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Understanding patient and caregiver perspectives using a dyad approach for data collection: A systematic review of the literature

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Cover Page Footnote

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Understanding patient and caregiver perspectives using a dyad approach for data collection: A systematic review of the literature

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Abstract

Treatments outside of a clinical setting may be managed independently by the pediatric patient, independently by a caregiver, or by the patient and caregiver together. Best practices for pediatric clinical outcome assessment (COA) recommend patient-reported outcome (PRO) and/or observer-reported outcome (ObsRO) measures to assess the patient experience of a condition or its treatment. However, a dyad approach where patients and caregivers can complete assessments together may be useful for assessing a shared treatment experience that may not be adequately captured by a PRO and/or an ObsRO. A systematic, targeted literature review of empirical literature was conducted to identify and describe published studies detailing dyad patient-caregiver outcome reporting approaches. The search was run in the MEDLINE®, Embase, and PsycINFO® databases using the OvidSP platform and was limited to English-language studies published within 10 years of the conducted search on 28 September 2021, and 13 articles were selected for full-text review based on pre-specified criteria. Advantages and disadvantages for use of a dyad data collection approach are discussed. Though not appropriate for all settings, dyad data collection may be useful for situations where the best practice approach to measurement does not capture all relevant perspectives, or the use of PRO and ObsRO also does not comprehensively capture all relevant concepts. In following, it may offer a pragmatic solution that can minimize the use of proxy assessment and limit missing data, particularly in research involving a shared patient and caregiver treatment experience.

Keywords

Clinical outcome assessment, data collection method, pediatric, dyad, caregiver, shared experience

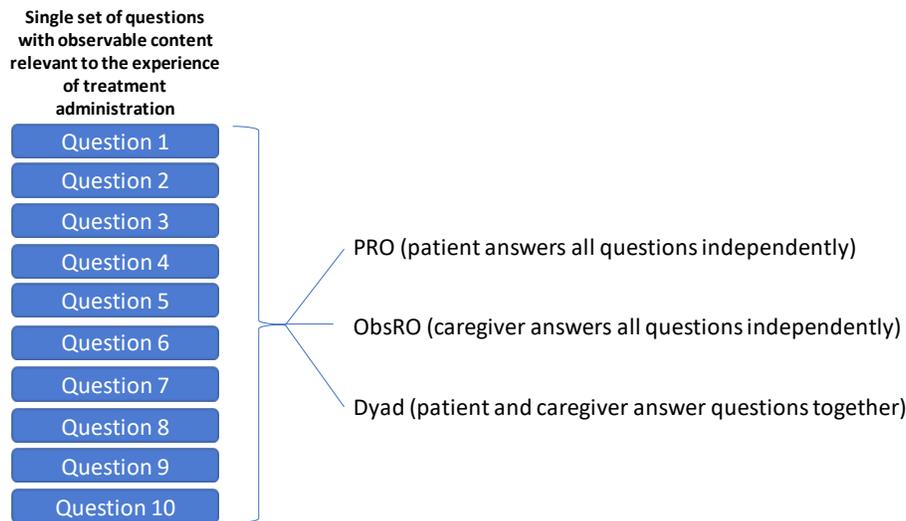
Introduction

Clinical outcome assessments (COAs) are used to measure a wide range of outcomes including those associated with treatments such as reduction in disease-related symptoms and health-related quality of life impacts or the burden of treatment on the lives of patients and caregivers. COA strategies for children and adolescents may involve patient self-report via patient-reported outcome (PRO) measures, and informant reports through observer-reported outcome (ObsRO) or proxy measures, depending on the ability of the patients.¹

PRO measures consist of questions answered by the patient themselves about the status of their health condition without interpretation of the response by an observer such as a clinician or a caregiver.² While PRO measures are the most direct approach to collecting the patient perspective, informant reports may be needed

when a child or adolescent is unable to reliably self-report (i.e., understand the question and independently select responses) using a PRO measure and in these cases ObsRO or proxy measures may be used (Figure 1). ObsRO measures include questions answered by someone other than the patient or clinician that require the respondent to answer based on directly observed behavior (what they have seen or heard, without interpretation or inference).² Proxy-reported outcome measures also include questions answered by someone other than the patient, but differ from ObsRO measures as they require the respondent to make inferences about the patient's subjective experience.² Proxy reports have been used historically to obtain data in scenarios where patients may not be able to provide input, and may provide useful data from the caregiver perspective, but responses on these measures can differ from PROs and the US Food and Drug Administration (FDA) guidance in COA^{2,3} discourages the use of proxy-reported outcomes for any

Figure 1. Reporting options suggested for the assessment of treatment administration experiences involving a patient and caregiver



age group, including children and adolescents. There are reports in the literature that the expressed perceptions of a child may differ in magnitude or importance from the caregiver. Research has demonstrated better agreement between child- and caregiver-report when the caregiver is more directly involved in the care of the child^{4, 5} and when events are directly observable by caregivers (e.g., physical function, activities of daily living) compared to experiences that are non-observable (e.g., symptom severity or emotional impacts).

