Initial Validation of GRASP: A Differential Diagnoses Algorithm for Children With Medical Complexity and an Unknown Source of Pain

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ABSTRACT

OBJECTIVES: Identifying the source of pain for children with medical complexity (MC) is challenging. The purpose of this study was the initial validation of a tool to guide the medical evaluation for identifying the source of pain in children with MC by using differential diagnoses. The tool is entitled Guidelines for Ruling Out and Assessing Source of Pain (GRASP).

METHODS: A mixed-methods approach that included expert review, focus groups, Web-based surveys, and a trial of the GRASP was used to determine validity as well as perceived clinical utility.

RESULTS: Focus groups were held with 26 inpatient and outpatient clinicians. Participants consistently responded in support of the GRASP. Participants advised several suggestions for tool organization such as designing the tool as a flow diagram. Seven clinicians participated in Web-based surveys and made specific suggestions for making the GRASP more comprehensive. Six participants trialed the GRASP for 14 children with MC and pain of unknown origin. Overall, participants found that the GRASP was a clinically effective tool for guiding medical evaluation.

CONCLUSIONS: These results provide preliminary evidence that the GRASP has content and face validity in evaluating the source of pain in children with MC. This tool can be used to systematically guide clinicians through a balanced approach to evaluation with a goal of determining the pain source, preventing harm, and relieving suffering without unnecessary tests.
Identifying the source of pain in a child with medical complexity (MC) is often challenging because the child cannot always localize pain or provide details of their experience. Because self-report is not possible for many children with MC, providers depend on parents and/or caregivers to provide a comprehensive history to guide the diagnostic evaluation. Children with MC have been described and, for the purposes of this article, are defined as having a “congenital or acquired multisystem disease, a severe neurologic condition with marked functional impairment, and/or technology dependence for activities of daily living.”

Throughout this article, we chose to identify the condition, not the child, with the acronym MC to write efficiently.

Unfortunately, pain in children with MC is common. When compared with other hospitalized children, children with MC tend to experience pain that is persistent and severe, which may be a result of underlying disease processes, comorbidities, and difficulties in pain assessment. Children with MC may experience both acute pain from fractures, otitis media, and pneumonia and chronic pain from spasticity or neuropathic pain. Some children with MC exhibit pain behaviors that are not typically associated with pain such as changes in mental status, laughter, and other vocalizations. Pain assessment tools validated for children who cannot provide self-reports of pain are effective for measuring the presence and intensity of pain; however, these tools do not guide clinicians in identifying the source of pain. Adding to the challenge of identifying the source of pain for these children is a prevailing thought among some clinicians that children with MC feel or experience less or even no pain. The challenges surrounding pain assessment in children with MC may contribute to lengthy and sometimes unnecessary medical workups and delays in identifying and addressing the source of pain.

In turn, such delays may contribute to increased morbidity for children with MC experiencing pain of unknown etiology. Although children with MC compose only 5.2% of hospitalizations, they account for 22% of hospital charges and 43% of hospital deaths. Although common pediatric conditions, such as otitis media and pneumonia, are typically treated in the outpatient setting, the hospitalization rate for these diagnoses is 6 times greater for children with MC than for neurotypical children. Hospital readmission rates for children with MC are higher than for the general pediatric population. In a case series of children with MC admitted to the hospital for an unidentified source of pain, children with MC stayed for nearly 2 weeks and required an average of 5 clinical images and 4 specialist consultations to identify a source of pain because of their MC. For all these reasons, a thorough, efficient, and standardized approach to the medical evaluation to identify the source of pain is needed for this vulnerable population.

The purpose of this study was the initial validation of a tool, the Guidelines for Ruling Out and Assessing Source of Pain (GRASP), to direct the medical evaluation for identifying the source of pain in children with MC by using differential diagnoses. Differential diagnoses are a list of possible causes of a patient’s clinical findings used to systematically consider, at times, evaluate for possible causes before identifying the final diagnosis. The specific aims included establishing (1) content validity (with expert and professional judgment to ensure the tool adequately represents the pain evaluation process by using differential diagnoses), (2) face validity (ensuring that nonexpert professionals determine that the tool appears to reflect the pain evaluation process), and (3) the perceived clinical utility of the tool.

