(Suggested) Title: Reducing the burden of pain from vaccination: updated recommendations for all age groups

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The impressive series of systematic reviews published in this issue by the HELPinKids&Adults team represents a significant undertaking in the provision of recommendations to reduce the burden of pain from vaccination. It constitutes the most comprehensive review of management of vaccination pain and needle fear to date, and updates the original Help ELiminate Pain in KIDS (HELPinKIDS) guidelines from 2010. One might question why it is important to address pain during vaccination. Three reasons can be broadly identified. Firstly, it is a form of neglected iatrogenic pain which deserves serious attention and mitigation strategies, similar to other forms of unintentional harm from medical procedures. Secondly, pain and fear of needles can, in severe cases, lead to avoidance of needle procedures in healthcare – even simple yet life-saving interventions such as glucose testing for diabetics. Finally, vaccination pain impacts vaccine hesitancy. In an era where vaccines are a victim of their own success, we need now, more than ever, to address all the reasons why people might refuse vaccines, including pain during immunization. Pain is an oft forgotten contributor to vaccine hesitancy which could have implications for vaccine uptake, herd immunity and outbreaks.

The series starts with an excellent overview of the core constructs addressed in the reviews (e.g., pain, fear, anxiety), which sets the stage for the systematic reviews to follow on different interventions in different target populations. The authors of this paper are to be applauded for outlining an innovative developmental framework with regard to the development of needle fear and transmission of needle fears from childhood to adulthood, its impact upon parenting, and the corresponding impact upon children. Subsequently, Taddio et al. provide an overview of the rigorous methodology (Grading of Recommendations Assessment, Development and Evaluation; GRADE) used for the different systematic reviews and meta-analyses included in this special series.

This series involved a huge undertaking: over 80,000 papers were screened before being narrowed to 136 publications informing the 55 interventions that were reviewed and discussed. Interventions were categorized as procedural, physical, pharmacological, psychological, or process-oriented. New from 2010 is separate guidance for adults, recognizing that adults experience negative consequences from needle pain as well. As such, the HELPinKIDS&Adults team has devoted separate reviews to psychological interventions for infants, for children and adolescents, and for adults. Furthermore, the reviews outlining physical, process-oriented, and pharmacological interventions were expanded to include studies involving adults. Interventions for individuals with high levels of needle fear were reviewed separately, in appreciation of the fact that such individuals require interventions not just to reduce pain but to confront their needle phobias.
With the publication of this body of work, we are now equipped with the knowledge necessary to reduce needle pain for people of all ages. Consideration thus needs to be given to the lofty work of knowledge dissemination and translation to all the various stakeholders in immunization programming, including front-line immunizers, program managers, policy-makers, parents, and vaccine recipients. Not only must uptake be ensured, but fidelity to the interventions according to context and local considerations should also be emphasized.

The World Health Organization’s (WHO) Strategic Advisory Group of Experts (SAGE) on Immunization has taken notice of the HELPinKids&Adults recommendations and, to this end, convened a Technical Consultation Group (TCG) in February 2015 consisting of immunization experts, pain researchers and immunization program managers, of which we were both privileged to be a part. Over the course of two days, the TCG deliberated the results of the HELPinKids&Adults systematic reviews and proposed recommendations to SAGE for adapting the findings to a global context. Such considerations included deliberating the balance of benefits and harms of the intervention particularly in low and middle income countries, resource use, opportunity costs and value for money, impact on health equity, acceptability (including anticipated cultural barriers) of the intervention for patients, parents and health care workers, and implementability in low-income settings.

In May 2015, SAGE issued a report\textsuperscript{11} concluding that effective, feasible, culturally acceptable and age-specific interventions exist for the mitigation of pain during vaccination. It has published a list of recommended interventions for national immunization programs and furthermore proposed specific recommendations for WHO and the health systems of individual countries. Specifically for WHO, SAGE recommended to: 1) include pain mitigation recommendations with immunization practice guidance materials, 2) disseminate these recommendations to its various stakeholders and partners, 3) monitor and evaluate the implementation of their recommendations, and 4) advocate that vaccine injection pain information be considered during licensing and included in product monographs. For countries, SAGE recommended that health systems: 1) include vaccination pain and distress mitigation as part of good clinical practice, 2) specify (where possible) the order of injections to health care workers so that immunizations are given from least to most painful, and 3) include immunization pain mitigation as part of health worker training.

To conclude, the systematic reviews included in this issue represent a substantial amount of research evidence with regard to different interventions for the mitigation of pain during vaccinations for infants, children, adolescents and adults. However, most individual recommendations are based on a small number of studies of unfortunately low quality. These limitations are addressed in the final chapter\textsuperscript{15}, in which relevant suggestions for future research are also delineated. An important direction of study may include the investigation of cultural appropriateness and feasibility of existing interventions in low and middle income countries (75\% of the 136 articles reviewed came from high income countries), and how the interventions may be modified to meet specific challenges related to particular settings (for example, in many developing countries facilities are not available for individuals to be immunized privately) and limited resources. The WHO report\textsuperscript{11} also recommended more research on effective interventions in adolescents and with regard to interventions that can be used in mass campaigns and school-based settings. Finally, systematic replication of the present recommendations is also needed using increased methodological rigor in the research designs. It is our hope that the publication of these reviews will encourage high quality research in order to heighten our knowledge on pain mitigation during
vaccination in diverse settings. It is clear that we need to continually add to our understanding of these evidence-based interventions in order to reduce iatrogenic pain, improve vaccine coverage, and positively impact public health overall.

**References**


