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Parents' and clinicians' views on conducting paediatric diagnostic test accuracy studies without prior informed consent. Qualitative insight from the Petechiae in Children study (PiC)

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Abstract

Objective The Petechiae in Children (PiC) study assesses the utility of presenting features and rapid diagnostic tests in the diagnosis of serious bacterial infection in feverish children with non-blanching rashes. An embedded qualitative study explored parents' and clinicians' views on the acceptability of the PiC study, including the use of research without prior consent (RWPC) in studies of diagnostic test accuracy.

Design Semi-structured qualitative interviews. Analysis was thematic and broadly interpretive, informed by the constant comparative approach.

Participants Fifteen parents were interviewed 55 (median) days since their child's hospital attendance (range 13 to 95). Five clinicians involved in recruitment and consent were interviewed.

Results Parents and clinicians supported RWPC for the PiC study and future emergency paediatric diagnostic test accuracy studies, as long as there is no harm to the child and emergency care is not delayed. Parents and clinicians made recommendations around the timing and conduct of a consent discussion, which were in line with RWPC guidance. Parents enrolled in the PiC study preferred a design which included consent discussions with the research team over the alternative of "opt-out" consent only.

Conclusions This embedded qualitative study demonstrates that RWPC is appropriate for use in paediatric emergency studies of diagnostic test accuracy and that the approach utilised in PiC was appropriate. Future diagnostic studies involving additional invasive procedures or an opt-out only approach to consent would benefit from exploring parent and clinician views on acceptability at the pre-trial stage.

Trial registration number ClinicalTrials.gov Identifier: NCT03378258

Introduction

Early recognition of serious bacterial infections (SBI) in childhood improves outcomes [1–6], though clinical features are often indistinguishable from self-limiting viral illnesses during the prodromal phase [1, 2, 4]. Many children are therefore given precautionary broad-spectrum antibiotics; while safe in the acute phase, this is linked to emergence of antimicrobial-resistance [7–10]. Clinical decision makers often face dilemmas in balancing the need for prompt treatment against antimicrobial stewardship, and in determining which children can be safely discharged, though anxiety related to these issues may be reduced where reliable test results are available.

An ideal test should give quick and accurate results which provide a diagnosis and/or aid clinical decision making. It is now possible to perform rapid-diagnostic tests in the emergency setting, with results available within minutes. These have shown promise when tested under laboratory conditions or using retrospective case-control methodology [11]. However to understand their true diagnostic accuracy and potential patient benefit they must be studied prospectively [11].

Studies investigating the diagnostic test accuracy (DTA) of rapid tests for SBI require research without prior consent (RWPC, also known as deferred consent) as the diagnosis and treatment of potentially life-threatening infections is time critical [12, 13], and by definition such studies are focused on obtaining very rapid test results. RWPC has successfully been used in paediatric emergency interventional studies, but there is a lack of knowledge about parent and clinician perspectives on the acceptability of RWPC in DTA studies[14–20]. Table 1 compares different models of consent including RWPC, prospective informed consent and opt-out consent.

The Petechiae in Children (PiC) study (summarised in Box 1) was designed in collaboration with Paediatric Emergency Research in the UK and Ireland (PERUKI), and the study protocol

has been published [21, 22]. It is the largest study evaluating the assessment and management of feverish children with non-blanching rashes and is the first UK study performed since the introduction of the Meningococcal B and C vaccinations onto the UK vaccination schedule. It aims to provide more robust evidence for those making decisions in the clinical care of these patients and includes evaluation of presenting features and point of care biomarkers. The PiC study opened to recruitment in November 2017, and enrolment is due to finish in June 2019. The objectives of the PiC study are to report on the diagnostic test accuracy of point-of-care testing for procalcitonin (PCT) and *Neisseria meningitidis* DNA, to validate existing clinical practice guidelines and the describe the aetiology of fever and non-blanching rash including the risk of serious bacterial infection such as meningococcal disease.

In this embedded qualitative study, we aimed to explore parents' and clinicians' views on the acceptability of the PiC study, including use of RWPC in DTA studies in emergency situations.

Methods

Study Design

The PiC study design (Box 1) utilises RWPC in accordance with clinical trials legislation and RWPC guidance[22–24]. The PiC study pilot took place at the Royal Belfast Hospital for Sick Children (RBHSC), a tertiary level children's hospital in the United Kingdom.

