CGM and CLS | | | |
| 3. Burchardt (2018) | Primary outcome: parental FPI on HFS | Least square mean difference control v CGM: 38.9% CI 12.2 to -4.4, p<0.005 | | | | |
| 4. JDF CWM Study Group (2010) | Primary outcome: HbA1c | No significant HbA1c changes in youth or parents | | | | |
| 5. Mayer-Davis (2018) | Primary outcome: HbA1c | No significant HbA1c changes in youth or parents | | | | |
| 6. Mueller-Godfrey (2018) | Primary outcome: time spent in hypoglycaemia | Only significant HbA1c reductions in children maintaining high BG in parents (p<0.005) and those exposed to high HbA1c levels (p<0.04) | | | | |
| 7. Patton (2019) | Primary outcome: HbA1c | | | | | |
| 8. Ziegler (2019) | Primary outcome: time spent in hypoglycaemia | | | | | |
### Appendix 2. Quality Assessment Tables (continued)

#### C. Pre-Post Prospective Studies (n = 5)

**NIH Quality Assessment Tool for Before-After (Pre-Post) Studies (NIH, 2018)**

| Study | 1 | 2 | 3 | 4 | 5 | 6 |
|-------|---|---|---|---|---|---|
| **First Author** | **Publication Year** | **Clearly stated objective** | **Clearly described eligibility criteria** | **Study participants representative** | **All eligible participants enrolled** | **Sample size sufficient** | **Intervention clear and consistent** |
| 1. Al Hayek (2017) | Yes (3m) FGM- Foh/Qol HbA1c | Yes: 13-19 years Minimum 6m T1DM No current SH/ DKA | Yes- of Saudi Arabia Limited demographics | Unclear | No (n=47) | No power calculation | Yes |
| 2. Ca (2017) | Yes (3m) Workshop- Foh/HbA1c | Yes: 8-16 years Minimum 6m T1DM No co-morbidity | Yes- of UK clinic population Ethnically diverse | No-pilot study Only 89 of 300- 33% recruitment | Almost (n= 22) Aimed 32 for pilot | Yes |
| 3. Ng (2019) | Yes (18m) CGM- Foh/ HbA1c | Yes: <8 years Minimum 12m CGM English speaking | Yes- of UK clinic population Limited demographics | Unclear | No (n=16) | No power calculation | Clear intervention 58% uncompliant |
| 4. Kamps (2010) | Yes Trauma- Foh/Angiopathy HbA1c | Yes: 4-16 years Minimum 6m T1DM No chronic illness | Yes- of US clinic population Higher income, education, duration in x2 completers | Most 89% recruitment | Moderate (n= 158) No power calculation | No | No measure of exposure/ stress |
| 5. Muller- Goddefroy (2009) | Yes (6m) CSII-Psychosocial | Yes: 18 years Minimum 6m T1DM Sufficient literacy | Yes-18 centres in Germany Limited demographics | Unclear | Almost (n=117) 80% power = 120 | Yes |

| Study | 7 | 8 | 9 | 10 | 11 | 12 |
|-------|---|---|---|---|---|---|
| **First Author** | **Publication Year** | **Outcomes defined, valid, reliable & consistent** | **Assessors blinded** | **Loss to follow up <20% and accounted for** | **P values provided for pre- to post- changes** | **Outcomes measured multiple times** | **Group-level intervention v. individual data** |
| 1. Al Hayek (2017) | Yes | HFS-C, Peds QL | No | Yes | Yes | No | NA |
| 2. Ca (2017) | Yes | HFS, Peds QL | No | Accounted for but high: 34% loss to follow-up | No Pilot intervention | Yes-outcomes at 1 and 3m | NA |
| 3. Ng (2019) | Yes | HFS/HbA1c | No | Yes | Only 8% loss to follow-up | Yes | Yes- HbA1c at 3, 6, 9, 12m | NA |
| 4. Kamps (2010) | Yes | CHI, RCMA/ HbA1c | No | Accounted for but high: 25% loss to follow-up | Yes | No | NA |
| 5. Muller- Goddefroy (2009) | Yes | HRQOL, RIP, HFS HbA1c | No | Accounted for but high: 23% in CYP 18% in parents | Yes | No | NA |
Appendix 2. Quality Assessment Tables (continued)

### D. Literature Reviews/Systematic Reviews (n = 2)

**CASP Systematic Review Checklist (CASP, 2018)**

| Study | 1 | 2 | 3 | 4 | 5 |
|-------|---|---|---|---|---|
| First Author Publication Year | Focused question | Appropriate papers | Important relevant studies included | Quality assessment | Results combination |
| 1. Bamford (2010) | Yes FoH in parents of young children | Yes Cross-sectional | Mostly CRD principles; 2 reviewers Multiple databases, meeting abstracts, bibliographies, experts, But only 6 studies; nil interventional | Yes: Cronbie criteria 2 reviewers X1 7/7 quality indicators x3 3 met 6/7; x2 met 4/7 | No Dissimilar cohorts/ outcomes Lack of data Narrative synthesis |