While PRO measures are the preferred approach to assessing the breadth of the patient experience, best practice guidelines^{1,2,6-9} recommend the use of ObsROs when children are not able to independently complete a PRO. ObsROs are limited to the assessment of observable concepts, based on direct observations of the child or what the child has said within a specified time period.¹

While PROs and ObsROs are appropriate for assessing direct and observable concepts from patients and informants (e.g., caregivers), respectively, another approach is needed to support the assessment of treatment experiences that are shared by the child and caregiver. This is particularly important as the level of involvement that caregivers have in treatment administration may vary from patient to patient based on a myriad of factors (e.g., age, experience, and cognitive ability).

Medicines administered outside of a clinical setting (i.e., at home, school, camp, etc.) to children and adolescents may involve varied routes of administration, including but not limited to oral (solid or liquid), nasal, inhaled, rectal,

cutaneous or transdermal, ear, eye, parenteral, subcutaneous or intramuscular injection, or IV infusion.¹⁰ Given the range of administration options and varied requirements in preparation and follow-up of these treatments, there are contexts involving a shared experience, in the management of a condition or its treatment, that may not be adequately captured through the administration of only a PRO and/or an ObsRO measure. For example, when administering medicines at home, there may be special considerations for regimen or schedule, dosing and measuring devices to aid administration, storage to support the optimal treatment effect for the patient, and supervision post-administration to monitor for side effects that require support from the caregiver. Assessing all of these factors within a shared treatment administration model can be challenging, particularly if the patient and caregiver are sharing the experience and responding to separate COA measures as responses may conflict, or the approach taken by the caregiver and the child may vary from administration to administration.

This literature review explored a dyad approach to data collection, wherein the child/adolescent and caregiver provide input together on a COA measure in the context of qualitative or quantitative data collection in instances where a separate PRO or ObsRO would not fully capture the treatment experience. Understanding the ways in which dyad reports have been employed in qualitative and quantitative research (for COA instrument development and other purposes), including the advantages and limitations of the approach, can provide useful information for future applications.

Methods

A systematic and targeted review of empirical literature was conducted to identify published studies detailing dyad patient-caregiver outcome reporting approaches. A search strategy was developed to identify abstracts for articles that may provide additional details on the dyadic data collection approach and the associated advantages/disadvantages. More specifically, the search strategy employed terms related to the dyad approach (e.g., dyad, dyadic, and shared decision), the parties involved in dyadic data collection (e.g., patient, caregiver, and parent), and the data collection method (e.g., PRO, questionnaire, and interview).

The search was run in the MEDLINE®, Embase, and PsycINFO® databases using the OvidSP platform and was limited to English-language studies published within 10 years of the conducted search on 28 September 2021. The resulting abstracts were screened using Abstrackr,¹¹ a web-based program used to screen abstracts and document whether or not each abstract was relevant to the research question (i.e., meets the study inclusion/exclusion criteria).

Abstracts were considered for inclusion if they were published in peer-reviewed journals and primarily focused on the administration or application of a dyad approach to data collection in a qualitative study or quantitative study and appeared to provide commentary on the advantages and disadvantages of the approach.

In addition to the systematic search, a grey literature search was conducted using Google, Google Scholar, and a review of reference lists in selected articles to identify additional literature related to the key research question.

The grey literature search was not restricted by publication year (i.e., articles published more than 10 years prior to the search were considered), though the same inclusion and exclusion criteria described above for the targeted search were applied.

Studies were excluded from full-text review if they focused on shared decision-making or dyad discussions in other contexts (e.g., treatment decision-making), or if study data were collected from a patient and caregiver independent of one another for comparative purposes. Studies that utilized a dyad approach to data collection but did not appear to provide additional commentary on the approach were not considered for full-text review but were recorded to better understand the frequency with which the dyad approach has been utilized within the published literature.

