BMJ Open

Protocol for the development of a patient-reported outcome measure for patients with hypospadias

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-088619
Article Type:	Protocol
Date Submitted by the Author:	10-May-2024
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Keywords:	UROLOGY, Patient Reported Outcome Measures, Paediatric urology < UROLOGY

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Key Words: PROMS, Hypospadias, Urology, Patient Reported Outcomes

Word Count: 1620

Awknowledgements: none to declare

Conflict of interest: none to declare

Author contributions: none to declare

Funding: This work was supported by Canadian Urological Association Research Foundation Award.

ABSTRACT

Introduction. Existing patient-reported outcome measures (PROM) do not meet accepted international criteria for measuring health outcomes of hypospadias treatment. This protocol describes the qualitative development (phase I) of a novel PROM to evaluate outcomes of hypospadias treatments.

Methods and analysis. Participants aged 7 years and older with hypospadias and caregivers of children under 8 years seeking treatment at Boston Children's Hospital, Children's Hospital of Eastern Ontario (CHEO), Children's Hospital of Philadelphia (CHOP) and McMaster Children's Hospital (MCH), will be invited to participate in concept elicitation and cognitive interviews. Concept elicitation interviews will be in-depth and semi-structured to understand concepts important to patients seeking treatment for hypospadias. Cognitive interviews will be performed concurrently to ensure that the scale items, instructions, and response options are relevant, understandable, and comprehensive. Cognitive interviews will be complemented by expert input. Concept elicitation and cognitive interview transcripts will be coded line-by-line. Participant quotes will be categorized into top-level domains, themes, and subthemes. The primary outcome of this research will be to develop a conceptual model representing the patient experience of hypospadias and a novel PROM.

Ethics and dissemination: Ethics approval was obtained from the Institutional Research Ethics Board (IRB) at BCH, CHOP, McMaster and CHEO. Findings from this research will be disseminated at national and international conferences and published in relevant peer-reviewed journals for the target audience.

Strengths and limitations of the study

- Recruitment of a heterogeneous sample of patients will ensure that concepts capture the patient's authentic experience of hypospadias and will enable the development of a novel patient-reported outcome measure (PROM).
- We adhere to published guidelines for establishing content validity and developing new PROMs.
- This new PROM will offer a clinically meaningful PROM, developed using a modern psychometric approach called Rasch measurement theory analysis.

INTRODUCTION

Patient-reported outcome measures (PROMs) are valid and reliable tools developed to enable direct reports of a patient's health status from their perspective [1]. PROMs are increasingly used to inform care delivery, comparative effectiveness research, and health policy decisions. Little is known about the most critical outcomes for young patients; therefore, including the patient (or proxy) perspective in pediatric surgical decision-making is critically important.

Hypospadias, a condition where the urethra opens on the underside or below the penis, which is associated with varying degrees of penile curvature and foreskin anomalies is the second most common congenital disability in boys, occurring in approximately one in every 200 male births in the United States [2] and a global prevalence of 20.9 per 10 000 births [3]. Since boys cannot outgrow this defect, surgical repair is often undertaken during infancy to improve urinary and sexual function and overall quality of life (QOL). Surgical success has been measured primarily by surgeon assessments of urine flow rates or complications. However, there is a need to incorporate the patient's perspective of health outcomes following hypospadias treatment.

Surgical outcomes for correcting hypospadias vary widely and may impose physical and psychosocial consequences on patients and their families. Recent advances in surgical technique have shown improved outcomes in hypospadias; however, eight percent of boys still experience complications [4]; this risk doubles to quadruples in boys with severe defects (i.e. proximal) or those with prior complications. Poor cosmetic or functional outcomes can lead to considerable long-term cognitive, behavioral, and self-esteem consequences, including poor school performance [5, sexual avoidance [6-7], and negative genital perception [8-9].

Presently, no PROM exists that meets the accepted international criteria for measuring health outcomes of hypospadias treatment [10-11]. A systematic literature review revealed a need for validated PROMs for patients with hypospadias [12]; PROMs were primarily ad hoc, with limited evidence of their development and validation. Existing PROMs do not address self-perception, embarrassment, satisfaction with voiding/sexual function, or QOL, therefore, lack content validity (i.e., they do not capture the full range of concerns experienced by patients and their families).

The lack of disease-specific and well-validated patient-reported endpoint has hampered the evaluation of surgical techniques or non-operative management of hypospadias. There is wide variation in the surgical technique, including non-intervention, with an unknown impact on the patient's QOL. Furthermore, commonly reported outcomes, such as surgical complications or urine flow rates, have not demonstrated benefits in patients' health status after treatment.

This research program aims to develop and validate a novel PROM for patients with hypospadias. This protocol describes the qualitative development (phase I) of the a new PROM to evaluate outcomes of hypospadias treatments.

METHODS AND ANALYSIS

Phase 1: Qualitative development

Best practice guidelines of the USA Food and Drug Administration (FDA) [11] and the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) [13] are being employed to inform the development of this new PROM. Interpretive description, an applied health services research approach, will be used. A systematic literature review was conducted to inform the development of a preliminary conceptual model [12]. ubsequent qualitative interviews with patients aged over 7 years, with a focus on children, teens, young adults with prior pediatric hypospadias care, and their proxies were undertaken to inform the conceptual model further and develop initial items for scale development.

Additional in-depth and semi-structured concept elicitation interviews will be conducted, including a more heterogeneous sample of patients aged 7 years or older to better understand concepts important to patients seeking treatment for hypospadias. Qualitative data will be used to develop the conceptual model and content further. Cognitive interviews will be performed concurrently to ensure that the scale items, instructions, and response options are relevant, understandable, and comprehensive. Cognitive interviews will be complemented by expert input.

Setting

Participants were recruited from the urology clinics at the Children's Hospital of Eastern Ontario (CHEO, Canada) and Boston Children's Hospital (BCH, USA) for the completed concept elicitation interviews.

For the subsequent concept elicitation and cognitive interviews, participants will be recruited from the urology clinics at McMaster Children's Hospital (MCH, Canada) and Children's

Hospital of Philadelphia (CHOP, USA). Given these sites' high volume of patients, we do not anticipate problems recruiting the necessary participants.