| 2. Driscoll (2016) | Yes FoH in CYP and parents Literature review | Yes Cross-sectional | Greater breadth- 16 studies | Unclear | No Narrative analysis |

| Study | 6 | 7 | 8 | 9 | 10 |
|-------|---|---|---|---|---|
| First Author Publication Year | Overall results | Result precision | Locally applicable | All-important outcomes considered | Benefits worth harms and costs |
| 1. Bamford (2010) | Parental FoH/ anxiety/ depression are common Hypoglycaemia severity predicts FoH > frequency | Some results precise p values given | Somewhat 4 studies representative Mostly US studies; similar to UK | Yes Except intervention/ education | NA |
| 2. Driscoll (2016) | Parent report of SH was the most common predictor o Most studies failed to find an association with Hba1c | Unclear | Somewhat 16 studies- mainly US/ European | Yes Associated factors, behavioural interventions, technology | NA |
| Paper First author | Study Design | Target population | Country | Recruitment site | Response rate | Number of participants | Exclusion criteria | Mean diabetes duration (range) | Mean HbA1c (range) | Insulin regime | Ethnicity | Marital Partner | SES |
|--------------------|--------------|--------------------|---------|-----------------|---------------|------------------------|-------------------|--------------------------|----------------|---------------|-----------|----------------|------|
| 1. Alders (2018)   | Cross-sectional | Parents | Netherlands | MILES Youth data | 421/533 | 79% | F 359 (85%) M 62 (15%) 43y (25-66) | NR | 4.6y (0-16) | MDAI 114 (27%) CSII 307 (73%) | 7.8% - parent report 355 | Non-Dutch 3% | 89% | High education 38% Paid job 83% |
| 2. Al Hayek (2015) | Cross-sectional | Adolescents | Saudi Arabia | Diabetes Centre | Jun 13-Feb 14 | NR | NA | 187 | M 95 (51%) M 92 (49%) 15.3y (13-18) | <1y T1DM | 7.1y | MDAI 15 (61%) CSII 36 (19%) | NR | Arabic 100% | NR | NR |
| 3. Amiri (2014)    | Cross-sectional | Young children | Iran | Diabetes Education Assoc 2000-12 | 61 | 75 | 81% | F 60 (57%) 36.2y (25-49) 45 M (43%) 42y (30-55) | <6m T1DM | 5.1y (5-10.5) | MDAI 61 (100%) CSII 0 | 9.4% - initiation (6.1-13.7) | Iranian 100% | NR | High School 66% Employed 25% F 95% M |
| 4. Amiri (2018)    | Cross-sectional | Same data 2014 | Iran | Diabetes Education Assoc | 61 | 75 | 81% | F 60 (57%) 36.2y (25-49) 45 M (43%) 42y (30-55) | <6m T1DM | 5.1y (5-10.5) | MDAI 61 (100%) CSII 0 | 9.4% - initiation (6.1-13.7) | Iranian 100% | NR | High School 66% F 64% M Employed 25% F 95% M |
| 5. Di Battista (2009) | Cross-sectional | Adolescents | North America | Nashville/Toronto May 04-Apr 07 | 72 | 307 | 23% US 10 of 22 45%Canada | NA | 7.6 | M 43 (57%) M 33 (43%) 15.9y (13-18) | <6m T1DM | 6.4y | NA | 8.9% - initiation | White 82% African 12% Other 4% | NR | Average income $40,000-$59,999 |
| 6. Forsander (2016) | Cross-sectional | Adolescents | Sweden | DIABKIDS database | 453 | 212 | 21% | F 59 (66%) 154 M (34%) 17.1y (15-18) | NR | 6.6y | MDAI 23 (53%) CSII 216 (47%) | 7.7% - current | NR | 69% | Economic status above average 90% |
| 7. Freckleton (2014) | Cross-sectional | Parents | Australia | Diabetes camp JDAF advised | 71 | 115 | 62% | F 71 (100%) M 0 | 71 | M 39 (52%) M 33 (47%) 9y (2-12) | NR | 3.1y (1-22) | MDAI 71 (100%) CSII 0 | 8.1% - initiation (5.6-12.9) | Australian born 63% | NR | NR |
| 8. Frederick (2011) | Cross-sectional | Children | US | Diabetes camp | Clinic Atlanta | NR | 127 | F 75 (59%) M 52 (41%) 11.8y (8-15) | <5y T1DM | 4.9y (1-13) | MDAI 60 (47%) CSII 67 (53%) | 8.0% - current | White 66% Black 32% Hispanic 2% | NR | NR |
| 9. Gonder - Frederick (2006) | Cross-sectional | Parents | US | Clinic Virginia | 78 | 124 | 63% | F 38 (97%) 1M (3%) | 39 | F 12 (44%) M 22 (56%) 15.3y (12-17) | <1y T1DM | 7.0y | MDAI 25 (64%) CSII 14 (36%) | 7.85% - 6-8 asks | Caucasian 87% of African 13% | 70% | Beyond high school 75% |
| 10. Gonder-Frederick (2011) | Literature review | Aggregated data Parents & CYP | US | Literature review | 94 | 24 articles | US lab Several datasets over 10y | NR | 2.55 | M 203 (81%) M 47 (19%) | <1y T1DM | 5.24y | MDAI 16 (62%) CSII 98 (38%) | 8.01% | Caucasian 88% | NR | Mean education 15.5y |