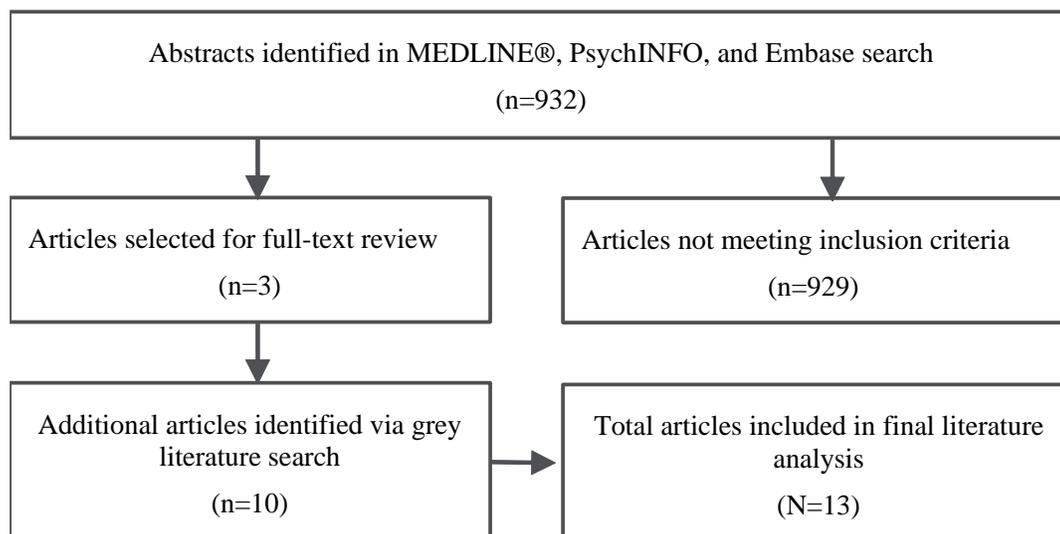
Articles selected for full-text review were reviewed in full and data related to the use of the dyad approach and the author's commentary on the approach were summarized. The holistic results of the study summarize the identified studies including the methodology employed, provide commentary on the use of the dyad approach as reported in prior studies, and highlight the advantages and disadvantages of the dyad data collection approach.

Results

Results of targeted search strategy and grey literature search

The targeted search strategy yielded 932 abstracts. All abstracts were reviewed, and ultimately three publications were selected for full-text review that appeared to primarily focus on a dyad data collection approach and the associated benefits and disadvantages (Figure 2). An additional 10 publications were identified via Google

Figure 2. Search flow diagram



Scholar search, as well as through a review of reference lists of selected publications, that met the study inclusion and exclusion criteria. Thus, a total of 13 full-text articles were included in the final analysis. Among these, 11 presented original research findings, one was a review article, and one was a guidance document. Table 1

presents an overview of the 11 articles presenting original research findings.

An additional 16 studies were identified that utilized a shared dyad approach to data collection in qualitative research (n=14 studies), quantitative COA data collection

Table 1. Overview of original research studies (n=11) included in review

Citation	Target patient population	Research focus	Data collection method	Country	Sample size n	Patients	
						Age (years) Mean (min-max)	Sex n
Coutant et al. 2017	Pediatric growth disturbance	Efficacy of injection device	Dyad questionnaires	France	409	11.3 (1.1-18.1)	Male: 225 Female: 184
Eisikovits Z. and Koren C. 2010	“Second couplehood” in old age	Effectiveness of dyad interview approach	Dyad and individual interviews	Israel	40	Not reported (66-92)	Not reported
Etschmaier M. et al. 2009	Growth hormone deficiency (GHD)	Development of dyad questionnaire to assess injection pen administration	Dyad interviews and focus groups	U.S.	8	Not reported	Not reported
Hey-Hadavi et al. 2010	GHD	Dyad perception of injection device	Dyad questionnaires	U.S.	133	12.4 (range not reported)	Male: 91 Female: 45
Morris, SM 2001	Cancer (breast, lung, colorectal, lymphoma)	Effectiveness of dyad interview approach	Dyad and individual interviews	UK	<i>Dyad:</i> 19 <i>Individual:</i> 41	<i>Dyads:</i> 58 (26-76) <i>Individual:</i> 57 (32-83)	<i>Dyads:</i> Male: 10 Female: 9 <i>Individual:</i> Males: 10 Females: 18
Neveus T et al. 1999	Enuresis and incontinence	Role of sleep on nocturnal enuresis	Dyad questionnaires	Sweden	1,413	7.9 (6.2-10.9)	<i>n-value not reported</i> Male: 49.3% Female: 50.7%
Pleil et al. 2012	GHD	Development and psychometric performance of dyad questionnaire to assess injection pen administration	Dyad questionnaires	U.S.	136	12.3 (range not reported)	Male: 91 Female: 45
Taylor B. and de Voche H. 2011	Cancer, motor neuron disease	Experience of sexuality and intimacy living with life-limiting illness	Dyad and individual interviews	UK and Netherlands	Not reported	Not reported	Not reported
Turner Bowker DM et al. 2020	GHD	Use of dyad questionnaire to assess human growth hormone injection treatment burden	Dyad and individual interviews	U.S.	21 <i>Adult:</i> 6 <i>Pediatric:</i> 15	<i>Adult:</i> 47.9 (32-60) <i>Pediatric:</i> 9.7 (4-15)	<i>Adult:</i> Male: 4 Female: 2 <i>Pediatric:</i> Male: 11 Female: 4
Ungar et al. 2006	Asthma	Ability of dyads to assess Health-related quality of life (HRQoL) in children	Dyad interviews	Canada	16	10.7 (8-15)	Male: 9 Female: 7
Ungar et al. 2012	Asthma	Ability of dyads to assess HRQoL in children	Dyad questionnaires	Canada	91	10.9 (8-17)	Male: 50 Female: 41

(n=1), and both qualitative shared dyad qualitative and quantitative COA data collection (n=1); however, these studies did not report details or advantages/disadvantages of the method.

