PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	'Looking for the needle in the haystack': a qualitative study of the pathway to diagnosis of type 1 diabetes in children
AUTHORS	Usher-Smith, Juliet; Thompson, Matthew; Walter, Fiona

VERSION 1 - REVIEW

REVIEWER	Jordan Pinsker, MD Tripler Army Medical Center, USA
REVIEW RETURNED	05-Oct-2013

GENERAL COMMENTS	A very nice paper by Usher-Smith, et al. discussing the time to diagnosis of type 1 diabetes and the barriers to making the diagnosis sooner. The structured interveiws offfered a standardized apporach to recalling events leading to diagnosis. Two very interesting findings are the need to stress to GP's the importance of simply performing a UA for diagnosis of diabetes, and that most parents learn of this disease on the internet, where a site devoted to parents on how to make the diagnosis sooner would be most helpful. Minor issues: 1) Recruitment: It says children age 1-16 years of age, then 6-16 years of age. Why is there an overlap? Was different receruitment done at different centers? Please explain. 2) Recruitment: Please explain in detail what is meant by families that were not suitable on clinical grounds? Often it is families undergoing social stress (eg, divorce) where the diagnosis is delayed. By exlcuding certain families, the data may be biased towards earlier diagnosis. Was this the reason only 32 of the 43 families were invited to participate? According to table 1, the DKA at presentation rate was much higher in the not included group. Major Issues: 1) Strengts and weaknesses: Of the 43 children diagnosed, only 32 were invited and only 16 participated. As noted above, the characteristics were not the same, in that the DKA rate was much higher. In addition, no mention is made of any particular family stress or socioeconomic status, which may play a role in time to diagnosis .The only results reported for socioeconomic status are in the results section, I believe this is for the 16 familes that participated. Please include both groups. Although it is a very small sample size, can a statistical comparison be done between the two groups? None is offered in the table. There is also no discussion of this is the strengths and weaknesses table.

REVIEWER	Kathleen Bethin, MD, PhD University at Buffalo USA
REVIEW RETURNED	08-Oct-2013

GENERAL COMMENTS	The Objective of this work is to explore the pathway to diagnosis of type 1 diabetes (T1D) in children from the perspective of the child, family and general practitioner (GP). The authors have a very well thought-out and written manuscript on the barriers that parents create or face in diagnosing their children with diabetes. However, the authors fail to give us any information from the children's point of view and only interview 5 general practitioners. Need to define what criteria made the families not suitable for inclusion. More information about the questions asked during interview needs to be included in the methods section. Reference 19- http://www.youthhealthtalk.org/Diabetes_type_1_in_young_people/Topic/1510 - does not contain any information that is helpful to understand the interview techniques used or anything related to this manuscript. Graphics for Figure 1 is poor and would need to be improved for publication. It would be more useful to have a table that demonstrated data rather than 4 tables of quotes from families. e.g., a table that supports the statements- "In most cases both parents appeared to be in agreement throughout the appraisal process. In the cases where there was conflict, it was consistently the mothers who were more concerned than the fathers." The authors also state in the discussion that "there was evidence that mothers in particular made use of a social network throughout this process and almost all parents also sought information from the internet." There should be a table that demonstrates which of the families used social networking resources and which used the internet in their appraisal phase. The authors state "Instead, the message to primary care physicians and nurses and health visitors providing first line care from this study is to have a low threshold for performing a dipstick test on urine of children who are non-specifically unwell." However, their data in Table 2 shows that every child that participated in this study had polyuria, polydipsia, nocturia, weight loss or a combination – all classic symptoms of diabetes. These data support checking a urine dipstick if any of those specific symptoms are present not testing a child who is non-specifically well. Overall, this is a very interesting manuscript. However, as written it does not support the objective. It is almost entirely about the parents and not the children or the GPs.

REVIEWER	Rasha Tarif Hamza Ain Shams University, Cairo, Egypt
REVIEW RETURNED	08-Oct-2013

GENERAL COMMENTS	Authors tried to explore the pathway to diagnose type 1diabetes in children from perspective of child, family and general practitioner which is an important topic since the prevalence of type 1 diabetes is greatly increasing.