| Study (Year) | Design | Country | Participants | Gender | Type | Data | Mean Age | N | Mean | SD | Mean | SD | % | % | Income | Notes |
|-------------|--------|---------|--------------|--------|------|------|----------|---|------|----|------|----|----|----|---------|-------|
| Grey (2009) | Cross-sectional | UK | Clinics | 70% of 177 | 40% | F 67 (10%) | M 105 (60%) | 27.2 (26-51) | 67 | F 67 (35%) | M 55 (44%) | 8.2 | 3.9 | 22 | >80,000 | 27% |
| Haugstedt (2010) | Cross-sectional | Norway | University Hospital | Dec 2006 | 115% of 161 | 71% | F 103 (52%) | M 97 (48%) | 15 | F 55 (50%) | M 57 (50%) | 8.1 | 1.0 | 28 | Norwegian | 14% |
| Haugstedt (2015) | Cross-sectional | Norway | University Hospital | Dec 2006 | 115% of 161 | 71% | F 91 (52%) | M 60 (48%) | 102 | F 50 (49%) | M 52 (51%) | 5.3 | 1.4 | 28 | College | 67% |
| Hawkes (2014) | Cross-sectional | Ireland | 3 clinics | 325 of 539 | 49% | 325 | NR | 325 | 3.0 | 1.0 | 28 | 3.0 | 1.0 | 28 | NA (not applicable) | 70% |
| Herbert (2014) | Cross-sectional | US | 3 clinics | 134 of 285 | 47% | 134 | NR | 3.0 | 1.0 | 28 | 3.0 | 1.0 | 28 | NA (not applicable) | 70% |
| Johnson (2013) | Cross-sectional | Western Australia | Clinic | Aug 09-Aug 10 | 325 of 539 | 49% | 325 | NR | 3.0 | 1.0 | 28 | 3.0 | 1.0 | 28 | NA (not applicable) | 70% |
| Kamps (2005) | Cross-sectional | US | ADA Summer Camp | Mid-West | 109 of 168 | 65% | 109 | NR | 109 | 1.0 | 28 | 1.0 | 28 | NA (not applicable) | 70% |
| Morkowitz (2012) | Cross-sectional | UK | Single-site of JDRF GCM trial | 100 of 141 | 88% | 100 | NR | 7.2 | 1.0 | 28 | 7.2 | 1.0 | 28 | NA (not applicable) | 70% |
| Mitchell (2009) | Cross-sectional | US | Clinic Mid-Atlantic | 100 of 141 | 88% | 100 | NR | 7.2 | 1.0 | 28 | 7.2 | 1.0 | 28 | NA (not applicable) | 70% |
| Pate (2019) | Cross-sectional | Slovenia Clinic Ljubljana | 125 | 120 of 215 | 62% | 125 | NR | 4.9 | 1.0 | 28 | 4.9 | 1.0 | 28 | NA (not applicable) | 70% |
| Patton (2007) | Cross-sectional | US | Clinic in Cincinnati | 24 of 28 | 86% | 24 | NR | 8.3 | 1.0 | 28 | 8.3 | 1.0 | 28 | NA (not applicable) | 70% |
| Patton (2008) | Cross-sectional | US | Clinic in Cincinnati | 81 of 109 | 75% | 81 | NR | 8.1 | 1.0 | 28 | 8.1 | 1.0 | 28 | NA (not applicable) | 70% |
| Patton (2011) | Cross-sectional | US | 2 clinics in the Midwest | 39 | 77 of 39 | 51% | 39 | NR | 8.3 | 1.0 | 28 | 8.3 | 1.0 | 28 | NA (not applicable) | 70% |
| Study ID       | Number of Children | Type of Study | Country/Region | Number of Centres | Data Source | Data Collection Period | Targets | Outcomes | Duration | Conclusion | Further Information |
|---------------|--------------------|---------------|----------------|-------------------|-------------|------------------------|---------|----------|----------|------------|---------------------|
| 24. Patton (2017) | 16 | Cross-sectional data analysis | Parents | 3 datasets over 5 years | NA | 116, 106 (93%) | 116, 58 (50%) | 59 (50%) | <6m T1DM | No English | 8.2% -last 3 m (5-12.7) | White 91% | NR | NR |
| 25. Shepard (2016) | 114 | Cross-sectional factor analysis | Parents + CYP | Virginia Lab 5 studies 2002-10 | NA | 250, 220 (8.8%) | 124 (48%) | 135 (52%) | <1y T1DM | Comorbidities | MDI 155 (60%) | 8.01% | Caucasian 93% | African 4% | 87% | Mean education 15y |
| 26. Strens (2011) | 68 | Cross-sectional | Parents | 2 city clinics | 80% | 134, 115 (86%) | 64 (48%) | 70 (52%) | <6m T1DM | | MDI 107 (90%) | 8.5% (5.6-14) | -last 6 m | Caucasian 79% | 84% | Hollinghead Class Ill 46% |
| 27. Van Name (2017) | 41 | Cross-sectional Parents of young children | US T1DM Exchange | 56 centres | 419 | 149 (31%) | 254 (46%) | 205 (54%) | <1y T1DM | | MDI 23 (42%) | 8.2% (2.6-6) | White 7 mm Hispanic 10% | Black 6% | NA | Income >$75,000 52% |
| 28. Vlaseanu (2017) | 63 | Cross-sectional | Parents | Belgium Single clinic centre | 63 | 53 (84%) | 26 (44%) | 35 (56%) | <6m T1DM | Non-Dutch speaking | MDI 17 (64%) | 8.2% (10%) | -last clinic | NR | 76% | NR |