Sample

Participants from the completed concept elicitation interviews were identified through a retrospective search of surgical billing codes within the Electronic Health Record system (EPIC) and new patient referrals to the urology clinic for hypospadias. New patient referrals and existing patients of the urology clinics for hypospadias will be approached to participate in the subsequent concept elicitation and cognitive interviews.

A maximum variation sample will be purposively selected to vary by disease severity (mild to severe disease), stage of treatment (pre- and post-operative), age of treatment, and clinical outcomes, urethral location, and the presence or absence of complications. Definitions of complications are based on a consensus statement from the International Pediatric Urology Task Force on Hypospadias [14].

Recruitment

A care team member recruited participants from the completed concept elicitation interviews, and those who consented to participate were invited to complete an in-person or virtual interview. Subsequent concept elicitation and cognitive interview recruitment will involve care team members asking patients if they would be interested in participating in the study. If the patient or caregivers express interest, the urologist will obtain verbal consent for a researcher to contact them later to obtain full consent, schedule the interview, and answer any further

questions the parents or caregiver might have. Patients or parents who consent to participate will be invited to an interview on an online platform (e.g., Microsoft Teams or Zoom) telephone interview with an experienced qualitative researcher.

Experts in the field of hypospadias known to our network will be invited via email invitation to provide feedback on the scales.

Data collection

Subsequent concept elicitation and cognitive interviews will follow the same data collection procedures used previously for the completed concept elicitation interviews. All interviews will be audio recorded, transcribed, and coded. Participants will be interviewed using a semi-structured qualitative interview guide, including surgical experience, appearance, function, and psychological well-being probes. Questions regarding perceptions of ideal hypospadias outcomes will be probed. Topics included in the interview guide will be informed by a systematic literature review of PROMs used in hypospadias. The interview guide will be adapted accordingly to each participant to avoid asking irrelevant questions (e.g., asking young participants about sexual well-being). The interview guide will be adjusted as interviews are conducted to include any new concepts identified after each interview. Recruitment will continue until saturation (i.e., no new concepts are elicited from the interviews) [15].

Multiple rounds of cognitive interviews will be performed with as many participants as necessary to establish the content validity of the scales. Participants will review the scales via an online Research electronic data capture (REDCap) survey [16] and will be encouraged to use the

'think aloud' approach with probing to obtain feedback on the relevance, comprehensibility, and comprehensiveness of the scale items, instructions, and response options [17-19].

Experts in hypospadias will review the scale content before the final round of patient cognitive interviews. A REDCap survey will be designed with targeted questions about the items' relevance, instructions, response options, and any missing content. Relevant changes suggested in each round of patient interviews and from expert input will be applied and reviewed in a final round of participant interviews.

Data analysis

Subsequent concept elicitation and cognitive interviews will follow the same data analysis procedures used previously for the completed concept elicitation interviews. Data collection and analysis will be conducted concurrently. Concept elicitation and cognitive interview transcripts will be coded line-by-line by a research team member and confirmed by a second member for the first five interviews or until an agreed-upon coding framework is achieved. Coded data will be transferred onto an Excel spreadsheet for analysis.

Participant quotes from the concept elicitation interviews will be categorized into top-level domains and themes/subthemes. Qualitative analysis will refine a conceptual framework covering the concepts concerning people seeking treatment for hypospadias. The coding framework will guide scale development, and codes will inform the development of a comprehensive item pool. Items will be devised such that they retain participant language to ensure that they resonate with patients and are easy to understand. A comprehensive set of

independently functioning scales will be formed from the item pool, alongside instructions, a time frame for responding to the scales, and a set of response options. Feedback obtained from the cognitive interviews will be categorized according to the following top-level domains: interpretation, relevance, clarity, missing content, and suggested changes.

ETHICS AND DISSEMINATION

The Institutional Research Ethics Board (IRB) approved the study at BCH, CHEO, CHOP, and McMaster. Participants will provide written and audio-recorded verbal consent. Participants will be de-identified from their transcripts, and institution rules for data storage will be followed.

Once developed, this new PROM will be made available to license free for all non-profit users. We will seek to advertise and promote its use through presentations at national and international meetings. Findings about the development will also be published in relevant peer-reviewed journals for the target audience.

Strengths and limitation

The strengths of this study include recruitment of a heterogenous sample of patients. This will ensure that concepts capture the patient's authentic experience of hypospadias and will enable the development of a novel patient-reported outcome measure (PROM) – the HYPOSPADIAS-Q.

- We adhere to published guidelines for establishing content validity and developing new PROMs.
- This new PROM will offer a clinically meaningful means to measure outcomes developed using a modern psychometric approach called Rasch measurement theory analysis.

Limitations

- This protocol is limited to patients that are English speakers, seeking care in a North American health care Setting. Future work should include more geographic and cultural diversity.

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Manuscript ID	bmjopen-2024-088619.R1
Article Type:	Protocol
Date Submitted by the Author:	26-Feb-2025
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Primary Subject Heading:	Urology
Secondary Subject Heading:	Urology, Patient-centred medicine
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Key Words: PROMS, Hypospadias, Urology, Patient Reported Outcomes

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Awknowledgements: none to declare

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Methods and analysis. Participants aged 7 years and older with hypospadias and caregivers of children under 8 years seeking treatment at Boston Children's Hospital, Children's Hospital of Eastern Ontario (CHEO), Children's Hospital of Philadelphia (CHOP) and McMaster Children's Hospital (MCH), will be invited to participate in concept elicitation and cognitive interviews. Concept elicitation interviews will be in-depth and semi-structured to understand concepts important to patients seeking treatment for hypospadias. Cognitive interviews will be performed concurrently to ensure that the scale items, instructions, and response options are relevant, understandable, and comprehensive. Cognitive interviews will be complemented by expert input. Concept elicitation and cognitive interview transcripts will be coded line-by-line. Participant quotes will be categorized into top-level domains, themes, and subthemes. The primary outcome of this research will be to develop a conceptual model representing the patient experience of hypospadias and a novel PROM.

Ethics and dissemination: Ethics approval was obtained from the Institutional Research Ethics Board (IRB) at BCH, CHOP, McMaster and CHEO (IRB-P00042425). Findings from this research will be disseminated at national and international conferences and published in relevant peer-reviewed journals for the target audience.