	Abstract: lines 20 & 21 “They felt the main challenges to diagnosing T1D in children were the rarity of the condition…” T1D is not rare nowadays !! (as mentioned by authors in introduction section). Strengths and limitations of this study: line 32 Authors mentioned only the strengths but a major limitation is the small number of participants (parents, children & GPs) especially that authors are trying to explore the etiology of a disease using a simple interview, thus, it was better to include a larger number of participants. Moreover, the prevalence of type 1 diabetes is not uncommon nowadays. Methods: - The details of included participants should be better included in “methods” section, not just describing them in “results”. - Describe clearly inclusion & exclusion criteria of selected subjects Results: In general, results need more accurate specification in the form of numbers & frequencies, not just descriptions using general phrases e.g. most of parents…etc.. - Line 38: better use a socioeconomic standard leveling (referenced) to clearly classify social class of studied subjects. - Line 26: describe the frequency of each alternative symptom among studied subjects. - Line 33: specify symptoms that concerned the parents & those that did not & describe their frequencies. - Lines 38-44: better described based on socioeconomic standard leveling (as previously mentioned). - Subtlety of symptoms: line 14: “many parents..” indicate the exact number & % - Influence of other family members and social network: line 42: “in most cases…” indicate the exact number & % Line 53: “In most cases where…” indicate the exact number & % - Sources of information: line 4: “most parents…” indicate the exact number & % - The help seeking interval: line 21: “most children” indicate the exact number & % Line 28: “a number continued to wait…” indicate the exact number & % Parents feeling they needed to push for investigations: line 20: “many parents…” indicate the exact number & % - Challenges for GPs diagnosing T1D in children: lines 35 & 36 “The GPs felt the main challenges to diagnosing T1D in children where the rarity of the condition and the difficulty obtaining urine samples or blood glucose measurements from children…”. As previously mentioned, T1D is no longer a rare disease. Moreover, I think it`s not a challenge obtaining urine samples or blood glucose measurements from children (except in infants). - Page 10, line 7: “in several cases…” indicate the exact number & % - Page 10, line 21: “in some cases…” indicate the exact number & % Discussion: - Page 11, line 29: mention the mean duration of symptoms prior to

	diagnosis (to be mentioned also in results). Figures & tables: - Table 4: Indicate number & % of each feature - Table 6: Indicate number & % of each reason

VERSION 1 – AUTHOR RESPONSE

Reviewer Name Jordan Pinsker, MD
Institution and Country Tripler Army Medical Center, USA

A very nice paper by Usher-Smith, et al. discussing the time to diagnosis of type 1 diabetes and the barriers to making the diagnosis sooner. The structured interviews offered a standardized approach to recalling events leading to diagnosis. Two very interesting findings are the need to stress to GP's the importance of simply performing a UA for diagnosis of diabetes, and that most parents learn of this disease on the internet, where a site devoted to parents on how to make the diagnosis sooner would be most helpful.

Minor issues:

1) Recruitment: It says children age 1-16 years of age, then 6-16 years of age. Why is there an overlap? Was different recruitment done at different centers? Please explain.

The reason for the separate statements about recruitment is that only children over 6 were eligible for inclusion in the study whilst the parents of children over 1 were eligible. Recruitment was the same at all centres. We have modified the sentence below in the methods section to clarify this:

> *"**Parents of all children aged 1 month to 16 years diagnosed with new onset T1D at the two participating hospitals were eligible for inclusion unless their clinical team felt that they were not suitable on clinical grounds. Children aged 6 years to 16 years were also eligible for inclusion in the study themselves.**"*

2) Recruitment: Please explain in detail what is meant by families that were not suitable on clinical grounds? Often it is families undergoing social stress (eg, divorce) where the diagnosis is delayed.

The study protocol included the option for the clinical team to choose not to invite those in whom they felt invitation would adversely affect the care the child received, either through a breakdown in relationships between the family and clinical team or due to specific clinical circumstances. Social reasons, such as divorce, would not have been considered clinical grounds. In the study only one family was not invited on clinical grounds and that was because the parents were refusing to accept the diagnosis of diabetes and subsequent treatment. Relationships were, therefore, already strained between the family and the clinical team and it was felt that the child's care might suffer if additional pressure was placed on the family.

To clarify this in the text, details of possible reasons for exclusion on clinical grounds have been added as below to the methods section:

> *"Parents of all children aged 1 month to 16 years diagnosed with new onset T1D at the two participating hospitals were eligible for inclusion unless their clinical team felt that they were not suitable on clinical grounds **(when the invitation would adversely affect the care the child received, either through a breakdown in relationships between the family and clinical team or due to specific clinical circumstances).** Children aged 6 years to 16 years were also eligible for inclusion in the study themselves."*

A sentence to clarify how many families this affected has also been added to the first paragraph of the results section which now reads:

> *"43 children were diagnosed with T1D in the 2 hospitals during the study period (1st January 2012 – 28th February 2013). Of those: 32 were invited to take part in the study; one family was not invited as they did not speak English; **one family was not invited on clinical***

grounds as the parents were not accepting the diagnosis of diabetes and so relationships were already strained between the family and the clinical team*; and the other nine were missed during follow up. 20 responded to the initial invitation and 16 agreed to take part."*

By excluding certain families, the data may be biased towards earlier diagnosis. Was this the reason only 32 of the 43 families were invited to participate? According to table 1, the DKA at presentation rate was much higher in the not included group.