| 29. Abraham (2016) | 49 | RCT | PLGM vs. SAPT | CYP | 49 | 31 (63%) | 18 (37%) | 2.5 (2.12) | <1y T1DM | 6m CSii use | MDI 16 (100%) | 8.2% <10% | +4 BGid | NR | NR | NR |
| 30. Barnard et al. (2014) | 45 | Open label Crossover RCT | CLS vs. SAPT Adolescents | England Clinic UCLH & Cambridge | 17 of 33 | 12 (92%) | 1 (6%) | 5 (18%) | | 5 (6%) | 15.6 (12-18) | Complications | TDD >20U/kg | MDI last 1m Pregnancy | BF | 7.2 | 5% -last clinic | NR | NR | NR |
| 31. Burchardt (2018) | 5 | Open label Crossover RCT | CYP | Australia | 5 | 49 | 31 (63%) | 18 (37%) | 2.5 (2.12) | <1y T1DM | 6m CSii last 6m | MDI 16 (100%) | 8.2% <10% | +4 BGid | NR | NR | NR |
| 32. DOJF CQM Study Group (2010) | 223 | RCT | CYP | 5 | 49 | 31 (63%) | 18 (37%) | 2.5 (2.12) | <1y T1DM | 6m CSii last 6m | MDI 16 (100%) | 8.2% <10% | +4 BGid | NR | NR | NR |
| 33. Mayer-Davis (2018) | 256 | Open label Crossover RCT | CYP | US Clinic Colorado | 256 | 187 (74%) | 128 (50%) | 130 (50%) | <1y T1DM | 6m CSii last 6m | MDI 75 (29%) | 9.5% (8-13) | White 7% Hispanic 13% | Black 4% | 87% | Public health insurance 18% |
| 34. Mueller-Godfrey (2016) | 211 | RCT | Open label | Germany | 211 | 77 (43%) | 102 (57%) | 119 (56%) | <1y T1DM | insufficient literacy | MDI 69 (49%) | 7.5% | NR | 69% medium-high SES | NR |
| 35. Patton (2018) | 36 | RCT | REDCh v. conventional | US | 36 | 34 (98%) | M 2 (2%) | 52 (35.2) | <6m T1DM | | MDI 8 (22%) | 8.01% -last clinic | Caucasian 95% | Hispanic 5% | 81% | Hollinghead index SES >47.6% |
| 36. Ziegler (2015) | 59 | RCT | CYP | International Clinic Germany, Israel, Slovenia | 59 | 75 (79%) | 45 (43%) | 25 (55%) | <6m T1DM | Comorbidities | MDI 9 (29%) | 8.12% (7-10) | 8.9% (4-18) | NR | NR | NR |
| 37. Al Hamzeh (2017) | 4.7 | Prospective | Pre-JSP | GDM Adolescents | 4.7 | 27 (57%) | 20 (43%) | <6m T1DM | Skin issue | SHI DKA | MDI 20 (62%) | 8.5% | NR | NR | NR | NR | NR |
| Study Code | Study Type                           | Location | Participants | Follow-up | Main Findings | Co-morbidity | Comorbidities  | Co-morbidity | Co-morbidity  |
|------------|-------------------------------------|----------|--------------|-----------|---------------|--------------|---------------|--------------|--------------|
| 38.Cai     | Prospective pre-plant workshop      | UK       | 22 of 89     | 22        |               | 6.2y         | NR            | 8.2%         | White 77%     |
|            |                                     |          | 25%          |           |               |              |               |              | Asian 14%     |
| 39.Ng      | Prospective pre-plant CGM study     | UL, NW England Single centre | NR | 16        |               | <12m         | 7.8y         | Min 12m      | 14.6%        |
|            |                                     |          |              |           |               |              |              |              | -3.6,12m     |
| 40.Kamps   | Longitudinal pre-plant trauma study | US       | 221 of 248   | 158      |               | <6m TDm      | NR            | 8.35%        | Caucasian 71% |
|            |                                     |          | 89%          |           |               | Chronic Illness, T2DM |              |              | African 23%  |
|            |                                     |          | 8 excluded   |           |               | LD           |              |              | Hispanic 4%  |
| 41.Muller- | Prospective pre-plant study         | Germany  | 117 of 143   | 117      |               | 3.9y         | MDI 117      | 7.7%         | NR           |
| Godeffroy  |                                     |          | completed    |           |               |              |              |              | NR           |
|            | (2009)                              |          | 82%          |           |               |              |              |              | NR           |
| 42.Barnard | Systematic review of young children | 6 studies | NA           | 79       | NA            | <3.5y       | MDI + CSI     | 8.19%        | NR           |