Children were enrolled into the PiC study by the treating emergency clinician, and informed consent (Summarised in Box 1) sought after the clinical condition was stable. Written consent for the use of data was sought from participants either in the emergency department (ED), on the ward, or after discharge, depending on the timing of the presentation, clinical course, and timing of discharge [21]. Participants who were approached after discharge received an initial telephone call outlining the study and then a follow up postal consent.

Recruitment and sampling procedure for embedded qualitative study

Consent for participation in an embedded qualitative study was sought in writing as part of the PiC consent process and then verbally re-confirmed at interview. To ensure sample variance in this embedded qualitative study, we invited parents to interview who had been approached for consent at the three possible time points.

We used previous research [14–20] to develop interview topic guides (supplementary file 1), which contained open-ended questions and prompts to explore views and experiences of the PiC study, including use of a RWPC approach. TW (Male Paediatrician) received qualitative research training from KW (Female Social scientist). TW conducted semi-structured telephone interviews with parents of recruited children, as well as face to face interviews with PiC clinicians at the RBHSC. All clinicians involved in PiC recruitment or consent conversations at the RBHSC were invited for interview. Interviews were digitally audio recorded and transcribed verbatim by a professional audio typist. Transcripts were anonymised and checked for accuracy by TW. Interviews were conducted until data saturation (where no new major themes are identified in the analysis of data) [26, 27]. There were no repeat interviews or additional field notes recorded.

Analysis

TW led the analysis with assistance from KW. Analysis was thematic and broadly interpretive, informed by the constant comparative approach [28–33] (supplementary file 2). We used NVivo Version 12 software to assist with the organisation and coding of data.

Study Registration

Registered at <https://www.clinicaltrials.gov> (trial registration: NCT03378258) on the 19/12/2017.

Ethical Approval

The Northern Ireland Research Ethics Committee (REC) and the Belfast Trust IRB approved the PiC protocol, including the embedded qualitative research (REC Reference - 17/NI/0169)(IRB Reference 16201MS-SW).

Results

Between the 11th November 2017 and 31st July 2018, 147 of 150 eligible patients were enrolled in the PiC study at the RBHSC. One participant declined participation; two were not approached as an interpreter was not available. 131 patients (89%) agreed to telephone interview. The one parent that declined to participate in the PiC study also declined interview.

Data saturation was reached at 15 interviews (where no new major themes are identified in the analysis of data). Parent and patient characteristics are presented in Table 2. No participants knew TW prior to the interview. All invited clinicians (n=8) agreed to participate in a face-to-face interview, of whom six (75%) had previous experience with clinical research (Table 3). Data saturation was achieved at five interviews (one research nurse, one junior doctor, three senior doctors). Interviews lasted between 22 and 44 minutes (supplementary file 3 contains selected quotations by theme).

Opinions on RWPC in PiC and future DTA studies

A definition of RWPC was read to participants (Box 2) who were then asked, "What do you think about the use of research without prior consent in an emergency situation?" All parents supported RWPC in PiC and future DTA studies, highlighting the need to avoid treatment delays *"I think the doctor should do what they can do as quick as they can"* (P2 Mother). Parents valued the speed of diagnostic tests which could be conducted alongside emergency clinical care: *"It was instant really that the results came back...I just thought that was a great thing"* (P5 Mother). However, three parents indicated that prior consent would be required for any research that involved additional interventions that would cause

pain or discomfort, such as an additional “pinprick” (P9 Mother) for blood samples:

“I think these tests can be done just as part of a blood sample anyway, I think I would say no, it’s fine the way it’s (RWPC) done” (P14 Mother)

Clinicians supported RWPC in PiC and future DTA studies, stating tests were quick, “*relatively easy*” (C3 Junior Doctor) to conduct, did not cause harm “*I know you’re not doing any extra harm physically*” (C2 Senior Doctor), or involve “*any more invasive tests that you already would be doing*” (C5 Senior Doctor). Clinicians described parents’ positive responses to consent discussions and cited “*all parents wanted to be on the study*” (C1 Research Nurse) as an indicator of study and RWPC acceptability.