Hopefully the results paragraph as above clarifies the reasons 11 families were not invited to take part. Whilst we cannot exclude bias towards earlier (or later) diagnosis, the selection of families was independent of the research team and, of particular note, four families in which the children had DKA were invited but chose not to take part. Furthermore, as a qualitative study, the aim of this study was to provide insights into the pathway to diagnosis from a range of perspectives. The aim was not to interview all families but to interview families from a range of backgrounds with a range of experiences leading up to the diagnosis. This was achieved by interviewing until data saturation, the point at which no new findings emerged from the data, was reached for the parental interviews. The fact that data saturation was reached suggests that inclusion of additional families would not have changed the overall study findings.

To provide further information about the families that did not take part, however, we have modified Table 1 to distinguish between those that were invited but chose not to take part and those that were not invited. We have not added statistical comparisons as we do not feel this is appropriate for qualitative work where the aim, as described above, is to sample a range of participants and details are often not collected on those that do not take part.

	Included in study (n = 16)	**Invited but did not take part (n = 16)**	**Eligible but not invited (n = 11)**
Age			
Less than 6 years	6	2	3
6-8 years	4	3	3
9-11 years	3	3	3
12-16 years	3	8	2
Mean ± s.d.	7.3 ± 4.1	10.1 ± 3.5	8.5 ± 4.1
Median (range)	6.5 (2 – 15)	11 (4 – 14)	(3 – 16)
Gender			
Male	9 (56%)	8 (50%)	4 (36%)
Female	7 (44%)	8 (50%)	7 (64%)
DKA			
Yes	2 (13%)	4 (25%)	3 (27%)
No	14 (87%)	12 (75%)	8 (73%)

Table 1. Characteristics of children included in the study compared with **those who were invited but did not take part and those who were eligible but not invited.**

The text in the relevant section of the results section has also been altered to read:

> *"The characteristics of those 16 children included in the study compared with the **children who were invited but did not take part and those who were eligible but not invited** are shown in Table 1. Included children were younger and less likely to have had DKA at diagnosis."*

Major Issues:

1) Strengths and weaknesses: Of the 43 children diagnosed, only 32 were invited and only 16 participated. As noted above, the characteristics were not the same, in that the DKA rate was much higher. In addition, no mention is made of any particular family stress or socioeconomic status, which may play a role in time to diagnosis .The only results reported for socioeconomic status are in the results section, I believe this is for the 16 families that participated. Please include both groups. Although it is a very small sample size, can a statistical comparison be done between the two groups? None is offered in the table. There is also no discussion of this is the strengths and weaknesses table.

Unfortunately it was not possible to obtain socioeconomic data for the families that did not consent to participate as the data on socioeconomic status was collected at the time of interview. It is, therefore, not possible to include details of socioeconomic status for this group in the results section.

We agree that family stress or other social issues may play a role in time to diagnosis. In these interviews, however, there was no mention of particular family stress or other social issues that appeared to influence the diagnostic pathway. To acknowledge this important negative finding we have added a sentence to the "Help-seeking" section of the results as below:

> *"Reasons for waiting before seeking help included concern about going with non-specific symptoms and wasting the GP's time, waiting to 'see how it goes', fear of the diagnosis and unawareness of the importance of a timely diagnosis (Table 6). **There was no evidence that particular family events or social issues influenced this process."***

To address your final point relating to the absence of mention of these issues in the strengths and weaknesses table, we have added an additional sentence so that it now reads:

> ***"STRENGTHS AND LIMITATIONS OF THIS STUDY***
>
> - *This study is the first exploration of the pathway to diagnosis and presentation of T1D in children in primary care and provides a novel perspective of areas in this pathway where future interventions may be targeted.*
> - *The inclusion of children and GPs as well as parents provided additional perspectives and triangulation of the findings.*
> - *The use of semi-structured interviews allowed in-depth exploration of the experiences of the participants **but the sample size was small with only 16 out of 43 eligible families taking part** and the accounts are necessarily retrospective and subject to recall and framing bias."*

Reviewer Name **Kathleen Bethin, MD, PhD**
Institution and Country **University at Buffalo**
USA

The Objective of this work is to explore the pathway to diagnosis of type 1 diabetes (T1D) in children from the perspective of the child, family and general practitioner (GP). The authors have a very well thought-out and written manuscript on the barriers that parents create or face in diagnosing their children with diabetes. However, the authors fail to give us any information from the children's point of view and only interview 5 general practitioners.