|            |                                     |          |              | (24-114)  |              |              |              |              | NR           |
|            |                                     |          |              | F 60-100% |              |              |              |              | NR           |
| 43.Dreisal | Literature review                   | 16 studies | NA         | NA       | NR            | NA          | NR          | NR           | NR           |

**Notes:**
- NA (not applicable), NR (not recorded)
- MDI: Medical Device Identification
- <6m: <6 months
- T1DM: Type 1 Diabetes Mellitus
- T2DM: Type 2 Diabetes Mellitus
- LD: Language Difficulty
- MDI: Medical Device Identification
- MDI 117: Medical Device Identification 117
- MDI + CSI: Medical Device Identification + Continuous Self-Management
- Recent: Recent study
- Not recorded (NR): Not recorded in the study
- Not applicable (NA): Not applicable in the study

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| Paper | First Author | FoH Tool | Other assessment tools | Hypoglycaemia (Hypo) Definition | Frequency | Results | Strengths & Limitations |
|-------|-------------|----------|------------------------|---------------------------------|-----------|---------|------------------------|
| 1.     | Alders      | HFS-P    | Parent-reported questionnaire | SH: requiring glucose, hospital admission or an emergency call | >1 SH in last 12m: 7% | Demographics, mindfulnlessness, clinical characteristics accounted for 19% FoH variance; younger parental age (p=0.006), low parental educational level (p=0.016), non-Italian nationality (p=0.003), higher number of BG readings/day (p=0.001) and less mindful parenting (p=0.006) were related to higher parental FoH. SH was not related | Only 35.5% parent-reported HbA1c levels; No data available on non-responders; Sample had higher employment, higher CSI use and lower HbA1c levels |
| 2.     | Al Hayek    | HFS-C    | Socio-demographic clinical questions Screen for Child Anxiety-Related Disorders (SACRED) | American Diabetes Association Hypo definition: <3.9 mmol/L, Hypo <12/12m: 41.8%, Hypo at school: 80.7%, Low BG big problem: 63.1% | Females had higher scores on HFS & SACRED (p=0.05) 16-18y had higher HFS & SACRED SAD scale scores (p=0.05) CSI users had lower levels of worry, panic, SAD (p=0.05) DM duration >7 years correlated with greater HFS & SACRED scores Higher hypo frequency had higher HFS scores (p=0.05) HFS scores correlated with SACRED scores; no effect HbA1c Risk factors for FoH = age, MLI, older DM duration, higher SH | Single centre study; Limited socio-demographic factors; No control group; Arabic translation of questionnaires |
| 3.     | Amiri       | HFS-C    | Diabetes History Questionnaire Self-Efficacy for Diabetes Scale-Child version (SED-C) | SH: requiring assistance | Hypo in the last 3m: 97%, Hypo at school: 7.2% | CYP <9y had higher HFS scores than those >10y (p=0.0001) CYP <9y also had lower mean SED scores (p=0.0005) CYP with significant FoH concerns had higher HFS scores (p=0.004) No significant association with HbA1c, demographics or SH | Selection of children from a database; SED-C not designed for 6-16y-adapted Questions read aloud- verbal answers; Persian translation of questionnaires |
| 4.     | Amiri       | HFS-P    | Diabetes History Questionnaire Paediatric Inventory for Parents (PIP) | SH: requiring assistance | Hypo in the last 3m: 97%, Hypo at school: 7.2% | HFS-P scores were higher for mothers than fathers (p=0.0022) HFS-P scores correlated positively with several PIP scores HFS scores did not correlate with number of hypo episodes Mothers with child DM duration >2 years had lower HFS-B (p=0.008) No significant association between HbA1c and HFS-P or SED | Persian translation of questionnaires; Lack of cultural adaptation of questionnaires; Reduced completion rate among fathers |