Strengths and limitations of the study

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Limitations

- This protocol is limited to patients that are English speakers, seeking care in a North American health care Setting. Future work should include more geographic and cultural diversity.

INTRODUCTION

Patient-reported outcome measures (PROMs) are valid and reliable tools developed to enable direct reports of a patient's health status from their perspective [1]. PROMs are increasingly used to inform care delivery, comparative effectiveness research, and health policy decisions [2]. Little is known about the most critical outcomes for young patients; therefore, including the patient (or proxy) perspective in pediatric surgical decision-making is critically important [3]. Hypospadias, a condition where the urethra opens on the underside or below the penis, which is associated with varying degrees of penile curvature and foreskin anomalies is the second most common congenital disability in boys, occurring in approximately one in every 200 male births in the United States [4] and a global prevalence of 20.9 per 10 000 births [5]. Since boys cannot outgrow this defect, surgical repair is often undertaken during infancy to improve urinary and sexual function and overall quality of life (QOL). Surgical success has been measured primarily by surgeon assessments of urine flow rates or complications [6]. However, there is a need to incorporate the patient's perspective of health outcomes following hypospadias treatment.

Surgical outcomes for correcting hypospadias vary widely and may impose physical and psychosocial consequences on patients and their families. Recent advances in surgical technique have shown improved outcomes in hypospadias; however, eight percent of boys still experience complications [7]; this risk doubles to quadruples in boys with severe defects (i.e. proximal) or those with prior complications. Poor cosmetic or functional outcomes can lead to considerable long-term cognitive, behavioral, and self-esteem consequences, including poor school performance [8], sexual avoidance [8, 9], and negative genital perception [8, 10, 11].

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This research program aims to develop and validate a novel PROM for patients with hypospadias. This protocol describes the qualitative development (phase I) of the a new PROM to evaluate outcomes of hypospadias treatments.

METHODS AND ANALYSIS

Phase 1: Qualitative development

Best practice guidelines of the USA Food and Drug Administration (FDA) [14] and the Consensus-based Standards for the selection of health status Measurement INstruments (COSMIN) [16] are being employed to inform the development of this new PROM. Interpretive description, an applied health services research approach, will be used. A systematic literature review was conducted to inform the development of a preliminary conceptual model [15]. Subsequent qualitative interviews with patients aged over 7 years, with a focus on children, teens, young adults with prior pediatric hypospadias care, and their proxies were undertaken to inform the conceptual model further and develop initial items for scale development.

Additional in-depth and semi-structured concept elicitation interviews will be conducted (May 2024-March 2025, including a more heterogeneous sample of patients aged 7 years or older to better understand concepts important to patients seeking treatment for hypospadias. Qualitative data will be used to develop the conceptual model and content further. Cognitive interviews will be performed concurrently to ensure that the scale items, instructions, and response options are relevant, understandable, and comprehensive. Cognitive interviews will inform the final scales which will be circulated to an international group of experts in hypospadias for feedback (estimated May 2025). Concepts elicited and changes proposed by expert informants will be reviewed with patient participants for final scale creation.

Setting

Participants were recruited from the urology clinics at the Children's Hospital of Eastern Ontario (CHEO, Canada) and Boston Children's Hospital (BCH, USA) for the completed concept elicitation interviews. All participants participating in concept elicitation and cognitive

interviews provided informed consent or assent (patients < 16 years) as approved by local institutional review boards or research ethics boards. For the subsequent concept elicitation and cognitive interviews, interested participants will be recruited from the urology clinics at Boston Children's Hospital (BCH, USA) Children's Hospital of Philadelphia (CHOP, USA) .

Sample

Participants from the completed concept elicitation interviews were identified through a retrospective search of surgical billing codes within the Electronic Health Record system (EPIC) and new patient referrals to the urology clinic for hypospadias. New patient referrals and existing patients of the urology clinics for hypospadias will be approached to participate in the subsequent concept elicitation and cognitive interviews.

A maximum variation sample will be purposively selected to vary by disease severity (mild to severe disease), stage of treatment (pre- and post-operative), age of treatment, and clinical outcomes, urethral location, and the presence or absence of complications. Definitions of complications are based on a consensus statement from the International Pediatric Urology Task Force on Hypospadias [17].

Recruitment

A care team member recruited participants from the completed concept elicitation interviews, and those who consented to participate were invited to complete an in-person or virtual interview. Subsequent concept elicitation and cognitive interview recruitment will involve care team members asking patients if they would be interested in participating in the study. Patients

will provide written or verbal consent (patients under 16 will assent). Patients or parents who consented to participate were invited to an interview on an online platform (e.g., Microsoft Teams or Zoom) telephone interview with an experienced qualitative researcher.

Experts in the field of hypospadias known to our network through the Hypospadias International Society (n=20) will be invited via email invitation to provide feedback on the scales and feedback will be captured through a REDCap survey. This step will ensure that the content of the proposed scales comprehensively measured outcomes that matter to patients and that instructions, response options and items are clear, meaningful and unambiguous.

Data collection

Subsequent concept elicitation and cognitive interviews will follow the same data collection procedures used previously for the completed concept elicitation interviews. All interviews will be audio recorded, transcribed, and coded. Participants will be interviewed using a semi-structured qualitative interview guide, including surgical experience, appearance, function, and psychological well-being probes (Appendix 1). Questions regarding perceptions of ideal hypospadias outcomes will be probed. Topics included in the interview guide will be informed by a systematic literature review of PROMs used in hypospadias. The interview guide will be adapted accordingly to each participant to avoid asking irrelevant questions (e.g., asking young participants about sexual well-being). The interview guide will be adjusted as interviews are conducted to include any new concepts identified after each interview. Recruitment will continue until saturation (i.e., no new concepts are elicited from the interviews) [18].

Multiple rounds of cognitive interviews will be performed with as many participants as necessary to establish the content validity of the scales. Participants will review the scales via an online Research electronic data capture (REDCap) survey [19] and will be encouraged to use the 'think aloud' approach with probing to obtain feedback on the relevance, comprehensibility, and comprehensiveness of the scale items, instructions, and response options [20, 21].