Timing of consent discussions

Analysis of parent and clinician accounts of recruitment processes suggested that clinicians followed the study protocol and appropriately timed study discussions. Clinicians described how they would assess the ability of parents to discuss the study on the ward or in ED based on: the condition of the child: “*It would be a little bit of time after I had taken the samples and made sure that the child was well and stable*” (C4 Senior Doctor); discussions with clinical staff: “*I will go up and speak to the nurse or a member of the nursing staff and ask how the patient was doing and whether they felt it was appropriate and usually I got the nurse to introduce me*” (C3 Junior Doctor); and perceived readiness of parents to discuss consent: “*I would be very much led by the parent*” (C2 Senior Doctor).

The majority (14 of 15) of parents advised against seeking consent prior to testing. They described how during the initial emergency parents would not have the capacity to discuss research as the priority is their child: “*you’re just more concerned that your child is going to*

get better" (P2 Mother). Some also stated that broaching a study at this time point could be perceived as disrespectful:

"For me I would say that maybe a wee bit of respect should be given... I will be thinking you know I'm trying to sort out my child here to see what's wrong with them and I have somebody coming in to try and talk about a study." (P3 Mother).

Parental decision making and understanding of PiC

The decision to provide consent for PiC was often described as being quick *"it was just a there and then kind of decision"* (P11 Mother) and easy: *"I mean it was a complete no-brainer"* (P12 Father). This was often attributed to the nature of the study, which parents perceived would not *"cause him any harm"* (P1 Father). Other reasons for consenting included parental support for medical research and a desire to help other children in the future. Parents also described how participation could help their own child, by enabling quick access to test results:

"I felt that it was a good idea maybe you know to help other children" (P3 Mother)

"I'm all for research" (P15 Mother)

"it was going to be like beneficial for [child name] to have a test that would bring back results quicker" (P7 Mother)

"we would find out within a few hours if it was meningitis" (P8 Mother)

All parents interviewed (up to 3 months after discharge) remained happy with their consent decision *"I think it was the right decision"* (P10 Mother). During interviews parents were able to describe the study in detail and displayed good understanding. *"it was a test, a swab on the back of the throat and it's a way of getting results back sooner to look for infections"* (P15 Mother).

Child assent

Parents recommended including children in the consent process where appropriate, assuming they are old enough to understand the discussion. *“If they understand and they are old enough to comprehend, then I don't see a problem with them having an input as well because if they're old enough to make their own mind up then they should be given some say”* (P1 Father)

However, parents and clinicians described how the majority of enrolled children were too young to participate in consent discussions. *“No they have all been little age, we did have one who was 5, he was at school. I did speak with him about the study with his parents there. I did offer them the assent form to have a look at, but he was fine and didn't want to”* (C1 Nurse).

Opt-out consent

Clinicians stated that some families suggested consent discussions for this type of research were not required *“Parents are really positive and often ask me why we even need consent, they say it's fine to use the data”* (C2 Senior Doctor). To explore this further, we sought parents' views on an alternative approach, which would involve provision of a study information sheet and the option to opt-out of the PiC study (i.e. no full consent discussion with a member of the research team and the child's data included in the study unless parents opted-out and chose for the data to be removed).

All parents stated that they would choose not to opt out: *“I would have just stayed in the study”* (P15 Mother). However, they stated that full consent discussions with families is preferable as the research team *“can explain more”* (P15 Mother). An opt-out approach that didn't involve a full research discussion was viewed as impersonal: *“a wee bit cold perhaps”* (P10 Mother), and limited opportunities to discuss the study: *“I think if I had any concerns it would have been more difficult to ask them”* (P10 Mother). Parents enrolled in the PiC study preferred a design which included consent discussions with the research team over the alternative of “opt-out” consent only without any discussion: *“It wouldn't be appropriate for extra procedures done that weren't to the benefit of the child”* (P12 Father).

Discussion

This study provides insight into parents' and clinicians' views on the acceptability of RWPC in the PiC study and future DTA studies. Previously, parents' views on their child's involvement in a trial without their prior consent were unknown and clinicians were apprehensive about conducting RWPC [18,19]. Our findings are consistent with other successfully conducted clinical and qualitative studies that have demonstrated parent and clinician acceptability of RWPC in paediatric emergency medicine [12, 13, 17-19, 34–37]. Parents supported RWPC provided emergency care is not delayed and their child does not come to any harm [14, 17]. This finding was also supported by the high consent rate for use of data in the PiC study.