| 5.     | Di Battista | HFS      | Self-report demographics/HbA1c Social Anxiety Scale for Adolescents (SAS-AQoL, Measure [SAS-AQoL]) Summary of Diabetes Self-Care | | NR | Social anxiety was positively correlated with HFS for boys (p=0.01) and girls (p=0.05) FoH = independent correlate of lower adherence (p=0.046) | Significant missing data for 6 CYP 10% incentive to participants; Self-report measures; Majority Caucasian US sample |
| 6.     | Fossero     | FoH scale 1 to 10 | Selected items from Diabetes Distress Scale | NR | Females scored twice as high on FoH scale (p=0.0001) Twice the proportion of females had moderate-severe DD FoH was associated with DD (p=0.044 F; 0.26 M) | No validity for FoH scale; 21% uptake; Participants had low HbA1c and tended to be female (p=0.0001) | No validity for FoH scale; 21% uptake; Participants had low HbA1c and tended to be female (p=0.0001) |
| 7.     | Frackton    | HFS      | Illness Perception Questionnaire 7 day diabetes diary management | Hypo <5mmol/L, IF 6-12y | HFS/P behaviour associated with high BG but not with hypo Model not significant in predicting HbA1c | Poor HbA1c record = different centres; Participants volunteers; only mothers | Pover HbA1c record; different centres; Participants volunteers; only mothers |
| 8.     | Frederik    | CHB      | Diabetes Behaviour Rating Scale | CHB | CHB was reduced by 7.4% for re-pet campers (>2 years) than those who had attended <2 years Total CHB reduced by 6.6% for every 1 year over 12 years age Lower self-management correlated with higher HbA1c | Convenience sample from camps/clinic; Socioeconomic data not collected | Convenience sample from camps/clinics; Socioeconomic data not collected |
| 9.     | Goederen-Frederik | HFS-P 0.89 | HFS-C 0.86 | State specific questionnaire State Traet Personality Inventory (STPI) State Traet Anxiety Inventory for Children (STAI) | MH: affecting functioning SH: requires assistance | MH 6.74/ year SH 0.46/ year | HFS-worry score higher for girls than boys (p=0.02) Adolescent trait anxiety and SH frequency (p=0.01) account for 45% variance in HFS score; nil predicted HFS-II HFS-P influenced by provision of emergency glucose (p=0.05) History of unconsciousness to higher HFS-C (p=0.011) Hypo at school → higher HFS-P (6.4 v. 43.8; p= 0.007) Parental & a adolescent anxiety scores correlated (p=0.01) No difference with CSI or MDEV; no correlation with HbA1c | 22 families failed to return questions; No demographic data on non-participating families; Only one father included |
| 10.    | Goederen-Frederik | HFS-P 0.86 | HFS-C 0.86 | STPI- STAI | NR | Good correlation between STPI and HFS scores Higher HFS-S scores vs 9.11y than 6-6y (p=0.04) | Cross-sectional design; Narrow sample sizes; No clear outcome measures | NA (not applicable), NR (not recorded) |
| Reference | Methodology | Measurement | Outcome | Notes |
|-----------|-------------|-------------|---------|-------|
| [11] | HFS | Center for Epidemiological Studies Depression Scale (CES-D) an = 0.88 | Variance in maternal depression: 27% of demographics, 7% FoH | Parents required to commit to 6-weeks RCT Only 2 fathers, so excluded in analysis |
| [12] | HFS-P | Hopkins Symptom Checklist-25 (HSCL-25) an = 0.92 | Problematic/hyp: as perceived by parent > 7 problematic/12m; 23% Unconsciousness: 21% | Higher HFS-P worry score associated with HBA1c and more problematic hyps, but not with hyp severity HFS-B score higher in MDI use, HSCL-25 correlated with maternal (p = 0.001) & paternal (p = 0.001) HFS-W; mothers HFS scores > fathers |
| [13] | HFS-P | HSCL-25 | > 7 problematic episodes/12m: 22% Unconsciousness: 24% | Worry subscale is a valid instrument to measure anxiety provoking aspects of hypoglycaemia; validity of behaviour scale is more questionable; weak correlations between the 2 HFS-B reflects both inappropriate behaviours related to fear and appropriate behaviour to avoid hypoglycaemia |
| [14] | HFS-PYC | Demographic questionnaire | Hypo-seizure 19.8% Hypo-disorientation 51.9% | Mean scores for parents of children 6-11y were higher at 70.7 versus 67.6 in 0’y (p = 0.025) and 61.6 >12y (p = 0.003) HBA1c > 7.5% associated with lower total scores (p = 0.025) No difference mothers versus fathers or CIIL versus MDI |