Thank you for your positive comments on our manuscript. We acknowledge your comments about the relative lack of information from the children's point of view and the small number of GPs and address those issues in more detail below.

Need to define what criteria made the families not suitable for inclusion.

We have added the following sentences to both the methods and results section to clarify this:

"Parents of all children aged 1 month to 16 years diagnosed with new onset T1D at the two participating hospitals were eligible for inclusion unless their clinical team felt that they were not suitable on clinical grounds ***(when the invitation would adversely affect the care the child received, either through a breakdown in relationships between the family and clinical team or due to specific clinical circumstances).*** *Children aged 6 years to 16 years were also eligible for inclusion in the study themselves."*

"43 children were diagnosed with T1D in the 2 hospitals during the study period (1st January 2012 – 28th February 2013). Of those: 32 were invited to take part in the study; one family was not invited as they did not speak English; ***one family was not invited on clinical grounds as the parents were not accepting the diagnosis of diabetes and so relationships were already strained between the family and the clinical team****; and the other nine were missed during follow up. 20 responded to the initial invitation and 16 agreed to take part."*

More information about the questions asked during interview needs to be included in the methods section. Reference 19- http://www.youthhealthtalk.org/Diabetes_type_1_in_young_people/Topic/1510 - does not contain any information that is helpful to understand the interview techniques used or anything related to this manuscript.

We have included both the parent and child and GP interview schedules as Appendices to provide complete transparency about the questions asked during the interviews. We have retained the reference to Youth Health Talk as this helped us inform the interview schedules prior to the start of the study.

Graphics for Figure 1 is poor and would need to be improved for publication.

We thank the reviewer for highlighting this and will improve the quality for publication.

It would be more useful to have a table that demonstrated data rather than 4 tables of quotes from families. e.g., a table that supports the statements- "In most cases both parents appeared to be in agreement throughout the appraisal process. In the cases where there was conflict, it was consistently the mothers who were more concerned than the fathers."

For qualitative studies, the data is indeed quotes from participants, and it is standard practice to include these in papers using these methods. Thank you for drawing to our attention the fact that we have not included any quotes to directly support this statement though. On careful review of the results section we have identified one additional statement which was not previously illustrated with quotes and so have added quotes to the text for both of these as below:

"In most cases both parents appeared to be in agreement throughout the appraisal process. In the cases where there was conflict, it was consistently the mothers who were more concerned than the fathers.

> ***'My husband thought I was being silly, you know, we've got no history in our family, nothing so there wasn't any reason to suspect really and to look at her you would never think, she was fine in herself, the only thing was she was drinking more and going to the toilet.' M1***

> ***'It was round about that time his mother was seeing [him losing weight], and we was not arguing but I'm saying no, he's fit enough' F9***

"In most cases where the views of others were in conflict with the mothers' own views, the mothers' ultimately allowed their own concerns to override the comments of others and chose to seek help.

> ***'I remember another friend at the school gate was just, sort of, saying, "Oh, my daughter was thirsty a lot and I didn't really think that much of it and I'm sure it'll be nothing," sort of thing. But I was, like, "Well, I'm just going to get him checked out anyway."' M6***

> ***'So I was still saying to family about me worries and they were still saying puberty and friends, oh it's puberty, you're worrying yourself and, you know, don't worry about it, I wouldn't worry' M15***

We feel the other four tables are useful in their current format as they provide illustrative quotes to support existing statements within the text.

The authors also state in the discussion that "there was evidence that mothers in particular made use of a social network throughout this process and almost all parents also sought information from the internet." There should be a table that demonstrates which of the families used social networking resources and which used the internet in their appraisal phase.