In line with RWPC guidance [38], clinicians assessed parents' ability to discuss the study in collaboration with clinical staff and timed their consent approach appropriately. As in other studies, motivations for providing consent were often altruistic, such as to help others in the future and support research [17, 34, 35].

Rapidity of test results and the nature of additional interventions may influence parents' views on the acceptability of RWPC in DTA studies. The PiC study and use of RWPC were acceptable to parents and clinicians as there were **no additional invasive procedures**. Similar concerns regarding additional phlebotomy events without prior consent were described by nurses and some parents involved in the CATheter infections in CHildren (CATCH) trial[18]. Future DTA studies involving invasive procedures or interventions in addition to usual clinical care would benefit from exploring parent and clinician views on trial acceptability and RWPC at the pre-trial stage.

Our findings in regard to opt-out consent for the PiC study were novel. Although some parents asked clinicians why consent was needed for the PiC study, when presented with a hypothetical alternative approach, parents favoured a full RWPC discussion with a member of the research team over provision of written materials and the opportunity to opt-out from

having their child's data included in the study. As consistently shown in previous studies exploring trial recruitment processes, parents valued conversations with clinicians above written information materials [14-20]. Parents stated they would not have opted out of the PiC study. However, only providing researcher contact details on written information sheet was viewed as impersonal and a potential barrier to voicing questions and concerns.

Strengths and limitations

Our findings fill an important gap in the existing literature by providing parent and clinician perspectives on RWPC for paediatric DTA studies. Our sample was limited as it involved parents and clinicians involved in the pilot phase. However, interviews were conducted until data saturation was reached and involved parents who experienced RWPC [32]. Interviews were conducted by TW who is the PiC study lead. TW was not known to parents or involved in their children's clinical care. However, TW was previously known to clinicians and his non-independent role may have impacted upon their willingness to voice concerns about the study during interviews. Due to the high consent rate and no bereavements in the PiC study, our sample is limited to the views of parents who consented to the PiC study and whose children recovered. Finally, as children involved in the PiC study were typically under five years of age their views are not represented in our findings.

Conclusion

This study demonstrates that RWPC is appropriate for use in paediatric emergency diagnostic test accuracy studies not involving additional invasive procedures. Parents were supportive of RWPC for diagnostic test accuracy provided emergency care is not delayed and their child does not come to any harm. Future diagnostic studies involving additional invasive procedures or an opt-out only approach to consent would benefit from exploring parent and clinician views on acceptability at the pre-trial stage.

- “What is already known on this topic”
 - Technological advances have resulted in a greater availability of rapid diagnostic testing for bacterial infection.
 - The assessment of these tests in different diagnostic pathways is challenging; especially in the emergency setting where prior informed consent cannot be sought.
 - No studies have explored the acceptability of RWPC for diagnostic test accuracy studies.

- “What this study adds”
 - Research without prior consent is appropriate for diagnostic accuracy studies as long as the test is being used in an emergency situation and does not delay or interfere with urgent care.
 - Consent discussions with a member of the research team are preferred to a written information only ‘opt-out’ approach.
 - Future diagnostic test accuracy studies involving invasive procedures or interventions in addition to usual clinical care would benefit from pre-trial feasibility work incorporating parent and clinician perspectives.

Declarations

- **Ethics approval** The Northern Ireland Research Ethics Committee (REC) and the Belfast Trust IRB approved the PiC protocol, including the embedded qualitative research (REC Reference - 17/NI/0169)(IRB Reference 16201MS-SW).
- **Consent for publication** Not applicable
- **Availability of data and material** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- **Competing interests** None
- **Funding** This study was funded by the Public Health Agency of Northern Ireland (EAT/5313/16). The funder had no involvement in the design or conduct of the study.
- **Authors Contributions** TW, MDS, JM, DF, MDL, DR, KW conceptualised and designed the study. TW and KW completed analysis, drafted the initial manuscript. TW, MDS, JM, DF, MDL, DR, KW edited and approved the final manuscript as submitted. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.
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Tables:

Table 1: Overview of consent models discussed in this manuscript

Consent Model	Description	Rationale/Enablers	Considerations
Prospective informed consent	Informed consent for participation in research is a key principle of good clinical practice. A potential participant (or parent/legal representative of a child) must be adequately informed about the research and their consent sought prior to their participation.	Prospective informed consent helps protect an individual's right to make an informed, un-coerced decision about their participation in research.	Informed consent is not feasible or appropriate in certain situations, including emergencies. Without alternatives to informed consent emergency research could not be conducted and critically ill patients would not benefit from evidence-based healthcare.
Research without prior consent	The research activity is performed and data are collected without prospective informed consent from the participant. Consent is sought to continue in the study at the earliest appropriate time (e.g. when the emergency situation has passed).	Enables the conduct of vital research in emergency situations.	Restricted to research, including drug trials in emergency situations where: the treatment is required urgently, it is not reasonably practicable to obtain consent prospectively and ethics committee approval has been given.
Opt-out consent	Research activity is performed and data are collected. Informed consent is not sought but study information is provided including how participants can opt-out (e.g. decline to have their data included in the study).	Used in certain types of low risk studies, such as epidemiological studies that do not involve additional procedures or change to clinical care.	Studies utilising opt-out only have to provide clear justification to an ethics committee. Opt-out is not suitable for studies such as drug trials or research involving additional interventions or changes to clinical care.

Table 2: Summary Data (Parents)

<i>Recruited Parents Summary Data</i>	
<i>Fathers</i>	2 (13%)
<i>Mothers</i>	13 (87%)
<i>Median Time to Interview</i>	55 Days (Range 13 to 95)
<i>Median Length of Stay</i>	2 Nights (Range 0 to 5)
<i>Consent Route</i>	Emergency Department n= 5 Ward n=6 After Discharge n=4
<i>Final Diagnosis</i>	Viral Illness 7 Group A Streptococcus 5 Pneumonia 1 Febrile Convulsion 1 Reactive Arthritis 1

Table 3: Summary Data (Clinicians)

<i>Experience</i>	Have Previous Research Experience	75%
<i>Study Responsibilities</i>	Screening	100%
	Consent	100%
	POCT	100%
	CRF Completion	40%
<i>Role</i>	Research Nurse	20%
	Senior Doctor	60%
	Junior Doctor	20%

POCT = Point-of-Care Testing, CRF = Case Report Form

Box 1:

- *The Petechiae in Children (PiC) study aims to; determine the diagnostic accuracy of point-of-care testing for identifying children with serious bacterial infection, to validate clinical practice guidelines and to describe the aetiology of fever and non-blanching rashes in children.*
- *The rapid point-of-care tests included molecular testing for Neisseria Meningitidis DNA on a throat swab and measurement of blood procalcitonin levels using 0.5ml of whole blood.*
- *There were no additional phlebotomy events, to obtain the additional 0.5ml of blood required for PiC, beyond those needed for routine care.*
- *Consent to include test result data and data from the attendance in the PiC study was then sought at the earliest appropriate opportunity. This was either during the inpatient stay, or after discharge depending on the timing of the presentation, clinical course and timing of discharge.*

Box 2:

Families involved in PiC provided consent after their child was tested for infection (within 24-48 hours). We call this deferred consent or research without prior consent.

There is specific legislation in place to allow for this type of research. This is because in emergency situations there's not time to have a discussion about the research and that actually having that discussion might delay important treatment.

Supplementary File 1. Example Topic Guide Questions

Table 1. Example interview topics and questions

Interview topics	Example questions
<u>PARENTS</u>	
Background and experience	<p><i>So just to get a background of what happened, what first prompted you to seek medical help when your child became unwell? (Prompt: explore what happened, how they were admitted to hospital)</i></p> <p><i>Has your child had a severe infection before this episode?</i></p> <p><i>Did the doctor give your child a diagnosis (e.g. did they tell you what had caused the illness?)</i></p>
PiC Study consent process	<p><i>Would you mind if I start by getting an overall picture of what happened when you first heard about the PIC Study... could you tell me a bit about that?</i></p> <p><i>At any point, were you aware of the clinical team mentioning PIC? If Yes, can you tell me a little bit more about this? How did this make you feel?</i></p> <p><i>Did the researcher check with you that it was a good time to talk about research?</i></p> <p><i>Was there anything that you found: a) unclear b) surprising?</i></p> <p><i>Did you have the opportunity to ask any other questions about the study? Did you ask any?</i></p>
Research without prior consent	<p><i>Families involved in PiC provided consent after their child was tested for infection (within 24-48 hours). We call this deferred consent or also known as research without prior consent. There is specific legislation in place to allow for this type of research. This is because in emergency situations there's not time to have a discussion about the research and that actually having that discussion might delay important treatment.</i></p> <p><i>What do you think about the use of research without prior consent in an emergency situation (for example, when a child has entered hospital via A&E or born very early)?</i></p> <p><i>How did the nurse/doctor explain RWPC to you? Was it explained clearly? If not, provide explanation. Check understanding.</i></p> <p><i>What did you think when you found out that your child had already been entered into the study before you were approached by the doctor or nurse about your consent?</i></p>