Dyad data collection in qualitative interview research

A growing body of literature describing the use of various dyadic approaches in qualitative research has emerged over the last few decades; in particular, for interview studies. Eisikovits and Koren (2010)¹² describe and compare the advantages and disadvantages of several dyadic qualitative interview approaches including separate interviews with each member of the dyad, single interviews conducted jointly with both dyad members, and a combined (i.e., separate and joint interview) approach.¹² Eisikovits and Koren (2010) suggest that the best quality data may be collected through interviewing each dyad partner separately, in order to capture each participant's unique perspective, and then use the dyad data (rather than individual data) as the unit of analysis.^{12,13} Still, Eisikovits and Koren (2010) also suggest that interviewing dyad participants jointly can provide a unique third perspective (i.e., the shared perspective of both dyad members) that is not captured through discussion with each individual dyad member and allows researchers to observe and analyze the interactions between dyad members that may be particularly helpful in some contexts (e.g., caregiver-patient relationships).^{12,14} The authors also note that when the goal of research is to compare and contrast the perspectives of individuals within a dyad, separate interviews with each individual may be ideal; one limitation of this approach is that it only provides the individual perspective of each dyad member rather than the "shared" perspective, which can be important in contexts where the patient and caregiver share in an experience together.¹² Another study, by Taylor and deVocht (2011) suggests that a limitation of interviews conducted jointly with both dyad members is that, while it can offer the perspective shared by both participants, the collected data does not necessarily represent an "average" perspective of the participants and similarly, the shared perspective cannot necessarily be presumed from interviews conducted individually. The authors therefore suggest using a dyad approach when the goal of the research is to explore the shared experiences among members of the dyad.¹⁵

Dyad approach in qualitative COA development research

In standard practice, qualitative concept elicitation interviews are commonly conducted with members of a target patient population to identify the important and relevant signs, symptoms, and impacts of a condition or its treatment. Converging evidence from patient concept elicitation interviews, meetings with clinical experts, and the empirical literature informs the selection of concepts to be measured in a COA. Once a COA has been selected or developed, qualitative cognitive debriefing interviews

are commonly conducted with members of the target patient population to evaluate respondent ability to understand and respond independently to questions.

In the context of concept elicitation interviews, the *ISPOR PRO Good Research Practices for the Assessment of Children and Adolescents Task Force*¹ mentions dyad administration. While the ISPOR Task Force's general recommendation is for pediatric concept elicitation interviews to be conducted without a caregiver present, it recognizes that there are "some context-specific exceptions to the recommendation that child concept elicitation interviews be conducted without a parent present" (p. 467). Matza et al (2013) note that when researchers are interested in collecting the shared perspective of patients and caregivers in a questionnaire, "it may be useful to develop the questionnaire based on dyadic rather than individual concept elicitation interviews" (p. 467).¹ The ISPOR Task Force further acknowledges that there is "some support for a parent-child dyad approach to assessment of the child's HRQOL, as opposed to the concept elicitation phase of PRO instrument development" (p.467).¹

While this approach has not been widely discussed, there are examples in the empirical literature of COA qualitative concept elicitation and cognitive debriefing interview research involving a dyad approach to data collection.

For example, one recent study conducted qualitative interviews¹⁶ with patient and caregiver dyads during the development of a novel COA, the Life Interference Questionnaire for Growth Hormone Deficiency (LIQ-GHD) (a modified version of the Injection Pen Assessment Questionnaire, or IPAQ),^{17,18} to capture the burden of long-term recombinant human growth hormone (r-hGH) replacement therapy administered via daily subcutaneous injections to treat growth hormone deficiency (GHD) in children, adolescents, and adults. The LIQ-GHD is novel as it includes several modules that can be used depending on who is completing the questionnaire. Specifically, the LIQ-GHD includes options for child/caregiver dyad-report (e.g., on shared injection administration experiences, such as those relating to pen preparation, dose settings, injection, storage), self-report (e.g., by children who independently manage their injections), or caregiver-report (e.g., by caregivers who manage all aspects of the injections for their child). For dyad-report modules, the dyads were instructed to read and answer questions together; however, the questions could be completed independently by the patient or caregiver given the wide target participant age range and varied ability levels. Data are collected relating to document "who reported" on the measure (i.e., the patient, the caregiver, or both as a dyad). A module has been included to allow patients 8-17 years of age to self-report symptoms associated with injections, and a caregiver-reported module assesses the injection-related

signs for pediatric patients <8 years. There are also caregiver-reported modules assessing the impact of daily injections on the caregiver and family.