By the phrase 'social network' in the section on "Influence of other family members and social network" in the results section we mean extended family, friends and work colleagues who parents spoke to during the appraisal interval. To clarify this and give more details we have changed the subtitle of the section and re-phrased the paragraph to read:

> ***"Influence of other family members, friends and work colleagues***
>
> *In most cases both parents appeared to be in agreement throughout the appraisal process. In the cases where there was conflict, it was consistently the mothers who were more concerned than the fathers. Apart from their husband or partner,* ***most mothers*** *discussed their concerns with their mother, friends* ***or work colleagues*** *before making an appointment to see a health care professional."*

The statement in the discussion has also been altered to read:

*"As previously described, there was evidence that mothers **~~in particular~~** made use of a social network **of extended family, friends and work colleagues** throughout this process and almost all parents also sought information from the internet."*

In relation to those parents who used the internet in their appraisal process, we have included a column in Table 2 to show which families used the internet and reference to this in the results section as below:

*"Most parents looked on the internet for explanations for the symptoms **(see Table 2)** and this either raised or confirmed concerns about diabetes."*

The authors state "Instead, the message to primary care physicians and nurses and health visitors providing first line care from this study is to have a low threshold for performing a dipstick test on urine of children who are non-specifically unwell." However, their data in Table 2 shows that every child that participated in this study had polyuria, polydipsia, nocturia, weight loss or a combination – all classic symptoms of diabetes. These data support checking a urine dipstick if any of those specific symptoms are present not testing a child who is non-specifically well.

We agree that our statement "Instead, the message to primary care physicians and nurses and health visitors providing first line care from this study is to have a low threshold for performing a dipstick test on urine of children who are non-specifically unwell." is not directly supported by the results of our study. We have, therefore, amended both that statement in the discussion section and the final sentence of the abstract to read:

*"Even when neither the parents nor GPs had thought specifically of T1D, however, the diagnostic interval was short and most diagnoses were made promptly as a result of urine tests requested as part of the assessment of a non-specifically unwell child. It is not clear, therefore, whether T1D specific educational interventions aimed at primary care physicians **in particular** would necessarily have much impact on the pathway to diagnosis. Instead, the message to primary care physicians and nurses and health visitors providing first line care from this study is to **consider T1D in non-specifically unwell children and perform a dipstick test on urine during the consultation for all children with polyuria, polydipsia, nocturia or weight loss**."*

*"Primary care physicians should also take parental concerns seriously and do urine dipstick tests **during the consultation for children with symptoms of T1D**."*

Overall, this is a very interesting manuscript. However, as written it does not support the objective. It is almost entirely about the parents and not the children or the GPs.

We completely agree that the manuscript largely focuses on the parents rather than the children or GPs. We were surprised ourselves by how little the children contributed to the interviews, and indeed the diagnostic pathway and were disappointed to only be able to interview five GPs. We strongly disagree with the reviewer in dismissing the importance of parents, indeed for children it is their parents who are the most important in interpreting changes in their child, contacting health services, and providing care. Therefore, understanding the role of parents and the parent-doctor relationship in accessing care for their children is fundamental for these types of diseases. We have made several changes to the text to reflect this:

1) *We have removed the words "from the perspective of the child, family and general practitioner" from the title so that it now reads and no longer claims to give equal weight to the perspectives of the three groups:*

'Looking for the needle in the haystack': a qualitative study of the pathway to diagnosis of type 1 diabetes in children

2) *We have also added several new sections of text within the Appraisal interval section of the manuscript describing the views of the children. These include:*

Difficulty recognising the symptoms was also evident in the children's accounts with several not noticing them until either their parents mentioned them or after the diagnosis.

> ***'I didn't think it was anything different 'til my mum said some stuff I started thinking' C16***

> ***'I didn't really realise it because I just felt probably tired for a long time. I just felt like, after the first time I had my insulin I felt more awake than I did before' C15***

In general, children were less concerned with finding explanations for their symptoms and more likely to just accept them.

> ***'I just felt hungry, I didn't know why, I just needed more food.' C16***

There was evidence, however, that some children found alternative explanations themselves.

> ***'I was just thinking that I was doing a lot of exercise and I was just getting thirsty' C13***

Whether the symptoms interfered with daily life was also a key factor in how the children responded to their symptoms. Symptoms such as increased appetite and thirst did not generally interfere with their lives and did not cause concern. Instead they thought it was 'great because I could eat more' or 'quite funny'. By contrast, urinary symptoms and lethargy did appear to impact on their lives and as a result led to concern.

> ***'So I woke up but it was just I didn't have time to sort of go, it didn't let me stop…that's why I got worried because it was just like normally just can wait a minute and get there, but it was just I couldn't wait' C13***

> ***'Well I was a bit tired and after three days I like didn't really want to eat anything and I was only in bed, I would do nothing, just bed…It wasn't good.' C4***

Notably, none of the children, even those who were worried about their symptoms, mentioned anything to their parents before they were diagnosed

with one child even admitting that he had been worried but kept saying there was nothing wrong each time his parents mentioned taking him to the doctor.