A retrospective medical chart review for children with MC admitted to a pediatric hospital for pain of unknown origin was used to identify the need for a standardized approach to medical evaluation. One author (JCS) considered the literature and clinical experiences and developed the first draft of the GRASP. The GRASP is an algorithm that guides a standardized approach to medical evaluation with the initial evaluation based on the severity of the child’s clinical condition and differential diagnoses organized by body system. The GRASP (Fig 1) uses both prognostic and probabilistic approaches to diagnosis. A prognostic approach to diagnosing prioritizes clinical conditions, which, if left undiagnosed and untreated, could be life-threatening. The first step in the GRASP suggests tests to complete if the child with MC has pain behaviors of unknown etiology and appears ill. Then the list of differential diagnoses takes a more probabilistic approach to diagnosing by considering diagnoses that are likely to occur in this population.

The tool was then reviewed and edited for wording and content on the basis of input from local experts, including authors SM, JH, and CDG, and additional experts, who are mentioned in the Acknowledgments. The study team then revised the tool for readability and organization.

Phase 1: Content and Face Validation
To determine content and face validity, 4 in-person focus groups with clinical experts on the care of children with MC were held. The specific goals of these groups included identifying overall impressions of the GRASP and determining if the listed differential diagnoses were both comprehensive and necessary to include in the tool.

Potential participants were identified as experts in this field by both the patient population that they care for and the years of experience caring for this population. Specifically, participants were determined to be experts on the basis of years of experience in the area of pediatric pain, pediatric complex care, or completion of specialized training in pediatric pain and/or complex care. Experts were invited via e-mail to the focus group sessions held.
on-site at 2 pediatric hospitals. One hospital was a 404-bed pediatric medical center, and the other was a 70-bed subacute rehabilitation center for children with MC. Both facilities offer comprehensive services for children with MC. The focus group invitation e-mail included a copy of the GRASP for review before the focus group. Refreshments were offered to incentivize participation.

Informed consent of all the participants was obtained. Participants completed a professional demographics survey for the purposes of describing the sample. Before the focus group, a brief presentation profiled the GRASP development and intended use with ground rules for the discussion. During the focus group, we reviewed the GRASP by each body system and used a discussion guide to facilitate conversations about the GRASP. Each participant was allowed time to answer questions including the following: What are your initial thoughts about the general usefulness of this tool in the clinical setting? Which, if any, of the differential diagnoses do you think can be eliminated from this tool? What, if any, differential diagnoses are we missing? Do you think this tool would be useful in your clinical setting? Focus groups were audio-recorded and transcribed verbatim.

Members of the study team (BLM, JCS, and SM) moderated the group sessions and recorded field notes. After analysis of focus group discussions, we made edits to the GRASP. After the revisions, the focus group participants reviewed the edited GRASP to ensure content and face validation. Participants were invited to complete a Web-based survey to share professional opinions regarding the importance of each component of the revised GRASP. Consent was embedded in the survey, and gift cards were offered to incentivize participation. Survey questions included the following: Are there any other additional differential diagnoses to consider? If so, list them and explain their significance. The survey also asked participants if they would recommend the revised GRASP to their colleagues and if so, to specify under what circumstances. The survey concluded with an open-ended question asking for any additional comments or suggestions. The collected data were analyzed to identify themes related to the usefulness, comprehensiveness, and practicality of the revised GRASP. The findings were presented to the focus group participants and the study team for feedback.