Decision making	<p><i>In making the decision about your child's participation in PIC, what sort of things went through your mind?</i></p> <p><i>Could you tell me if you found anything about the study unclear or confusing?</i></p> <p><i>Was there anything you found particularly helpful in making up your mind?</i></p> <p><i>Was there anything specific that influenced your decision?</i></p> <p><i>Would you mind telling me what were your reasons for (providing consent/not providing consent)?</i></p> <p><i>Did you feel that your child may benefit from taking part in the study?</i></p>
Child assent	<p><i>Did the nurse or doctor explain the PIC study to your child and give them an information sheet to seek their permission to take part? IF YES:</i></p> <p><i>a) Could you tell me a bit more about that?</i></p> <p><i>b) Did they ask any questions?</i></p> <p><i>What do you think involving children more in making the decision about the use of their information in a study?</i></p>
<u>CLINICIANS</u>	
Professional role and involvement in PIC	<p><i>What is your profession? (Explore: junior nurse, senior nurse, junior doctor, senior doctor)</i></p> <p><i>How would you describe your role and what you have contributed to the PIC study?</i></p> <p><i>(Explore: screening patients, helping with randomisation or consenting)</i></p>
Patient identification and recruitment	<p><i>Who would usually identify patients for inclusion?</i></p> <p><i>Do you think the identification process could be improved?</i></p> <p><i>Were there any barriers to recruitment?</i></p> <p><i>E.g. Time, equipment failure, lack of training?</i></p>
Research without prior consent	<p><i>Before PIC, did you have any experience of research without prior consent?</i></p> <p><i>What were your initial thoughts when you first heard that the PIC study was to use a RWPC approach? [Prompt: Did you have any concerns?]</i></p> <p><i>Have your views about research without prior consent changed over time?</i></p> <p><i>If yes, could you tell me a bit more about that?</i></p>

	<p><i>At what point did they change before/after SIV? After experience of RWPC?</i></p> <p><i>Have you had direct experience of discussing the study with parents and seeking permission to use their child's data in PIC?</i></p> <p><i>If yes, could you describe to me what happens when a patient included and you are preparing to approach the parents?</i></p> <p><i>Explore:</i></p> <ul style="list-style-type: none"> • <i>At what time (post inclusion) have you usually approached parents? (Explore minimum and maximum time frames)</i> • <i>What do you look for when establishing when best to approach parents?</i> • <i>Do you speak to the clinical care team?</i> • <i>Have you ever asked the clinical team to introduce you to the parents?</i> • <i>Are there ever any times when you've identified an eligible child but you feel it might not be appropriate to approach the family?</i> <p><i>How have parents reacted to finding out that their child has been entered into a clinical study without their prior consent?</i></p> <p><i>Explore: Have any parents been angry/ upset etc. What happened?</i></p>
Child assent	<p><i>Have you involved children in PIC discussions?</i></p> <p><i>Explore: barriers and whether age appropriate PIS have been given/ taken home?</i></p>