Experts in hypospadias will review the scale content before the final round of patient cognitive interviews. A REDCap survey will be designed with targeted questions about the items' relevance, instructions, response options, and any missing content. Relevant changes suggested in each round of patient interviews and from expert input will be applied and reviewed in a final round of participant interviews.

Data analysis

Subsequent concept elicitation and cognitive interviews will follow the same data analysis procedures used previously for the completed concept elicitation interviews. Data collection and analysis will be conducted concurrently. Concept elicitation and cognitive interview transcripts will be coded line-by-line by a research team member and confirmed by a second member for the first five interviews or until an agreed-upon coding framework is achieved. Coded data will be transferred onto an Excel spreadsheet for analysis.

Participant quotes from the concept elicitation interviews will be categorized into top-level domains and themes/subthemes. Qualitative analysis will refine a conceptual framework covering the concepts concerning people seeking treatment for hypospadias. The coding

framework will guide scale development, and codes will inform the development of a comprehensive item pool. Items will be devised such that they retain participant language to ensure that they resonate with patients and are easy to understand. A comprehensive set of independently functioning scales will be formed from the item pool, alongside instructions, a time frame for responding to the scales, and a set of response options. Feedback obtained from the cognitive interviews will be categorized according to the following top-level domains: interpretation, relevance, clarity, missing content, and suggested changes.

Subsequent phases

The phase II field-test study will involve recruitment of a large international sample of participants. We will use the data collected to refine and validate the Hypospadias PRO scales using RMT analysis. This will allow us to identify the items in each scale that can that serve as more accurate indicators of patient outcomes, thereby reducing the length of the scales for patient ease of completion and creating clinically meaningful and valid scales. Once developed and validated, we will conduct further psychometric research to determine each scales' ability to measure clinical change following hypospadias repair.

Patient and public involvement

Our patient-oriented approach engages patients with hypospadias and parents of children and teenagers with hypospadias and healthcare providers in all stages of our research as experts and research team members whose input is crucial to the design of the study and development of content for our hypospadias scales. Participants involved in qualitative and cognitive interviews will be invited to continue to collaborate in our study by taking part in scale refinement

interviews where they can provide feedback on our findings and help to refine the final set of scales. We are collaborating with patients and families to host a patient-centered hypospadias conference in the Summer of 2026, where study results will be presented for discussion and further dissemination in patient centered research.

ETHICS AND DISSEMINATION

The Institutional Research Ethics Board (IRB) approved the study at BCH, CHEO, CHOP, and McMaster (IRB-P00042425). Participants will provide written and audio-recorded verbal consent (assent for patients <16). Participants will be de-identified from their transcripts, and institution rules for data storage will be followed.

Once developed, this new PROM will be made available to license free for all non-profit users. We will seek to advertise and promote its use through presentations at national and international meetings. Findings about the development will also be published in relevant peer-reviewed journals for the target audience.

Author contributions

MAK initiated the study at BCH and CHOP, designed the qualitative interview guide, conducted qualitative interviews, coded interview transcripts, drafted and revised the paper. ET conducted qualitative and cognitive interviews, coded interview transcripts and drafted and revised the manuscript. SG designed interview guide, conducted qualitative and cognitive interviews and coded interview transcripts. CL implemented the study at CHOP, participated in research planning meetings and revised the manuscript. EM and LB participated in research planning

meetings and revised the manuscript. AK provided mentorship in designing the interview guide, provided mentorship in coding interview transcripts, scale design and revised the manuscript. MK is the guarantor.

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Appendix 1: Hypospadia Interview Guide.

(Note: Confirm Consent Form was Reviewed & Understood on Tape).

Preamble: This study is to create a new questionnaire for children and teenagers or young adults with hypospadias. I would like you to tell me stories that will help me to understand what it has been like for you to have had a hypospadias, or possible hypospadias surger. Should any question make you uncomfortable, you are free to decline responding. Further, you may stop the interview at any time, and you have the right to withdraw your participation.

Background Questions:

1. Can you us how you learned that you had hypospadias? [Probe: age, informed by parent/health provider, description of the condition, at what age?]

2. Tell me about how you felt when you learned that you had hypospadias? [Probe: feelings, emotions, concerns, past versus present feelings]

Experience of Care:

3. Based on what you remember, what treatments have you had for your hypospadias? [Probe: how old were you when you had your treatment? personal experience/knowledge vs. what you have been told]

4. What was helpful about the treatment(s)? [Probe: what did you like, did you feel better - how]

5. What did you dislike about the treatment? [Probe: problems/bad things associated with treatment]

6. Who did you (OR who do you still) see at the hospital or clinic? [Probe: doctor, nurse, receptionist].

7. What were the people who cared for you like? [Probe: friendly, made you feel comfortable, easy to talk to, listened to you, explained things to you, anything you disliked?]

8. At the hospital, who explained your hypospadias to you? [Probe: understanding] How did they explain your hypospadias to you? [Probe: talking, showing pictures, drawings, written information]

9. Tell me about how recent decisions were/are made about your treatments (e.g., getting surgery)? Were you involved in making decisions about your treatments? If yes, then ask:
    a. What factors influenced your decision to go through (or not go through) these treatments? [Probe: appearance, function]
    b. Did anyone influence your decision regarding treatments? [Probe: family, health providers]

10. Did you have any recent surgeries/treatments that you can remember? If so, what kind of information (verbal, written, visual) did they give you to prepare for surgery? [Probe: about nature of surgery; did you understand the information; did you get to ask questions; did they provide information about how to care for yourself after the surgery]

11. Tell me about anything you remember regarding your recovery (OR getting better after your surgeries OR what happened after your surgeries)? [Probe: any pain, swelling, or bruising; were you taking medications; any trouble with catheters/dressings; any difficulty urinating/peeing; any infections/fevers; any itching; how long has the recovery time been so far]

Complications:

12. Did you notice any problems after the surgery OR did anything go wrong after the surgery? [Probe: any complications]. If yes, then ask:
    a. How did you know something was wrong? [Probe: did you know OR did someone else notice it; did you tell anyone – who/when]
    b. How did you feel about these problems (complications)? [Probe: emotions, fear, worry]
    c. What happened after the complication occurred (saw physician, went to ER, seen in follow-up). What was the outcome of these visits? (surgery, plan to watch)
    d. Were you happy with how any problems regarding your treatments were handled?