Though it has limitations, the LIQ-GHD may offer a practical solution for the collection of treatment injection experience data, given that the level of caregiver involvement in the preparation and administration of injections varies from dyad to dyad, and is not necessarily dictated by the age of the patient.¹⁶ This dyad method of data collection can be used to address challenges in consistency of data collection in a clinical trial setting as the approach recognizes that the characterization of the treatment administration may not adequately be captured by separate PRO and ObsRO measures and could result in missing data on those questions not relevant to the experience of the patient (on the PRO) or to the caregiver (on the ObsRO), if one or the other has not been responsible for certain tasks in the injection procedure.

As part of the broader LIQ-GHD development study,¹⁶ 90-minute in-person combined concept elicitation and cognitive debriefing qualitative interviews were conducted with 15 patient/caregiver dyads. The patients were children 4-12 years of age and adolescents 12-17 years of age. During interviews, participants were first asked open-ended questions about the burden and impact of the injection treatment. Questions were initially directed to the pediatric patient; after the patient shared their perspective, the interviewer prompted the caregiver to share any additional comments. Some questions (e.g., symptom experience) were asked only of the patient while other questions (e.g., impacts on the caregiver and family life) were asked only of the caregiver.

The second part of each interview focused on cognitive debriefing of the draft LIQ-GHD, during which the child/adolescent and caregiver participants were asked to read the questionnaire and answer questions to support evaluation of the tool's relevance, comprehensiveness, and comprehensibility. During cognitive debriefing, participants were not provided instructions or guidance as to which participant should respond to the question and instead allowed the patient and caregiver to read the instructions and choose which participant responded to each question. Given the broad range of patient ages (4-15 years of age), and that the responsibilities for preparing and administering the injections differed for each patient/caregiver dyad, the way in which each pair read and answered the questions varied. Overall, the content of the LIQ-GHD core questions, relative to the age and ability of patients, dictated who was able to respond to each question. Findings indicated that generally, the person or persons primarily responsible for the task responded to the questions. If the patient completed the task, the patient suggested the answer to the question or led that discussion with the caregiver and vice versa. For

example, caregivers were more likely to lead the discussion on a reply to the question on the preparation and storage of the injection pen if they were the dyad member responsible for those tasks. When patients and caregivers responded together to a question as a dyad, it took the form of a negotiation and in this study no overt coercive behavior (i.e., pressuring the child to change their reply) was observed on the part of caregivers during the interviews.

While results from this interview study were useful in defining age limits for self-reporting on symptom questions (ages 8 years and older), findings also suggest that it is not appropriate to consider a single age-based cut-off for the administration of questions to assess shared injection experiences; for example, in this study, a 7 year old managed injections and reported independently on the experience, and two participants, ages 11 and 13 years, managed injections together with their caregiver and responded to questions in a dyad fashion (see Table 2).

In another example, Ungar et al (2006)¹⁹ conducted a joint qualitative interview study that employed a "complete" dyad approach involving 16 pediatric patients ages 8-15 years with asthma, and their primary caregiver, to investigate a dyad approach when answering standardized health-related quality of life (HRQOL) measures developed for patient-reported administration. Two disease-specific and two generic HRQOL PRO measures were administered to pediatric patients and their caregivers. The objective was to observe and describe the interaction between the pediatric and caregiver dyads during questionnaire completion. The approach employed a dyad reporting "option." While the introduction to the questionnaire focused assessment by the child, the children were also encouraged to ask the parent for help when needed; likewise, the parent was instructed that they intervene to assist their child when needed. The response represents some combination of input from the child and caregiver, a "shared response" that may contribute a unique perspective beyond that which may be possible through individual and separate reports from the child or caregiver.

Findings suggest that parents were an important resource to their child during completion, helping with issues involving recall, response bias, frustration, anxiety/discomfort, and comprehension; though the authors report some evidence of parental coercion. During the completion of questions, parents supported the pediatric patient with the recall period by providing a "bookmark" (specific reference point/event that happened in the same timeframe) to help the child recall the time period. Parents also supported the child in avoiding social desirability bias (e.g., tendency to provide answers expected to be socially desirable rather than the truthful

Table 2. LIQ-GHD hybrid concept elicitation and cognitive debriefing using a dyad-report approach

Patient	Age (years)	Primary CE Respondent	Primary CD Respondent
01	4	Caregiver	Caregiver
02	5	Dyad (patient and caregiver)	Dyad (patient and caregiver)
03	6	Dyad (patient and caregiver)	Caregiver
04	6	Dyad (patient and caregiver)	Dyad (patient and caregiver)
05	7	Dyad (patient and caregiver)	
06	9	Dyad (patient and caregiver)	Dyad (patient and caregiver)
07	10	Dyad (patient and caregiver)	Dyad (patient and caregiver)
08	11	Dyad (patient and caregiver)	Dyad (patient and caregiver)
09	11	Dyad (patient and caregiver)	Patient
10	11	Dyad (patient and caregiver)	Patient
11	11	Dyad (patient and caregiver)	Patient
12	13	Dyad (patient and caregiver)	Dyad (patient and caregiver)
13	13	Patient	Patient
14	13	Patient	Patient
15	14	Patient	Patient

response) by reminding and reassuring the child that they can respond based on their experience (i.e., “there are no right and wrong answers”) with no negative repercussions. Parents identified moments of frustration on behalf of the child (e.g., restlessness, disinterest) and suggested times when the child may need a break.