FIGURE 1 GRASP This guide is a (not exhaustive) list of sources of pain and irritability in children with intellectual disability who are unable to verbalize symptoms or localize pain. If the patient is ill-appearing and/or is not himself or herself, a thorough evaluation as suggested in boxes A, B, and C should be done rapidly in succession. AXR, abdominal radiograph; CBC/diff, complete blood cell count with differential; CK, creatine kinase; CRP, C-reactive protein; CT, computed tomography; CXR, chest radiograph; ECG, electrocardiogram; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; G/J, gastro-jejunostomy; HCG, human chorionic gonadotropin; HIDA, hepatobiliary iminodiacetic acid; KUB, kidney ureter bladder study; MRCP, magnetic resonance cholangiopancreatography; NSAID, nonsteroidal antiinflammatory drug; PE, physical examination; PMH, past medical history; PUD, peptic ulcer disease; SSRI, selective serotonin reuptake inhibitor; UA, urinalysis; UTI, urinary tract infection; VP, ventriculoperitoneal; WOB, work of breathing; √, check.
diagnoses you would include in the tool? Should we include any further tests in the initial workup section of the tool? On review of the survey results, the study team discussed participant suggestions to improve the GRASP and revised the tool.

**Phase 2: Perception of Clinical Utility**

The study team invited focus group participants and medical residents of the study sites that provide care to children with MC to test the GRASP. Participants were asked to use the GRASP on ≥1 patient and then to share their experience via a Web-based survey. Survey prompts included the following: Please describe aspects of the GRASP that were most helpful; Please describe aspects of the GRASP needing improvement; and Compared to previous evaluation practices, do you think using the GRASP helped you identify a source of pain?

Consent was embedded in the survey, and gift cards were offered to incentivize participation. Again, the study team reviewed all participant suggestions after use and made final adjustments to the GRASP.

**RESULTS**

**Phase 1**

Twenty-six inpatient and outpatient providers of children with MC participated in 4 separate focus group sessions at 2 pediatric hospitals. The participants were mostly medical doctors (n = 14 [53.8%]) and nurse practitioners (n = 8 [30.7%]) (Table 1). On average, participants had almost 17 years of clinical practice, and participants estimated caring for 23 children with MC and pain behaviors of unknown etiology annually. Participants rated the difficulty evaluating the source of pain in children with MC as 7.6 (SD = 1.22, range = 5–10) on a scale of 0 to 10.

On initial review of the GRASP, participants (N = 26) consistently responded in support of the GRASP and communicated the need for this clinical tool. Participants reported that this tool was especially important for inexperienced clinicians, those who infrequently cared for children with MC, and clinicians who did not have previous clinical experience with the particular child with MC. Some participants reported that this tool would be helpful as a teaching tool for new clinicians, as well as parents, guardians, and/or caregivers with concerns about the comprehensiveness of pain evaluations. During the discussions, several participants recalled challenging patients and ensured that we accounted for certain diagnoses within the tool. Participants provided some suggestions for the tool, including tool organization, accessibility (eg,
TABLE 1  Participant Demographics Across Study Phases

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Focus Groups</th>
<th>Web Survey</th>
<th>GRASP Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n)</td>
<td>Mean (SD)</td>
<td>Range</td>
</tr>
<tr>
<td>Provider type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>30.7 (8)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Outpatient</td>
<td>42.3 (11)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Inpatient and outpatient</td>
<td>26.9 (7)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>License</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical doctor</td>
<td>53.8 (14)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Nurse practitioner</td>
<td>30.7 (8)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Physician assistant</td>
<td>3.8 (1)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Registered nurse</td>
<td>7.6 (2)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Social worker</td>
<td>3.8 (1)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Practice years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All practice</td>
<td>—</td>
<td>16.84 (11.81)</td>
<td>3–37</td>
</tr>
<tr>
<td>Pediatric practice</td>
<td>—</td>
<td>17.26 (10.6)</td>
<td>4–37</td>
</tr>
<tr>
<td>Complex care practice</td>
<td>—</td>
<td>12.56 (11.01)</td>
<td>0–35</td>
</tr>
<tr>
<td>Months of past year caring for children with complex needs</td>
<td>—</td>
<td>9.93 (5.99)</td>
<td>0–12</td>
</tr>
<tr>
<td>Children per year cared for with pain behaviors of unknown origin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>—</td>
<td>23.61 (24.62)</td>
<td>0–100</td>
</tr>
<tr>
<td>Difficulty faced evaluating pain in children with complex needs</td>
<td>—</td>
<td>7.8 (1.22)</td>
<td>5–10</td>
</tr>
</tbody>
</table>

—, not applicable.  
<sup>a</sup> Defined as children presenting with pain behaviors with an absence of self or parent, guardian, or caregiver localization.

a Web-based tool versus a paper tool), user-friendliness, and the addition of a flow diagram.