Supplementary File 2. Approach to qualitative data analysis

Phase	Description
Transcription and data cleaning	Interviews transcribed by a professional audio typist and were checked for accuracy. Personal information (<i>e.g.</i> names) were removed to ensure anonymity.
Familiarising with data and generating initial themes	TW read and re-read a sample of transcripts noting down initial ideas around main themes and potential codes.
Developing the coding framework	Using NVivo 12 Software, TW created codes for initial main themes (<i>e.g.</i> , thoughts on PiC; thoughts on RWPC; decision-making in the emergency setting; and misunderstandings and misconceptions) and began developing a coding framework using line by line coding, comparing between transcripts as part of a constant comparative approach
Initial coding meeting	TW and KW met to discuss early themes and develop the coding framework.
Second coding	KW second coded a sample (3 parent and 2 clinician interviews; 25%,) of transcripts and made notes on any new themes identified and how the framework could be refined.
Second coding meeting	TW and KW met to discuss, reflect and refine the specifics of each theme in the coding framework.
Completion of coding of transcripts	TW completed coding of all transcripts in preparation for write-up.
Write-up and final revision of coding	TW and KW developed the manuscript using themes to relate back to the study aims ensuring key findings and recommendations were relevant to the PiC trial design and RWPC in studies of diagnostic test accuracy. Final discussion and development of selected themes occurred during the write-up phase.

Supplementary File 3. Selected quotations from parents by theme

Theme	Sub-theme	Example quotes
Support for research		<p>"I felt that it was a good idea maybe you know to help other children" (P3 Mother)</p> <p>"I'm all for research" (P15 Mother)</p> <p>"Yes I do absolutely. Given the opportunity I think it's important because if it helps some other kid then that has to be a positive thing" (P10 Mother).</p>
Support for RWPC		<p>"Yeah, I think I'd be happy enough with it, I wouldn't have an issue afterwards you know" (P8 Mother)</p>
	Suitable for emergencies	<p>"In an emergency it's fine" (P13 Mother)</p> <p>"I think the doctor should do what they can do as quick as they can" (P2 Mother)</p>
	If no harm to child	<p>"if the child isn't being tortured if you know what I mean" (P9 Mother)</p>
	See additional diagnostic tests as a potential benefit	<p>"Yeah so I thought they might be able to find something out" (P3 Mother)</p> <p>"Well maybe if it had it turned out to be anything sort of worse she probably would have benefited from it." (P6 Mother)</p> <p>"I think if it was going to be like beneficial for [Name] to have a test that would bring back results quickly" (P7 Mother)</p> <p>"My children benefited in that we knew straight away" (P8 Mother)</p> <p>"That said parents do really appreciate getting that result and that negative rather than waiting a few days in the lab." (C2 Senior Doctor)</p> <p>"It was instant really that the results came back...I just thought that was a great thing." (P5 Mother)</p> <p><i>"we would find out within a few hours if it was meningitis"</i> (P8 Mother)</p>

	No perceived harm	<p>Interviewer” Did you envisage any possible risks for [Child Name] taking part in the study?</p> <p>Parent “No not at all” (P12 Father)</p> <p>“I think these tests can be done just as part of a blood sample anyway, I think I would say no, it’s fine the way it’s (RWPC) done” (P14 Mother)</p> <p>“I know you’re not doing any extra harm physically” (C2 Senior Doctor)</p>
Timing of consent discussions is important	Do not approach immediately at presentation	<p>“For me I would say that maybe a wee bit of respect should be given because at the end of the day if you’re in you’re trying to find out about your child, I personally probably wouldn’t have went for it because I will be thinking you know I’m trying to sort out my child here to see what’s wrong with them and I have somebody coming in to try and talk about a study. I don’t think there would be much consideration for the parents and the child at the time” (P3 Mother),</p>
	Don’t have capacity to think about research during the initial emergency	<p>“Well you’re definitely not taking it in, you’re just more concerned that your child is going to get better” (P2 Mother).</p>
	<p>Approach after the initial emergency is favourable</p> <p>Clinicians appropriately timed consent discussions</p>	<p>“I got the letter and I could make a decision in a calm environment (P 10 Mother)”</p> <p>“It would be a little bit of time after I had taken the samples and made sure that the child was well and stable” (C4 Senior Doctor)</p> <p>“I will go up and speak to the nurse or a member of the nursing staff and ask how the patient was doing and whether they felt it was appropriate and usually I got the nurse to introduce me” (C3 Junior Doctor)</p> <p>“I would be very much led by the parent” (C2 Senior Doctor).</p>
Decision making	The decision to participate was easy	<p>“I mean it was a complete no-brainer.” (P12 Father)</p> <p>“Being bluntly honest it wasn’t, as soon as it was mentioned we were more than happy to go ahead that was really it.” (P1 Father)</p> <p>“Parents are really positive and often ask me why we even need consent. They say its fine to use the data” (C2 Senior Doctor)</p>