| [15] | HFS-PYC | Demographic medical questionnaire 24h recall interview of DM tasks Pittsburgh Sleep Quality Index (PSQI) SED-P (an = 0.76) | NR | 36% parents indicated overall sleep quality was fairly bad or very bad 34% performed daily night-time BG checks FoH worry was negatively correlated with parents confidence in managing diabetes (p = 0.01), and higher scores > greater PSQI scores |
| [16] | HFS | PerQDL Diabetes Module Clarke’s questionnaire Clinical data from W Australia Childhood Diabetes Database | MH: requiring assistance SH: seizure/ coma SH: 19% | Primary outcome: PerQDL score; primary variable: HFS Patients & children with highest FoH had 20% & 22% lower QOL, compared to those in lowest fear quartile; not associated with SHMH Children with highest FoH had 0.6% higher HBA1c (+ in 13-18y) Parents with SH children had 6.3 point higher FoH (p = 0.004) |
| [17] | HFS-C | RocAMAS Hypoglycaemia History Form | NR | CHI positively correlated with HFS-C and ROCAMAS Demonstrated good convergent validity and internal consistency Good test/retest reliability SH consistent predictor of situation and general fear scale of CHI |
| [18] | HFS | Pediatric GQL Inventory STAI, PAID, CDI, CES-D, DPCS BGM Communication Questionnaire | NR | No differences in reported FoH between CUM and BGM Parents reported more FoH than youth (p = 0.01) |
| [19] | HFS | Pediatric QOL Inventory STAI, SED, Hope Scale SED-P (an = 0.76) | NR | Low levels of FoH 16 (7–44) and low state anxiety compared to mothers in other studies. However, fathers completed <20% of diabetes related tasks |
| [20] | HFS-P | Positive and Negative Affect Schedule (PANAS) Satisfaction with Life Scale (SWLS) | STAI and DOL | SH: 8.5% parents Higher parental FoH associated with higher HBA1c Higher FoH more frequent monitoring at night (p < 0.01) At least one SH +: more preventivive behaviours p < 0.03 Mothers > FoH than fathers and more engaged in daily tasks |
| [21] | HFS-PYC | Self-report demographics Self-report hypoglycaemia history SMBG for 2 weeks using study meter HBA1c at enrolment + 3 months later | Hypo: BG <60mg/dl 3-5 hypo/week: 50% Hypo seizure in 6m: 25% | Mean total HFS-SPYC score 81 (26-130) moderate FoH FoH correlated positively with mean daily BG level (p = 0.05) Parents with hypo seizures worried more (50.7 vs 41.7) HFS-B score correlated with HBA1c at 3m (p = 0.04) Higher socioeconomic status protected from FoH |
| [22] | HFS-PYC | Self-report demographics Self-report hypoglycaemia history SMBG for 2 weeks using study meter | Hypo: <600mg/dl U/RX 3-5 hypo/week: 38% Hypo seizure: 32% Average 4.1 hpy/2 weeks | Mothers’ HFS-SPYC score > fathers (75 y 65.6; p = 0.006) Positive correlation between mothers HFS-W and frequency of hypoglycaemic events (p = 0.05) Higher scores with seizures No correlation with HBA1c average BG readings and internal consistency & test/retest reliability for HFS-SPYC |
| [23] | HFS-PYC | Behavioural Pediatric Feeding Scale Pediatric Inventory for Parents (PPIP) Beck Depression Inventory (BDI) | NR | RFS associated with greater HFS scores and higher BDI Parents’ depressive symptoms and FoH accounted for 68% of the variance in parents stress difficulty |

Appendix 3. Data Extraction Table (continued)
| Paper Authors | Project Title | Description | Methodology | Reference |
|--------------|--------------|-------------|-------------|-----------|
| 24. Patton | HFS-PYC | Self-report demographics | SMAI for 2 weeks using glucometer | NR |
| 25. Shepard | HFS-C HFS-P | Self-report hypoglycaemic history | STAI an 0.8-0.87 | Hypo HbA1c 70mg/dL Mean number of hypog | 2017 |
| 26. Snead | HFS-C | Demographic and Medical History | Diabetes Family Responsibility Questionnaire (DFRQ) 86.82 PIP 94.6 SEAI an 0.87 | NR |
| 27. Van Name | HFS-P | Worry scale | Self-report DKA & SH history | SH: seizure loss of consciousness >1SH in 3m: 7% |
| 28. Viswanath | HFS-P | Njgun Parenting Stress Index: Short form (NPSI-S) an 0.96 | Greater FSH associated with greater parenting stress: Greater stress associated with increased HBA1c Parental FSH not directly related to metabolic control | Higher age, diabetes duration not linked to FSH |