Seven of the 12 invited participants responded to the Web-based survey. Respondents were mostly medical doctors (n = 6 [85.7%]) providing inpatient care (n = 5 [71.4%]) with over 13 years (SD = 10.47, range = 2–27) of experience and nearly 8 years (SD = 8.17, range = 1–23) of complex care experience. The respondents reported that evaluating pain in children with MC was difficult (7.8 on a scale of 0 to 10 [SD = 0.75, range = 7–9]) (Table 1). Participants again responded in support of the GRASP and communicated the need for this tool in the clinical setting. They noted that the tool would be especially helpful for newly practicing clinicians when caring for children with MC in pain.

Participants offered specific suggestions for making the GRASP more comprehensive. Participants suggested that erythrocyte sedimentation rate (a marker of inflammation) should be added to the initial workup section of the tool. The differential diagnosis of appendicitis was moved from the infection section to the gastrointestinal section. An echocardiogram was added to the infection section to the gastrointestinal examination and reported a difficulty level of 7.66 (SD = 0.18, range = 7–9; Table 1) when evaluating these children for a source of pain.

The participants reported several benefits of using the GRASP. All participants commented on the utility of the checklist or framework format of the GRASP, noting the systems-based approach was “helpful so as not to overlook specific [differential diagnoses].” The organization of the GRASP by body system was especially helpful when working with trainees. Some respondents found that the GRASP helped increase efficiencies in care, reporting that “it allowed me to be more thorough from the very beginning in my history/physical exam, so this may have allowed me to rule out more possibilities for source of pain more quickly.” Other respondents reported that although using the GRASP lengthened the evaluation process, it was time well spent and helped them avoid unnecessary workups. After participant suggestions, we edited the heading of GRASP columns, added more specific instructions for signs and symptoms (eg, otoscopic examination positive for otitis media) and consultation (eg, consult dentist for suspected dental abscess), and incorporated emerging evaluation methods (eg, procalcitonin for cellulitis).

**DISCUSSION**

These results provide preliminary evidence that the GRASP has content and face validity of questionnaires and assessments. The Difficulties of Pain in Children in the Hospital Setting: Systematic Review and Meta-analysis provides evidence for the usefulness of a comprehensive approach to pain assessment and management in children. The GRASP was found to be effective in improving the care of children with pain in the hospital setting.

**Phase 2**

To evaluate its clinical utility, the GRASP was used as a trial on 14 patients who entered a complex care practice (n = 8) were mostly medical doctors providing inpatient care with 13 years of practice experience (SD = 7.96, range = 8–25) and nearly 7 years (SD = 5.15, range = 2–15) of complex care experience. On average, respondents each estimated caring for 15 children (SD = 8.01, range = 10–30) with pain behaviors of unknown origin per year and reported a difficulty level of 7.66 (SD = 0.18, range = 7–9; Table 1) when evaluating these children for a source of pain.

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in determining the source of pain in children with MC. This is an important first step in tool validation for this high-risk population of children who cannot verbally describe their pain experience.

Throughout the study, participants confirmed the importance of such a tool for clinical care, especially related to the limitations in obtaining self-reports in this patient population. Typically, the patient’s self-reported history directs the medical evaluation through first-person accounts of symptoms over time. On the basis of patient history, the use of differential diagnoses in medicine is well established to evaluate potential conditions that share similar signs and symptoms.\(^\text{5-7}\) The authors of one study reported that 83% of diagnoses were identified by using only the first-person accounts in the patient history.\(^\text{27}\) Although behavioral changes in children with MC provide valuable information to attentive providers and caregivers, the verbal history of children with MC is typically third-person reports from parents and caregivers.\(^\text{4,8,15-15,17}\) In most circumstances, even excellent third-person reports of the subjective signs and symptoms are inferior to first-person reports.\(^\text{28-32}\)

During the focus group discussions, participants described the different ways that the GRASP could be used. The obvious and original purpose is to guide the evaluation process for identifying a source of pain in a child with MC, depending on the child’s presenting signs and symptoms. Clinicians can initiate this guideline whenever there are changes in behavior or appearance and the child appears ill and not themselves.