While children were encouraged to answer questions, there was discussion and negotiation for answers to questions that occurred between the child and parent. However, parental coercion/influence was observed to some degree in 10 interviews as evidenced by the caregiver questioning the accuracy of the child’s answer, encouraging the child to reconsider their answer, pressing the child to answer quickly when it was evident the child needed more time, and/or silencing/redirection of the child. Instances of coercion appeared to occur more in dyads with children ages 8-10 years. Some participants also appeared to answer a certain way to avoid perceived inter-relational conflict. In this study, interviewers redirected questions to the child participant to overcome parental coercion and reminding the dyad that the interviewer was interested in hearing the child’s perspective.

Some children expressed feelings of anxiety or discomfort when asked questions about their past, present, or future health state. As a strategy to address this issue, the parent or interviewer assured the child that it was okay to answer based on how they feel, or that they do not need to answer at all. During the dyad interviews, parents were found to play an important role as advocate and enabler including the provision of additional information to the interviewer and ensuring that the child was comfortable with the interview process (advocacy) and encouraging the child to answer based on their own feelings and perceptions, translating questions into words that the parent knows the child understands, and guiding the child through the response options (enabling). Comprehension issues were common, particularly among those 8-10 years old, and

strategies used by the parent encouraged the child to ask clarifying questions, to ask the interviewers to repeat a question, or to explain the meaning of a questions or words or phrases.

Ungar et al. noted that while parental coercion is an important limitation to consider, it may be managed through interviewer-administration of the COA with a skilled facilitator using targeted redirection strategies. Ungar et al also suggest that dyad questionnaire administration may better capture “multi-factorial aspects of paediatric HRQOL” than individual assessments of the child or parent. These findings suggest that future studies involving the administration of HRQOL measures to dyads may benefit from interviewer-administration, which provides the opportunity for clarification of instructions and redirection when needed. The authors recommend that findings from this interview study can be used to inform the development of an interview guide to support administration of HRQOL measures with child/parent dyads.

Dyad report in quantitative research

Following best practices for questionnaire development, after COA content has been evaluated in cognitive debriefing research, the finalized version is administered to participants as part of a quantitative study to enable the analysis of item distributional properties, factor structure, score psychometric performance (reliability, validity, ability to detect change) and score interpretation (e.g., clinically meaningful change). COAs can then be implemented in a wide variety of research studies.

Currently there are a limited number of published studies documenting the use of a dyad approach in quantitative COA studies, and of those identified and summarized below, the details describing administration procedures vary by study.

Coutant et al (2017)²⁰ conducted a cross-sectional observational survey study to evaluate the use of SurePal™, a reusable self-injection system for use in pediatric patients (ages 1-18 years) who have growth disturbances. Approximately 57% of children completed the questionnaire independently, while 43% had assistance from another person (e.g., a family member). No details are provided on the procedure utilized for shared questionnaire completion among this latter child/caregiver group. In this same study, half of the children prepared the injection on their own, while nearly half had a family member (47%) or nurse (2%) prepare the device for them. Of those reporting, 44% of children performed the injections themselves; 52% of children had a family member perform the injection; and 2% had a nurse perform the injection. The authors do not report instances when injections were performed as a shared task between the child and family member.

The IPAQ (pre-cursor to the prior described LIQ-GHD)¹⁸ was developed to assess child/adolescent (≥ 8 and ≤ 18 years of age) and caregiver perceptions regarding ease of use and preference for attributes of injection pens used to administer daily injections of r-hGH.^{17,18} The IPAQ was intended for completion by child/caregiver dyads as the experiences and responsibilities associated with r-hGH injection therapy (e.g., the injection process) are often shared by children and their caregivers. Results reported in the IPAQ psychometric evaluation study provide a glimpse at these varied responsibilities, with the child (17.6%), mother (64.0%), father (16.2%) or other caregiver (2.1%) responsible for preparing the injection, and the child (26.5%), mother (56.6%), father (15.4%), or other caregiver (1.4%) responsible for administering the injection.¹⁸ The developers suggest that a dyadic approach is particularly useful in measuring activities that involve high parent-child interaction and may help overcome concordance issues that are sometimes found when assessing the child and parent separately.¹⁸