	<p>"I think it was all pretty clear from what [Clinician Name] said and what was on the form" (P6 Mother)</p> <p>"it was just a there and then kind of decision" (P11 Mother)</p> <p>"it was positive and if anything, people are quite quick to agree to it (C4 Senior Doctor)"</p> <p>"all parents wanted to be on the study" (C1 Research Nurse)</p>
Should discuss severe infection prior to the research team approaching	"It's a bit worrying when you hear it like that" (P7 Mother)
Parents do not show a preference for who should consent e.g. nurse/doctor/researcher	"Anybody really it doesn't have to be a doctor it wouldn't matter if it was the doctor or the nurse but just someone with a professional manner" (P3 Mother)
Parental understanding of the study was good	<p>"From what I remember it was, I could be totally wrong, it was a test, a swab on the back of the throat and it's a way of getting results back sooner to look for infections or whatever because the blood tests that they do take 48 hours and so as far as I know this is a test to try and get results back sooner, within 30 minute" (P15 Mother)</p> <p>"They all seem to understand it well" (C5 Senior Doctor)</p>
Decision hadn't changed over time	"Yes I'm still happy with my decision I think it was the right decision." (P10 Mother)
No pressure	<p>"Yeah well when I got the phone call it was basically asking did I want to take part in it and you were given the option there whether you were wanted to or not. So for me if I didn't want to take part in it well you have an option" (P3 Mother)</p> <p>No not at all no, it didn't feel pressured in either way to be honest with you no." (P14 Mother)</p>
Parents recommend including children in the consent process where appropriate	"If they understand and they are old enough to comprehend, then I don't see a problem with them having an input as well because if they're old enough to make their own mind up then they should be given some say." (P1 Father)

**Using opt out alone
not appropriate**

“It wouldn't be appropriate for extra procedures done that weren't to the benefit of the child” (P12 Father)

“No I think probably it would be better to discuss it with the family”(P15 Mother)

“I would have just stayed in the study.” (P15 Mother)

“I think if I had any concerns it would have been more difficult to ask them”(P10 Mother)

” “I feel it's a wee bit cold perhaps”(P10 Mother)

Would still take part
though

Harder to raise concerns

A little “cold”

Manuscript:

Parents' and clinicians' views on conducting paediatric diagnostic test accuracy studies without prior informed consent. Qualitative insight from the Petechiae in Children study (PiC)

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Developed from:

Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
<i>Personal Characteristics</i>		
1. Inter viewer/facilitator	Which author/s conducted the inter view or focus group?	Pages 4,5
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	Page 4
3. Occupation	What was their occupation at the time of the study?	Page 4
4. Gender	Was the researcher male or female?	4
5. Experience and training	What experience or training did the researcher have?	4
<i>Relationship with participants</i>		
6. Relationship established	Was a relationship established prior to study commencement?	Pages 5,6,10
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Pages 5,6,10
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	Page 4

Domain 2: study design		
<i>Theoretical framework</i>		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Page 5 and supplement 2
<i>Participant selection</i>		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Pages 4,5
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Pages 4,5
12. Sample size	How many participants were in the study?	Pages 5,6
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Page 5
<i>Setting</i>		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Page 4
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	Page 4
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	Page 5, Tables 1,2
<i>Data collection</i>		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Pages 4,5, Supplement 1
18. Repeat interviews	Were repeat inter views carried out? If yes, how many?	Page 5
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	Page 5
20. Field notes	Were field notes made during and/or after the inter view or focus group?	Page 5
21. Duration	What was the duration of the inter views or focus group?	Page 6

22. Data saturation	Was data saturation discussed?	Page 6
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	Page 5
Domain 3: analysis and findings		
<i>Data analysis</i>		
24. Number of data coders	How many data coders coded the data?	Page 5, supplement 2
25. Description of the coding tree	Did authors provide a description of the coding tree?	Supplement 2
26. Derivation of themes	Were themes identified in advance or derived from the data?	Pages 4,5, Supplement 2
27. Software	What software, if applicable, was used to manage the data?	5
28. Participant checking	Did participants provide feedback on the findings?	5
<i>Reporting</i>		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	Yes
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Yes
31. Clarity of major themes	Were major themes clearly presented in the findings?	Yes
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Yes