Appearance and General Function:

13. At this time (presently), how satisfied you are with your urinary function (i.e. going to the bathroom or peeing)? [Probe: easier/difficult, better/worse than before, level of satisfaction – happy]

14. Can you describe what it looks like, or feels like when you go pee? (probe pee goes straight, downwards, looks narrow/thin/spray, stream, pain, urgent/uncomfortable, accidents or dribbling, etc)

15. I know some of these questions may be difficult or personal, so share whatever information you feel comfortable sharing. Are you happy with the way that your penis looks now? [Probe: skin, shape, position of opening, curvature, size, scars, foreskin, scrotum, testicles etc.]. If you are not happy with how your penis looks (as are many men), what would you like to change?

16. Are you comfortable to use public bathrooms or change in public? Do/did you ever hide your penis/private region (genitals) from others (e.g., when going to the bathroom, changing in change room, etc)? If yes, how did you do this? Why did you do this?

17. Have others ever made comments about the appearance of your genitals or about how you pee/void? Can you give us some examples? How did those comments make you feel?

Psychological Wellbeing

18. How has having hypospadias impacted your overall life? Has it had any major impact on your wellbeing? Relationships with others (parents, siblings, friends, girlfriends etc)

19. How does the appearance of your penis make you feel? [Probe: happy, sad, anxious, worried, frustrated, self-conscious, self-esteem, body image]

20. How does the urinary function (peeing/voiding) of your penis make you feel?

Social Life:

21. Do you talk to others (family members, friends) about hypospadias? Do you feel that having hypospadias has impacted you socially in a positive or negative way?

22. More specifically, does your hypospadias/penis (AND/OR treatment/hospital care) affect your life at home? [Probe: siblings, relatives, friends, time management]

23. Does your hypospadias/penis affect your experience at school/college? [Probe: in classroom; in sports and activities; in change rooms; in the bathroom]

24. Does your hypospadias affect your social life such as your interactions with other same-aged peers, friends, etc? [Probe: possibility of being teased/bullied; meeting new people; dating; sex life]

25. Is/was there things you would have liked to do but didn't because of your hypospadias/penis? [Probe: swimming, changing in public locker rooms, sports, sleepovers]

26. Do/did people treat you differently because of your hypospadias? [Probe: family; friends; students; teachers; others]

Puberty, and Sexual Function & Wellbeing

27. [Determine if child identifies/describes going through puberty – if has adult male voice (aka – deep not pre-pubescent]. I know this question might be difficult, but in order to ask some other questions, it is important for us to know if you have any signs of puberty (voice change, pubic hair etc)
    a. Do you remember when you started puberty? (can explain, voice change, new body hair, penis/testicles became larger?)
    b. Did you have any concerns regarding your hypospadias when you went through puberty. Did you notice any improvements (urinary flow?) or new problems (curvature/appearance)?
    c. When you have erections, do they appear straight? (probe curved) Is there any pain, discomfort?
    d. Do you have any concerns about your erections or penile sensation? (curvature, lack of sensation where scars are, pain, impotence). Probe regarding ejaculation, any concerns (decreased amount/flow/sensation)
    e. Have you ever dated anyone? Been in a relationship? If not, did your hypospadias have any impact on this? Other reasons?
    f. Does your hypospadias/penis influence your dating behaviours [Probe: present/future concerns, feelings/emotions]

g. Have you had prior sexual activities (masturbation, sexual contacts). If yes, do you find that your hypospadias interferes with your ability to masturbate/fool around/have sex? [Probe: how so; erection/orgasm difficulty, embarrassment/in the dark only/ avoid sexual contact with others. If sexually active – curvature, ejaculation, difficulties obtaining, maintaining erection.]

Other Questions

28. If you could talk to a young boy or a family of a young boy with hypospadias, what do you think would be important for them to know?

29. Is there anything about your care for hypospadias that you would have like to have done differently? [probe: timing of surgery, number of follow-ups, how it was talked about by MDs/family]

30. Is there anything I have not asked you that you think it is important for me to know in order to understand young people's experience with hypospadias?

BMJ Open

Protocol for the development of a patient-reported outcome measure for patients with hypospadias

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-088619.R2
Article Type:	Protocol
Date Submitted by the Author:	31-Mar-2025
Complete List of Authors:	Keays, Melise; Boston Children's Hospital, Tsangaris, Elena; Boston Children's Hospital Gulati, Sonia; Carleton University Long, Christopher; Children Hospital of Philadelphia, Urology McNamara, Erin ; Children's Hospital Boston, Braga, LH; McMaster Children's Hospital, Surgery Klassen, Anne; McMaster University, Pediatrics
Primary Subject Heading:	Urology
Secondary Subject Heading:	Urology, Patient-centred medicine
Keywords:	UROLOGY, Patient Reported Outcome Measures, Paediatric urology < UROLOGY, Adolescents < Adolescent

Manuscript Title: Protocol for the development of a patient-reported outcome measure for patients with hypospadias

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Key Words: PROMS, Hypospadias, Urology, Patient Reported Outcomes

Word Count: 1910

Acknowledgement: none to declare

Conflict of interest: none to declare

Author contributions: none to declare

Funding: This work was supported by Canadian Urological Association Research Foundation Award.

ABSTRACT

Introduction. Existing patient-reported outcome measures (PROM) do not meet accepted international criteria for measuring health outcomes of hypospadias treatment. This protocol describes the qualitative development (phase I) of a novel PROM to evaluate outcomes of hypospadias treatments.

Methods and analysis. Participants aged 7 years and older with hypospadias and caregivers of children under 8 years seeking treatment at Boston Children's Hospital, Children's Hospital of Eastern Ontario (CHEO), Children's Hospital of Philadelphia (CHOP) and McMaster Children's Hospital (MCH), will be invited to participate in concept elicitation and cognitive interviews. Concept elicitation interviews will be in-depth and semi-structured to understand concepts important to patients seeking treatment for hypospadias. Cognitive interviews will be performed concurrently to ensure that the scale items, instructions, and response options are relevant, understandable, and comprehensive. Cognitive interviews will be complemented by expert input. Concept elicitation and cognitive interview transcripts will be coded line-by-line. Participant quotes will be categorized into top-level domains, themes, and subthemes. The primary outcome of this research will be to develop a conceptual model representing the patient experience of hypospadias and a novel PROM.