As part of a US multicenter, open label study, Hey-Hadavi et al (2010)²¹ collected data from 133 children ages 8-18 years currently being treated with r-hGH and their caregivers using the IPAQ to assess ease of use and preference for a new disposable r-hGH injection pen. Here, one section of the IPAQ was administered at baseline (assessing perceptions of the reusable pen) and other components of the IPAQ were administered after two months of using the new pen (assessing ease of use of both pens, comparative ease of use of the two pens, and pen preference). Specific instructions were provided to the child and caregiver for how to work together when completing the IPAQ. Dyads were asked to select a single response to each question, agreed upon by both the parent and caregiver. Any disagreement around what response to select was to be resolved by the dyad with no intervention from the study coordinators. In this study, most (82.4%)

caregivers were the child's mother, and in most cases the caregivers were responsible for the preparation (82.0%) and administration (72.9%) of the injections.²¹

In research that quantitatively evaluated the LIQ-GHD (as previously described), Turner-Bowker et al (2020)¹⁶ conducted an online, cross-sectional observational study to test the tool's hypothesized factor structure and score reliability and validity in a sample of clinician-diagnosed adult (≥ 18 years) and pediatric (child [3-11 years] and adolescent [12-17 years]) patients receiving daily r-hGH injections for GHD. A total 224 patients participated, including 70 child/caregiver dyads, 79 adolescent/caregiver dyads, and 75 adults. The child/adolescent dyad version of the LIQ-GHD included questions for completion by the child/adolescent only (e.g., sign and symptom questions for self-report when ≥ 8 years of age); questions for completion by the caregiver only (e.g., caregiver and family impact questions); and questions with the option for dyad completion (e.g., treatment impact on HRQOL; shared injection experience). For the dyad administration, the patient and caregiver participants were instructed to read and answer the questions together. Results, reported for the overall sample and by age subgroup, demonstrated that the collection of quantitative data using dyad administration is feasible and indicate that the scores produced by the LIQ-GHD are reliable and valid.

Extending upon initial qualitative research¹⁹ in this area, Ungar et al (2012)²² evaluated the psychometric performance of HRQOL and utility scores from measures that used a parent-child dyad approach for data collection. Specifically, data were collected from 91 child/adolescent patients who have asthma and their caregivers via the Health Utilities Index (HUI) 2 and 3, the Pediatric Quality of Life Inventory™ (PedsQL™) Core and Asthma modules, and the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) using a dyad approach. The questionnaires were interviewer-administered to the dyad with the interviewer serving as moderator, facilitating dialogue between parent and child as they completed the questionnaire and selected responses. This dyadic approach, promoting discussion among members of the dyad and clarifying perspectives, was described as one that more closely resembles real-life communications. Two interviewers were trained on the study instruments and administered the HRQOL measures in a random order between dyads (no counter-balancing within the dyad) with questionnaires first administered by interviewers to the parent and child separately, and immediately following this, were then administered again but to the child and parent together as a dyad. Cards with response options printed on them were provided to the respondents. Questions were read out loud and the respondent could answer aloud or point to the selection on card. During the dyad administration, one trained interviewer administered

the questionnaires to the child and parent using an interview guide. The interviewer encouraged the child and parent to share their thoughts out loud as they considered a response to a question; moderated to keep the discussion on track; and validated comments using repetition of words used by the child and/or parent. The interviewer encouraged the child and parent to discuss the questions together (rather than with the interviewer) and to resolve disagreements by clarifying their respective perspectives, although achieving consensus in perspectives was not required. Only the child's responses to the questions were recorded. No differences were found between dyad and independent administrations for the time to complete questionnaires, and for the dyads, the time to complete decreased over time.

Ungar et al described their perspectives on the advantages and disadvantages of their approach. They noted that since some younger children are still developing cognitively, a parent can help in the elicitation of preference data; help to “mitigate the confounding effect of changing cognitive skills” (page 9); help a child's recall ability (bookmarking the recall timeframe to events in the child's life); and/or “lend some objectivity to observable symptoms and behaviors in children of all ages” (e.g., noting, for example, that children may not know that what they are experiencing are symptoms of a disease, or what constitutes “normal” for a domain). Ungar et al also noted that a parent's presence can inhibit response bias or the patient selecting the same response across multiple questions (which can minimize missing or unreliable data) and noted that the findings from their study demonstrate the volume of missing data for the HUI decreased from 21% to 2%.

Ungar et al emphasize how their method (interviewing a child and parent together) closely resembles how information is obtained about a child's health status in a clinic setting. In terms of disadvantages, Ungar et al, acknowledged that those serving in the role of interviewer require special training to administer, facilitate, and “ensure accurate capture of information” (p.10) and that the child's preferences may be influenced by the parent. Noting how important it is for the young child's voice to be heard, they describe that “careful steps were taken to mitigate bias or coercion by the parent and only the child's preferences and responses were recorded...[and] the interviewer's role as a facilitator will encourage expression by the child” (p.10).

Discussion

A dyad reporting approach provides another option to be considered in selected contexts that may enable the collection of data representing a shared experience. Dyad-report may be a relevant approach to take when the condition or treatment includes significant and shared

involvement of the caregiver, and when events are observable (such as in asthma management or injection preparation and administration). Further, this approach may be valuable when there are no specific age thresholds for patient independence, as would be the case of injection treatment administration, as it allows for flexibility in the COA administration approach for each individual dyad. In particular, the dyad approach may be of value in a rare disease setting which frequently involves pediatric populations, and the disease management may involve a shared experience.