The GRASP can also be used as an educational tool for health care providers and for parents and other caregivers. The evaluation of pain in a child with MC requires in-depth understanding of medical conditions and potential comorbidities. There is a need for education for providers regarding evaluating and treating pain in children with MC.\(^\text{15,33-38}\) Pain education, in general, is limited for health care providers across specialties and disciplines.\(^\text{37-41}\)

Supervising clinicians may use the GRASP to help trainees gain knowledge and skills in identifying sources of pain in children with MC.

The GRASP can also be used to educate parents. When a source of noiceptive pain is not identified in a patient with a chronic pain syndrome, parents, guardians, or caregivers may be worried about the lack of a positive diagnostic test result. For example, children with MC may experience recurrent pain from both acute nociceptive sources and chronic pain without a confirmatory test to indicate a source due to the altered nervous system. Clinicians may find it helpful to share a tool like the GRASP with the parents to clearly illustrate the evaluation and ruling-out processes used.

**Future Research Priorities**

We chose this population because children with MC cannot verbally self-report and often have potential sources of pain due to MC such as infections from implanted hardware, fractures related to osteopenia, and dysmotility from immobility. For these reasons, children with MC were our focus in this initial validation study. However, most of the differential diagnoses would certainly apply to neurotypical children and could be useful for preverbal children. We plan to explore the need, if any, for a tool for preverbal children.

As medical knowledge and diagnostic tests and interventions evolve, the GRASP will require periodic revision based on current practices and latest research. For example, some laboratory tests may be replaced by more specific or, alternatively, more inclusive measures. Additionally, our study was only a first step in preparing the GRASP for widespread adoption in the clinical setting. We next aim to conduct a more rigorous validation study of the GRASP. Finally, whereas parents, guardians, and other caregivers notice the changes in behavior, activity, or affect in children with MC and seek care for their children, researchers should aim to better understand the experiences of parents surrounding pain identification and evaluation processes.

**Limitations**

This study was conducted with providers of 2 pediatric hospitals within the same city in the Northeast United States. One hospital has a specialty service for children with MC, and the other is a center specializing in subacute care for children with MC. A greater number of inpatient providers participated in this initial validation than outpatient providers (~66% and 33%, respectively, across study phases). In the future, we aim to test this tool in multiple sites with diversity in the training, experience levels, practice settings, and resources available to providers. There may be differences in institutional procedures and practices that may influence tool limitation. For example, serum lipase is a more specific marker for pancreatitis than amylase. At the study institutions, amylase and lipase are reported together, and we use amylase as a general inflammatory marker. Clinicians may need to modify specific diagnostic tests on the basis of availability or standards of practice of different institutions.

Additionally, in this study, we relied on the professional opinions and experiences of participants. Respondents providing such a self-report may have answered interview questions and survey items on the basis of perceived best practices and social desirability.

The focus of the GRASP is guiding the medical evaluation after an acute change in the child with MC. Children with MC have risks for comorbid acute and chronic pain sources. This includes chronic sources due to the altered nervous system, such as central neuropathic pain and visceral hyperalgesia. There is also the challenge of positive findings that may not be the source of pain symptoms, such as a positive culture result from a tracheostomy tube due to colonization or a positive EEG result due to intractable seizures. Cognitive bias may result in anchoring on positive test results and may thereby lessen consideration of chronic pain sources, which is an area in need of further study.

**CONCLUSIONS**

Clinicians face challenges in identifying sources of pain for children with MC. Some challenges, such as the inability of children with MC to localize or clearly state the presence of pain, are not easily overcome.
The GRASP can be used to systematically guide clinicians through a balanced approach to a medical evaluation with a goal of determining the pain source, preventing harm, and relieving suffering without unnecessary tests. Research is needed to establish further clinical utility and to measure benefits related to length of admission, time to diagnosis, and other factors surrounding pain in children with MC.

Acknowledgments

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