Ethics and dissemination: Ethics approval was obtained from Boston Children's Hospital's Institutional Review Board (HHS Registration: IRB00000352; Protocol number IRB-P00042425). CHOP, McMaster and CHEO have reliance agreements with Boston Children's Hospital. Findings from this research will be disseminated at national and international conferences and published in relevant peer-reviewed journals for the target audience.

Strengths and limitations of the study

- Recruitment of a heterogeneous sample of patients will ensure that concepts capture the patient's authentic experience of hypospadias and will enable the development of a novel patient-reported outcome measure (PROM).
- We adhere to published guidelines for establishing content validity and developing new PROMs.
- This new PROM will offer a clinically meaningful PROM, developed using a modern psychometric approach called Rasch measurement theory analysis.

Limitations

- This protocol is limited to patients that are English speakers seeking care in a North American health care setting, therefore, lacking geographic and cultural diversity.
- This study lacks the perspective of middle-age/senior adult hypospadias population and lacks patients with moderate to severe uncorrected hypospadias as most are fixed in infancy.

INTRODUCTION

Patient-reported outcome measures (PROMs) are valid and reliable tools developed to enable direct reports of a patient's health status from their perspective [1]. PROMs are increasingly used to inform care delivery, comparative effectiveness research, and health policy decisions [2]. Little is known about the most critical outcomes for young patients; therefore, including the patient (or proxy) perspective in pediatric surgical decision-making is critically important [3]. Hypospadias, a condition where the urethra opens on the underside or below the penis, which is associated with varying degrees of penile curvature and foreskin anomalies is the second most common congenital disability in boys, occurring in approximately one in every 200 male births in the United States [4] and a global prevalence of 20.9 per 10 000 births [5]. Since boys cannot outgrow this defect, surgical repair is often undertaken during infancy to improve urinary and sexual function and overall quality of life (QOL). Surgical success has been measured primarily by surgeon assessments of urine flow rates or complications [6]. However, there is a need to incorporate the patient's perspective of health outcomes following hypospadias treatment.

Surgical outcomes for correcting hypospadias vary widely and may impose physical and psychosocial consequences on patients and their families. Recent advances in surgical technique have shown improved outcomes in hypospadias; however, eight percent of boys still experience complications [7]]; this risk doubles to quadruples in boys with severe defects (i.e. proximal) or those with prior complications. Poor cosmetic or functional outcomes can lead to considerable long-term cognitive, behavioral, and self-esteem consequences, including poor school performance [8], sexual avoidance [9-10], and negative genital perception [11-12].

Presently, no PROM exists that meets the accepted international criteria for measuring health outcomes of hypospadias treatment [13-14]. A systematic literature review revealed a need for validated PROMs for patients with hypospadias [15]; PROMs were primarily ad hoc, with limited evidence of their development and validation. Existing PROMs do not address self-perception, embarrassment, satisfaction with voiding/sexual function, or QOL, therefore, lack content validity (i.e., they do not capture the full range of concerns experienced by patients and their families).

The lack of disease-specific and well-validated patient-reported endpoint has hampered the evaluation of surgical techniques or non-operative management of hypospadias. There is wide variation in the surgical technique, including non-intervention, with an unknown impact on the patient's QOL. Furthermore, commonly reported outcomes, such as surgical complications or urine flow rates, have not demonstrated benefits in patients' health status after treatment.

This research program aims to develop and validate a novel PROM for patients with hypospadias. This protocol describes the qualitative development (phase I) of a new PROM to evaluate outcomes of hypospadias treatments.

METHODS AND ANALYSIS

Phase 1: Qualitative development

Best practice guidelines of the USA Food and Drug Administration (FDA) [12] and the Consensus-based Standards for the selection of health status Measurement Instruments (COSMIN) [13] are being employed to inform the development of this new PROM. Interpretive description, an applied health services research approach, will be used. A systematic literature review was conducted to inform the development of a preliminary conceptual model [15]. Subsequent qualitative interviews with patients aged over 7 years, with a focus on children, teens, young adults with prior pediatric hypospadias care, and their proxies were undertaken to inform the conceptual model further and develop initial items for scale development.

Additional in-depth and semi-structured concept elicitation interviews will be conducted (May 2024-March 2025, including a more heterogeneous sample of patients aged 7 years or older to better understand concepts important to patients seeking treatment for hypospadias. Qualitative data will be used to develop the conceptual model and content further. Cognitive interviews will be performed concurrently to ensure that the scale items, instructions, and response options are relevant, understandable, and comprehensive. Cognitive interviews will inform the final scales which will be circulated to an international group of experts in hypospadias for feedback (estimated May 2025). Concepts elicited and changes proposed by expert informants will be reviewed with patient participants for final scale creation.

Setting

Participants were recruited from the urology clinics at the Children's Hospital of Eastern Ontario (CHEO, Canada) and Boston Children's Hospital (BCH, USA) for the completed concept elicitation interviews. All participants participating in concept elicitation and cognitive

interviews provided informed consent or assent (for participants <16: guardian consent, participant assent) as approved by local institutional review boards or research ethics boards. For the subsequent concept elicitation and cognitive interviews, interested participants will be recruited from the urology clinics at Boston Children's Hospital (BCH, USA) Children's Hospital of Philadelphia (CHOP, USA).

Sample

Participants from the completed concept elicitation interviews were identified through a retrospective search of surgical billing codes within the Electronic Health Record system (EPIC) and new patient referrals to the urology clinic for hypospadias. New patient referrals and existing patients of the urology clinics for hypospadias will be approached to participate in the subsequent concept elicitation and cognitive interviews.

A maximum variation sample will be purposively selected to vary by disease severity (mild to severe disease), stage of treatment (pre- and post-operative), age of treatment, and clinical outcomes, urethral location, and the presence or absence of complications. Definitions of complications are based on a consensus statement from the International Pediatric Urology Task Force on Hypospadias [16].