While in some cases caregivers may unduly influence a child's “voice” in the response, the involvement of a caregiver as part of a dyad may offer important emotional support to the child which would otherwise be lacking, if only the child were the respondent, and may better reflect a “real life” scenario in which patients and caregivers engage in a dialogue. Acting as an advocate and enabler for the pediatric participant during a dyad interview, the caregiver may help provide context, resolve issues involving recall, response bias, and frustration which may occur. Importantly, comprehension issues may be addressed by the caregiver reading question content aloud when needed, encouraging the child to answer honestly, or to explain the meaning of a question or specific words but being careful not to paraphrase item content or coerce or influence the child's responses. The dialogue between child and caregiver may result in less missing data, as would be the case when a separate PRO and/or ObsRO measure is administered with the intention of capturing relevant aspects of a treatment experience. Depending on the specific method used for data collection, a dyad option may also limit and help to avoid unreliable proxy reporting.

It should be noted that there are some contexts for which a dyad approach should never be used. For instance, when collecting subjective symptom severity data or the impact of emotional functioning on the patient, because only the patient can describe their experience of symptom severity or emotions they are feeling. Additionally, the dyad approach would not be suggested for use when collecting data using questionnaires designed for completion by a single party (i.e., patient- or caregiver-reported outcome measures).

The inherent differential power dynamics in a caregiver/patient relationship have been observed and can lead to parental coercion or influence, either by imposing their own views onto the child, by questioning the child's answer or pressing the child to answer the questions more quickly than they would naturally. Ungar et al., observed some evidence of coercion and recommended mitigating the effects of potential caregiver coercion/influence (e.g., facilitation and re-direction of the dyad completion of a questionnaire by a trained interviewer) that may be

possible in some contexts. Whilst in theory, a trained interviewer could facilitate a dyad-report approach to questionnaire completion as described by Ungar et al. and may even have the advantage of mimicking what occurs in a clinic setting, caution is recommended with this approach since it may not be practical to implement and the involvement of an interviewer may be leading or may unintentionally bias participant responses.

There are several recommendations to consider when planning a dyad option for data collection as part of a COA measurement strategy. First, consideration should be made for the overall goals of measurement and the use of a “complete” dyad approach (e.g., COA designed with the intention for dyad-report on all questions) versus a dyad reporting “option” (e.g., selected COA questions offering a dyad, PRO, or ObsRO report option; qualitative interview conducted intending to collect data from the patient). It is important to consider the concepts being assessed in the questionnaire when determining which approach to take. For example, subjective internal sensations such as pain or nausea should only be evaluated by the patient as there is no way for the caregiver to *truly* know what the patient is experiencing.

When providing respondents with a dyad reporting option, it does beg the question “who reported on what” in the single questionnaire. Therefore, it is recommended that data should be collected on “who reported” (child alone, caregiver alone, child/caregiver together) at questionnaire and also ideally at the item level to enable sensitivity analyses, if needed. Where possible, electronic data capture should be used to facilitate the collection of these additional data, and ease administration burden for respondents.

During the dyad interaction, when the question and response options are discussed by the patient-caregiver pair, in instances where the caregiver must read questionnaire instructions or item text aloud to the child, instructions should be provided to remind the caregiver to use caution in communicating with the child regarding the question content (e.g., paraphrasing the question content is not preferred and can change the meaning of the question). The recommendation would be for the questions be read verbatim and discussion to focus on an appropriate response. In a questionnaire that contains modules inviting patient self-report, caregiver-report, or dyad-report options, instructions can be included to orient the respondent accordingly.

Consistency in reporting is another important consideration. In a clinical study setting, where dyad reporting may occur at different timepoints, it is important that the same caregiver be involved and reports at each time period to provide consistency and minimize any changes to the administration approach throughout the

study. Further, setting expectations with each member of the dyad and confirming what their role will be during completion should be done ahead of implementation.

Conclusions

The dyad reporting approach has not been widely studied. The research described here presents very few instances in growth hormone treatment and asthma; however, it could have a wider utility and application. While there are limitations to a dyad approach, we have described its application and shown it offers a pragmatic solution in certain contexts, may help to avoid proxy report, and minimize missing data. Dyad reporting has the potential to positively or negatively impact overall data quality, and when elected, should be used with intent, appropriate instructions, and documentation, and should collect sufficient administrative data for “who reports” to enable sensitivity analyses, if needed. This approach offers insights to the relational aspects of shared health experiences and may yield more robust outcomes of the treatment or condition. When there is a shared treatment experience to be captured (beyond what may be measured by a PRO or ObsRO alone), this approach provides additional information to characterize the patient and caregiver shared experience which is unique and may be more comprehensive. It may be of particular value in rare diseases, which disproportionately impact children and their caregivers.

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