Reviewer Name Rasha Tarif Hamza
Institution and Country Ain Shams University, Cairo, Egypt

Authors tried to explore the pathway to diagnose type 1diabetes in children from perspective of child, family and general practitioner which is an important topic since the prevalence of type 1 diabetes is greatly increasing.

Abstract: lines 20 & 21
"They felt the main challenges to diagnosing T1D in children were the rarity of the condition…"

T1D is not rare nowadays !! (as mentioned by authors in introduction section).

We accept that the incidence of T1D is increasing but, even in Finland which has the highest incidence worldwide, it is still only 64.2 per 100,000 per year (Harjutsalo et al. 2008 Time trends in the incidence of type 1 diabetes in Finnish children: a cohort study. Lancet 371(9626):1777-82). An average UK Primary Care practice with 6,487 registered patients (The Kings Fund. General practice in England: An overview 2009) will have approximately 1230 children under 16 registered at any one time (http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2011-and-mid-2012/sty---uk-population-estimates.html - accessed 17 Oct 2013). Even with an incidence of 64.2 per 100,000 per year, the practice will, therefore, only see a child with new onset T1D once every 15 months and, as we already mention in the discussion, the average GP in the UK will, therefore, make a diagnosis of T1D only once or twice in a career (Ali et al 2011 Type 1 diabetes in children BMJ 342:d294). To put this into context, adult type 2 diabetes is almost thirty times more common with an incidence of 4.31 per 1,000 per year (Masso Gonzalez et al 2009. Trends in the prevalence and incidence of diabetes in the UK: 1996-2005) J Epidemiol Community Health 63:332-336) so the same practice will see an adult with new onset type 2 diabetes every 16 days. We therefore feel it is appropriate to refer to T1D in children as a rare condition in primary care.

To clarify that we are referring to T1D in Primary care, we have amended the first paragraph of the introduction to read:

"Type 1 diabetes (T1D) is one of the commonest endocrine diseases in children, with an estimated 65,000 children world-wide under 15 years developing the disease each year and the global incidence in children continuing to increase at a rate of 3% per year(DIAMOND Project Group, 2006; EURODIAB ACE Study, 2000). ***Despite this, the condition remains rare in primary care: In a large UK General Practice a child with new onset T1D will be seen only about once every two years (Ali et al 2011).*** *Differentiating the rare child with T1D from the large number with minor undifferentiated illness is, therefore, challenging for both families and primary care physicians."*

Strengths and limitations of this study: line 32
Authors mentioned only the strengths but a major limitation is the small number of participants (parents, children & GPs) especially that authors are trying to explore the etiology of a disease using a simple interview, thus, it was better to include a larger number of participants. Moreover, the prevalence of type 1 diabetes is not uncommon nowadays.

We would like to clarify that the aim of this study was not to explore the aetiology of a disease. The aim was to explore the experiences of the parents, children and GPs throughout the diagnostic process, and perhaps the reviewer is less familiar with this methodology. The sampling methods used in qualitative research such as this are, therefore, very different to those of quantitative studies. Whilst quantitative research aims to test pre-determined hypotheses and produce generalizable results and needs sufficient participants to perform statistical tests, qualitative studies aim to describe and provide understanding of

complex psychosocial issues. We direct you towards an article by Marshall (Marshall 1996. Sampling for qualitative research. Family Practice Vol 13, No 6. 522-525) which describes some of the differences in more detail. Briefly, the appropriate sample size for a qualitative study is, therefore, one that adequately answers the question and is usually not pre-determined. Sampling stops when a thorough understanding of the question under study has been reached, an end point often termed saturation. Saturation is reached when interviews with new participants no longer bring up trends or themes not already raised by previous participants. In this study we continued to sample parents until saturation was reached and, in this case, that number was 16.

To acknowledge the small number of participants further in the text, however, we have amended the final bullet point in the strengths and limitations box and the strengths and limitations section of the discussion to read:

> *"The use of semi-structured interviews allowed in-depth exploration of the experiences of the participants* ***but the sample size was small with only 16 out of 43 eligible families taking part*** *and the accounts are necessarily retrospective and subject to recall and framing bias."*
>
> *"We believe this is the first study to examine the pathway to diagnosis of T1D in children, and provides a novel perspective of the areas in this pathway where future interventions may be targeted. We used semi-structured interviews soon after diagnosis to allow participants to speak freely about the period leading up to the diagnosis, and also framed our analysis using a theoretical model.* ***The sample size was small but*** *data saturation for the parents was reached before the total sample had been interviewed and together with the similarity among key characteristics between children included and not included in the study, suggests that our findings are robust and representative of children diagnosed with T1D in this region.*

Methods:

- The details of included participants should be better included in "methods" section, not just describing them in "results".