Recruitment

A care team member recruited participants from the completed concept elicitation interviews, and those who consented to participate were invited to complete an in-person or virtual interview. Subsequent concept elicitation and cognitive interview recruitment will involve care

team members asking patients if they would be interested in participating in the study. Patients will provide written or verbal consent (patients under 16 will assent, their guardians will consent). Patients or parents who consented to participate were invited to an interview on an online platform (e.g., Microsoft Teams or Zoom) telephone interview with an experienced qualitative researcher.

Experts in the field of hypospadias known to our network through the Hypospadias International Society (n=20) will be invited via email invitation to provide feedback on the scales and feedback will be captured through a REDCap survey. This step will ensure that the content of the proposed scales comprehensively measured outcomes that matter to patients and that instructions, response options and items are clear, meaningful and unambiguous.

Data collection

Subsequent concept elicitation and cognitive interviews will follow the same data collection procedures used previously for the completed concept elicitation interviews. All interviews will be audio recorded, transcribed, and coded. Participants will be interviewed using a semi-structured qualitative interview guide, including surgical experience, appearance, function, and psychological well-being probes (Appendix 1). Questions regarding perceptions of ideal hypospadias outcomes will be probed. Topics included in the interview guide will be informed by a systematic literature review of PROMs used in hypospadias. The interview guide will be adapted accordingly to each participant to avoid asking irrelevant questions (e.g., asking young participants about sexual well-being). The interview guide will be adjusted as interviews are

conducted to include any new concepts identified after each interview. Recruitment will continue until saturation (i.e., no new concepts are elicited from the interviews) [17].

Multiple rounds of cognitive interviews will be performed with as many participants as necessary to establish the content validity of the scales. Participants will review the scales via an online Research electronic data capture (REDCap) survey [17] and will be encouraged to use the 'think aloud' approach with probing to obtain feedback on the relevance, comprehensibility, and comprehensiveness of the scale items, instructions, and response options [18-21].

Experts in hypospadias will review the scale content before the final round of patient cognitive interviews. A REDCap survey will be designed with targeted questions about the items' relevance, instructions, response options, and any missing content. Relevant changes suggested in each round of patient interviews and from expert input will be applied and reviewed in a final round of participant interviews.

Data analysis

Subsequent concept elicitation and cognitive interviews will follow the same data analysis procedures used previously for the completed concept elicitation interviews. Data collection and analysis will be conducted concurrently. Concept elicitation and cognitive interview transcripts will be coded line-by-line by a research team member and confirmed by a second member for the first five interviews or until an agreed-upon coding framework is achieved. Coded data will be transferred onto an Excel spreadsheet for analysis.

Participant quotes from the concept elicitation interviews will be categorized into top-level domains and themes/subthemes. Qualitative analysis will refine a conceptual framework covering the concepts concerning people seeking treatment for hypospadias. The coding framework will guide scale development, and codes will inform the development of a comprehensive item pool. Items will be devised such that they retain participant language to ensure that they resonate with patients and are easy to understand. A comprehensive set of independently functioning scales will be formed from the item pool, alongside instructions, a time frame for responding to the scales, and a set of response options. Feedback obtained from the cognitive interviews will be categorized according to the following top-level domains: interpretation, relevance, clarity, missing content, and suggested changes.

Subsequent phases

The phase II field-test study will involve recruitment of a large international sample of participants. We will use the data collected to refine and validate the Hypospadias PRO scales using RMT analysis. This will allow us to identify the items in each scale that can that serve as more accurate indicators of patient outcomes, thereby reducing the length of the scales for patient ease of completion and creating clinically meaningful and valid scales. Once developed and validated, we will conduct further psychometric research to determine each scales' ability to measure clinical change following hypospadias repair.

Patient and public involvement

Our patient-oriented approach engages patients with hypospadias and parents of children and teenagers with hypospadias and healthcare providers in all stages of our research as experts and

research team members whose input is crucial to the design of the study and development of content for our hypospadias scales. Participants involved in qualitative and cognitive interviews will be invited to continue to collaborate in our study by taking part in scale refinement interviews where they can provide feedback on our findings and help to refine the final set of scales. We are collaborating with patients and families to host a patient centered hypospadias conference in the Summer of 2026, where study results will be presented for discussion and further dissemination in patient centered research.

ETHICS AND DISSEMINATION

Ethics approval was obtained from Boston Children's Hospital's Institutional Review Board (HHS Registration: IRB00000352; Protocol number IRB-P00042425). CHOP, McMaster and CHEO have reliance agreements with Boston Children's Hospital. Participants will provide written and audio-recorded verbal consent (for participants <16: guardian consent, participant assent). Participants will be de-identified from their transcripts, and institution rules for data storage will be followed.

Once developed, this new PROM will be made available to license free for all non-profit users. We will seek to advertise and promote its use through presentations at national and international meetings. Findings about the development will also be published in relevant peer-reviewed journals for the target audience.

Author contributions

MAK initiated the study at BCH and CHOP, designed the qualitative interview guide, conducted qualitative interviews, coded interview transcripts, drafted and revised the paper. ET conducted qualitative and cognitive interviews, coded interview transcripts and drafted and revised the manuscript. SG designed interview guide, conducted qualitative and cognitive interviews and coded interview transcripts. CL implemented the study at CHOP, participated in research planning meetings and revised the manuscript. EM and LB participated in research planning meetings and revised the manuscript. AK provided mentorship in designing the interview guide, provided mentorship in coding interview transcripts, scale design and revised the manuscript. MK is the guarantor.

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Appendix 1: Hypospadia Interview Guide.

(Note: Confirm Consent Form was Reviewed & Understood on Tape).

Preamble: This study is to create a new questionnaire for children and teenagers or young adults with hypospadias. I would like you to tell me stories that will help me to understand what it has been like for you to have had a hypospadias, or possible hypospadias surger. Should any question make you uncomfortable, you are free to decline responding. Further, you may stop the interview at any time, and you have the right to withdraw your participation.

Background Questions:

1. Can you us how you learned that you had hypospadias? [Probe: age, informed by parent/health provider, description of the condition, at what age?]