| 29. Abraham | HFS-P | Clarke’s hypoglycaemia awareness | Pump satisfaction questionnaire | HbA1c score decreased for CYP but increased in parents Night BG >60mg/dL less in closed loop (10% v17%; p<0.01) No difference in HBA1c levels, HFS and PediQL scores |
| 30. Bernard | HFS-P | Semi-structured interviews | Diabetes Technology Questionnaire | Hypo <70mg/dL Tired spent hypo: very low |
| 31. Burchardt | HFS-P | PedriQL | Depression Anxiety Stress Scale | NR |
| 32. DORF CCM | HFS-W | PedriQL | Problem Areas in Diabetes (PAID-P) CCM Satisfaction Questionnaire | SH: requires assistance |
| 33. Mayer-Osav | HFS-P | Diabetes-specific module of KINDL-R | Social Problem-Solving Inventory Diabetes Self-Management Profile CES-D, PediQL, DICS | Hypo <3.5mmol/L | Hypo experienced: 37.48% Median time spent hypo:24h: 17.30 minutes |
| 34. Mueller | HFS-P | Diabetes specific module of KINDL-R | HRQL questionnaire | NR |
| 35. Patton | HFS-PYC | PIP | PIP-PR | 1-2 hypo/ week: 60% |
| 36. Zerger | HFS-P | Technology Acceptance Model Questionnaire (TAM) a = 0.91 | Satisfaction with use of an AP | NR |
| Reference | Design | Tool/Screening | Outcome | Description | Sample Characteristics |
|-----------|--------|----------------|---------|-------------|------------------------|
| Al-Nayek (2017) | HFS-C | PeqQL Diabetes Module | SH: BG <70mg/dL 1-2/mo | Use of flash glucose monitor resulted in significant reduction in HFS (p = 0.0001), HbA1c (p = 0.008), QoL (p = 0.02) and hypoglycaemia (p = 0.023) - reduced to 0.37 per month; monitoring 0.84d to 6.76d | Small sample, single centre; Arabic translation; 3m use of sensor |
| Cai (2017) | HFS | Acceptability rating 1 to 10 Follow-up questionnaires / feedback | Hypo last 1m: 9 | Primary outcomes: acceptability and feasibility of intervention HFS scores reduced in adolescents post sessions High Foh: 68% CYP and 91% parents | 11 failed to complete follow up; No1 powered to detect pre-post test differences |
| Ng (2019) | HFS-HFS-P | NA | SH: 3rd party assistance/ hospitalization | Primary outcomes: HFS/ HbA1c (no power calculation) Significant improvements in parental (p = 0.001) and patient (p = 0.003) Foh scores. No change in HbA1c | Small sample size; Poor compliance in 58% |
| Kamps (2010) | CHE | Revised Children’s Manifest Anxiety Scale (RCMAS) a = 0.87 | %time BG <70mg/dL: 11.6% | Hurricane-Interrupted group higher % of BG readings >300mg/dL (p = 0.05) and higher RCMAS scores (p = 0.05) High Foh in specific situations at time 1 associated with higher HbA1c at time 2 if hurricane-interupted | Participants: higher income (p = 0.01), paternal education (p = 0.05), duration diabetes (p = 0.05); no difference age; HbA1c; hurricane exposure unmeasured |
| Muller-Godeffroy (2009) | HFS-P | KIDSSCREEN10-Index (HRQOL) PIP, DPICS a = 0.7 in all scales translated except KINDOLOM (a = 0.99) and MC frequency subscale of PIP (a = 0.44) | Hypo: ISPAD definitions | Sample of 100 for 80% power on 0.05 probability level DRiQOL improved in all age groups (p = 0.001) Reduced frequency/difficulty of parenting stress & HFS-W (p = 0.001) No significant decrease in SH frequency; HbA1c reduction only teens | Required 3m commitment to CSIs; No demographics on 8 nonresponders; German translation questionnaires; Loss to follow up 23% CYP/15% parents; No difference between groups: no control |
| Barnard (2010) | HFS-P | Multiple | Multiple | Severity more important than frequency in predicting Foh Maternal depression & anxiety associated with greater Foh Fear of nocturnal hypoglycaemia independent of hypo risk | Only 6 studies; no intervention's Lack of power calculation Poor response rates |
| Dissoldt (2016) | HFS-ChI | Multiple | Multiple | Most common predictor of Foh was parent report of their children experiencing SH episodes (not verified on downloads) Majority of studies failed to find a relationship with HbA1c interventions focused on CBT/ BG awareness training/technology | Cross-sectional studies; No behavioral intervention studies in CYP |