As suggested by the reviewer we have added a section entitled "Participants" which provides details of the included participants in the methods section and accordingly edited the results sections. The methods section now reads:

> *"**Participants***
> ***43 children were diagnosed with T1D in the 2 hospitals during the study period (1st January 2012 – 28th February 2013). Of those, 32 were invited to take part in the study; one family was not invited as they did not speak English and the others were missed during follow up. 20 of those responded to the initial invitation and 16 agreed to take part. Of the 16 children included in the study, 12 saw a GP at their registered surgery prior to diagnosis. One saw a nurse and three contacted the Out Of Hours service and were directed from there to hospital. One family was interviewed three months after diagnosis so it was not possible to also invite and interview the GP within three months of diagnosis. Of the remaining 11 GPs who were invited to take part, five agreed to be interviewed.***

And the results section:

> ***~~"43 children were diagnosed with T1D in the 2 hospitals during the study period (1st January 2012 – 28th February 2013). Of those, 32 were invited to take part in~~***

~~***the study; one family was not invited as they did not speak English and the others were missed during follow up. 20 of those responded to the initial invitation and 16 agreed to take part.***~~ *The characteristics of* ***the*** *16 children included in the study compared with the 27 who were eligible but did not take part are shown in Table 1. Included children were younger and less likely to have had DKA at diagnosis.*

~~***Of the 16 children included in the study, 12 saw a GP at their registered surgery prior to diagnosis. One saw a nurse and three contacted the Out Of Hours service and were directed from there to hospital. One family was interviewed three months after diagnosis so it was not possible to also invite and interview the GP within three months of diagnosis. Of the remaining 11 GPs who were invited to take part, five agreed to be interviewed.***~~*"*

- Describe clearly inclusion & exclusion criteria of selected subjects

To clarify the inclusion and exclusion criteria we have amended the paragraph on recruitment in the methods section so that it now reads:

> *"Parents of all children aged 1 month to 16 years diagnosed with new onset T1D at the two participating hospitals were eligible for inclusion unless their clinical team felt that they were not suitable on clinical grounds* ***(when the invitation would adversely affect the care the child received, either through a breakdown in relationships between the family and clinical team or due to specific clinical circumstances).*** *Children aged 6 years to 16 years were also eligible for inclusion in the study themselves."*

Results:
In general, results need more accurate specification in the form of numbers & frequencies, not just descriptions using general phrases e.g. most of parents…etc..

> *Our paper is a qualitative study exploring the pathway to diagnosis of T1D in children. By it's very nature, qualitative research involves 'the collection, analysis and interpretation of data that are not easily reduced to numbers' (Murphy et al 1998. Qualitative research methods in health technology assessment: a review of the literature. Health Technology Assessment Vol 2 No 16). In contrast to quantitative research, which sets out to test hypotheses using predetermined methods to measure a quantity and then analyse the results using statistics to explain those measurements and generate conclusions that are generalizable, qualitative research approaches are interested in understanding the social world and the concepts and behaviours within it. Rather than seeking to measure and explain observations and provide generalizable results, we see qualitative research approaches as exploratory or explanatory, seeking to address questions of 'How?' or 'Why?'. Qualitative research studies are also not seeking to be generalizable but instead to provide adequate information for the reader to assess the transferability of the results to their population of interest. Our interpretation and presentation of the results, therefore, aims to provide a description of the main findings with as much importance placed on the unusual experiences as the usual. We are not trying to 'count' experiences but instead describe the range of experiences and common themes. We, like most other qualitative researchers, therefore, feel that it is not meaningful to include exact numbers and frequencies of findings and, instead, describe our findings using descriptive terms such as 'most' or 'many'.*

- Line 38: better use a socioeconomic standard leveling (referenced) to clearly classify social class of studied subjects.

> *As we describe in the manuscript, we collected data on income and education level. We are not aware of any standard socioeconomic levels that combine these three variables without additional information, for example on current employment. We, therefore, feel that it is best*

not to try and combine these measures. Instead, we have added additional columns to Table 2 to include the educational level and income bracket of studied subjects to allow the reader to more clearly assess the individual socio-demographic backgrounds.

- Line 26: describe the frequency of each alternative symptom among studied subjects.

We have already included details of the presence or absence of each symptom for each child in Table 2. The reader is therefore able to see which were the most common symptoms and the frequency of each symptom. For the reasons discussed above, we do not feel that calculating the frequency and presenting that in numerical format in the text is appropriate but we have made reference to the table at the appropriate point in the text so that the reader is referred to that for more detail:

> *"All experienced at least one of the key symptoms of diabetes (polydipsia, polyuria, lethargy or weight loss) and most were diagnosed at their first consultation with a healthcare professional* ***(Table 2)****.*

- Line 33: specify symptoms that concerned the parents & those that did not & describe their frequencies.