2. Tell me about how you felt when you learned that you had hypospadias? [Probe: feelings, emotions, concerns, past versus present feelings]

Experience of Care:

3. Based on what you remember, what treatments have you had for your hypospadias? [Probe: how old were you when you had your treatment? personal experience/knowledge vs. what you have been told]

4. What was helpful about the treatment(s)? [Probe: what did you like, did you feel better - how]

5. What did you dislike about the treatment? [Probe: problems/bad things associated with treatment]

6. Who did you (OR who do you still) see at the hospital or clinic? [Probe: doctor, nurse, receptionist].

7. What were the people who cared for you like? [Probe: friendly, made you feel comfortable, easy to talk to, listened to you, explained things to you, anything you disliked?]

8. At the hospital, who explained your hypospadias to you? [Probe: understanding] How did they explain your hypospadias to you? [Probe: talking, showing pictures, drawings, written information]

9. Tell me about how recent decisions were/are made about your treatments (e.g., getting surgery)? Were you involved in making decisions about your treatments? If yes, then ask:
    a. What factors influenced your decision to go through (or not go through) these treatments? [Probe: appearance, function]
    b. Did anyone influence your decision regarding treatments? [Probe: family, health providers]

10. Did you have any recent surgeries/treatments that you can remember? If so, what kind of information (verbal, written, visual) did they give you to prepare for surgery? [Probe: about nature of surgery; did you understand the information; did you get to ask questions; did they provide information about how to care for yourself after the surgery]

11. Tell me about anything you remember regarding your recovery (OR getting better after your surgeries OR what happened after your surgeries)? [Probe: any pain, swelling, or bruising; were you taking medications; any trouble with catheters/dressings; any difficulty urinating/peeing; any infections/fevers; any itching; how long has the recovery time been so far]

Complications:

12. Did you notice any problems after the surgery OR did anything go wrong after the surgery? [Probe: any complications]. If yes, then ask:
    a. How did you know something was wrong? [Probe: did you know OR did someone else notice it; did you tell anyone – who/when]
    b. How did you feel about these problems (complications)? [Probe: emotions, fear, worry]
    c. What happened after the complication occurred (saw physician, went to ER, seen in follow-up). What was the outcome of these visits? (surgery, plan to watch)
    d. Were you happy with how any problems regarding your treatments were handled?

Appearance and General Function:

13. At this time (presently), how satisfied you are with your urinary function (i.e. going to the bathroom or peeing)? [Probe: easier/difficult, better/worse than before, level of satisfaction – happy]

14. Can you describe what it looks like, or feels like when you go pee? (probe pee goes straight, downwards, looks narrow/thin/spray, stream, pain, urgent/uncomfortable, accidents or dribbling, etc)

15. I know some of these questions may be difficult or personal, so share whatever information you feel comfortable sharing. Are you happy with the way that your penis looks now? [Probe: skin, shape, position of opening, curvature, size, scars, foreskin, scrotum, testicles etc.]. If you are not happy with how your penis looks (as are many men), what would you like to change?

16. Are you comfortable to use public bathrooms or change in public? Do/did you ever hide your penis/private region (genitals) from others (e.g., when going to the bathroom, changing in change room, etc)? If yes, how did you do this? Why did you do this?

17. Have others ever made comments about the appearance of your genitals or about how you pee/void? Can you give us some examples? How did those comments make you feel?

Psychological Wellbeing

18. How has having hypospadias impacted your overall life? Has it had any major impact on your wellbeing? Relationships with others (parents, siblings, friends, girlfriends etc)

19. How does the appearance of your penis make you feel? [Probe: happy, sad, anxious, worried, frustrated, self-conscious, self-esteem, body image]

20. How does the urinary function (peeing/voiding) of your penis make you feel?

Social Life:

21. Do you talk to others (family members, friends) about hypospadias? Do you feel that having hypospadias has impacted you socially in a positive or negative way?

22. More specifically, does your hypospadias/penis (AND/OR treatment/hospital care) affect your life at home? [Probe: siblings, relatives, friends, time management]

23. Does your hypospadias/penis affect your experience at school/college? [Probe: in classroom; in sports and activities; in change rooms; in the bathroom]

24. Does your hypospadias affect your social life such as your interactions with other same-aged peers, friends, etc? [Probe: possibility of being teased/bullied; meeting new people; dating; sex life]

25. Is/was there things you would have liked to do but didn't because of your hypospadias/penis? [Probe: swimming, changing in public locker rooms, sports, sleepovers]

26. Do/did people treat you differently because of your hypospadias? [Probe: family; friends; students; teachers; others]

Puberty, and Sexual Function & Wellbeing

27. [Determine if child identifies/describes going through puberty – if has adult male voice (aka – deep not pre-pubescent]. I know this question might be difficult, but in order to ask some other questions, it is important for us to know if you have any signs of puberty (voice change, pubic hair etc)
    a. Do you remember when you started puberty? (can explain, voice change, new body hair, penis/testicles became larger?)
    b. Did you have any concerns regarding your hypospadias when you went through puberty. Did you notice any improvements (urinary flow?) or new problems (curvature/appearance)?
    c. When you have erections, do they appear straight? (probe curved) Is there any pain, discomfort?
    d. Do you have any concerns about your erections or penile sensation? (curvature, lack of sensation where scars are, pain, impotence). Probe regarding ejaculation, any concerns (decreased amount/flow/sensation)
    e. Have you ever dated anyone? Been in a relationship? If not, did your hypospadias have any impact on this? Other reasons?
    f. Does your hypospadias/penis influence your dating behaviours [Probe: present/future concerns, feelings/emotions]

g. Have you had prior sexual activities (masturbation, sexual contacts). If yes, do you find that your hypospadias interferes with your ability to masturbate/fool around/have sex? [Probe: how so; erection/orgasm difficulty, embarrassment/in the dark only/ avoid sexual contact with others. If sexually active – curvature, ejaculation, difficulties obtaining, maintaining erection.]

Other Questions

28. If you could talk to a young boy or a family of a young boy with hypospadias, what do you think would be important for them to know?

29. Is there anything about your care for hypospadias that you would have like to have done differently? [probe: timing of surgery, number of follow-ups, how it was talked about by MDs/family]

30. Is there anything I have not asked you that you think it is important for me to know in order to understand young people's experience with hypospadias?