As we describe in the text and in Table 4, symptoms that concerned parents were those that were different or unusual for their child, those with physical signs such as weight loss and vomiting that could not easily be attributed to behaviour and those that started to interfere with daily life. By comparison, symptoms that were intermittent, not unusual for the child or not making the child 'unwell' did not cause concern to parents. The same symptom, for example increased thirst, could therefore be both a non-concerning symptom when it was intermittent and one that caused concern when it started to interfere with daily life. It is not, therefore, possible to provide a list of symptoms that concerned the parents and those that did not or to describe their frequencies.

- Lines 38-44: better described based on socioeconomic standard leveling (as previously mentioned).

Please see our response above.

- Subtlety of symptoms: line 14: "many parents.." indicate the exact number & %
- Influence of other family members and social network: line 42: "in most cases…" indicate the exact number & %

Line 53: "In most cases where…" indicate the exact number & %

- Sources of information: line 4: "most parents…" indicate the exact number & %
- The help seeking interval: line 21: "most children" indicate the exact number & %

Line 28: "a number continued to wait…" indicate the exact number & %

Parents feeling they needed to push for investigations: line 20: "many parents…" indicate the exact number & %

As described above, due to the nature of the research, we do not feel it appropriate or helpful to add the exact number and percentages of parents in the examples you list above. We have, therefore, not amended the text.

- Challenges for GPs diagnosing T1D in children: lines 35 & 36

"The GPs felt the main challenges to diagnosing T1D in children where the rarity of the condition and the difficulty obtaining urine samples or blood glucose measurements from children…".

As previously mentioned, T1D is no longer a rare disease. Moreover, I think it`s not a challenge obtaining urine samples or blood glucose measurements from children (except in infants).

As we described above, although the incidence of T1D is increasing, the incidence is still such that the average GP will make the diagnosis only once or twice in a career. It, therefore, does not surprise us that the GPs interviewed considered the diagnosis rare and felt this was one of the main challenges to the diagnosis.

We acknowledge that you do not feel it is a challenge obtaining urine samples or blood glucose measurements from children but the GPs interviewed in this study did feel it was a challenge and, as the aim of this paper was to report the results of our interview study, we stand by our original statement in the text which is supported by quotes from the interviews themselves.

- Page 10, line 7: "in several cases…" indicate the exact number & %
- Page 10, line 21: "in some cases…" indicate the exact number & %

Please see our comments above regarding the use of exact numbers and percentages in qualitative research such as this.

Discussion:
- Page 11, line 29: mention the mean duration of symptoms prior to diagnosis (to be mentioned also in results).

Although we feel the range is more appropriate for qualitative research, as requested, we have added the mean duration of symptoms to the text in the discussion and results sections. They now read:

> *"The total duration of symptoms prior to diagnosis ranged from 6 to 127 days* ***(mean 44 ± 37 days)*** *with over half having symptoms for more than a month before diagnosis."*
>
> *"The interval from onset of symptoms to diagnosis ranged from 6-127 days* ***(mean 44 ± 37 days)*** *with the appraisal interval the longest in almost all cases."*

Figures & tables:
- Table 4: Indicate number & % of each feature
- Table 6: Indicate number & % of each reason

Please see our comments above regarding the use of exact numbers and percentages in qualitative research such as this.

VERSION 2 – REVIEW

REVIEWER	Jordan Pinsker, MD Tripler Army Medical Center, USA
REVIEW RETURNED	02-Nov-2013

- The reviewer completed the checklist but made no further comments.

REVIEWER	Kathleen Bethin University at Buffalo, USA
REVIEW RETURNED	03-Nov-2013

GENERAL COMMENTS	Strengths of this manuscript are that this is study does appear to be the first study to explore the pathway to diagnosis and presentation of T1D in children in primary care and provides a novel perspective of areas in this pathway where future interventions may be targeted. It also attempted to include the viewpoint of children, GPs and the parents. However, this is also a weakness of the manuscript—see below. Again, this is a very well written manuscript. The authors

	have done a very complete job addressing the reviewer comments. Weaknesses of this manuscript is that it is a small study. As stated above, the authors attempted to get the viewpoint of the children, GPs and parents. However, they have very little data from the children and the viewpoint of only 5 GPs. These limitations have been acknowledged by the authors.