

## Report Supplementary Material File 9

### Request for Project Advisory Group input on group analysis

#### Choosing international studies

At our last meeting you helped us to make some really important decisions. Just to remind you, we have 25 good or excellent UK studies on chronic pain to answer our project questions. We also found 122 international (non-UK) studies that we could include, which is too many for a meta-ethnography. So, we asked you how we should choose which international studies to include.

Based on your advice and suggestions we have chosen international studies we should include. We selected and then assessed studies which:

1. look at pain conditions/illnesses for which we had no UK studies.
2. look at infants and pre-schoolers (aged 0 to 5 years) because we had few UK studies on this age group.
3. have material to answer our project question 'what would a 'good' treatment/ service be like?' because we had few UK studies on this.
4. have an aim similar to ours that were published recently (in the last 15 years) because they will have useful material.

This gave us 50 international studies which we assessed. 17 of these were excellent or good in detail and will be included in the project. So we now have 42 studies in total – 25 UK and 17 non-UK.

We now have information on 24 conditions/illnesses and 11 studies have material on good services or treatments.

**Grouping studies - Now we want to ask you if you agree with how we want to group the 42 studies to analyse them.**

#### Why group studies for a meta-ethnography?

It can be a challenge to pull together and make sense of 42 studies! So, we plan to group the studies in a logical way. We will create smaller groups of studies which have something in common with one another. We will pull together each of the smaller groups of studies first. Then we will pull together what we find from across all the groups of studies.

### How shall we group the studies to start with?

We have looked at the studies and thought about different ways to group them, for example:

- By who took part in the studies, e.g., children or parents - but a lot of studies include both children and parents
- By age of the children with chronic pain the studies looked at, e.g., babies, pre-school children, primary or secondary children - but most studies look at a wide range of ages

So, we think the most sensible way to **group studies is by health condition/ illness** e.g. there are 6 studies on juvenile arthritis, 6 on sickle cell disease, 2 on abdominal (tummy) pain. This would also mean that we could spot any differences and similarities between people's experiences of different conditions when we pull together findings from all the groups of studies.

**Please can you tell us if you agree or disagree with how we plan to group the studies by 9 July 2021, if possible? Also please make any other suggestions if you want to.**

### **Email asking pain specialists and clinicians from PAG on how to group studies**

Thank you again for supporting the CHAMPION project. As we updated you in our previous email, we are trying to group our studies by pain condition – this is a preliminary step in the analysis before looking across all of the studies, regardless of condition. We have a total of 42 studies focusing on 24 conditions. We would like your expert clinical and methodological advice on how best to group the conditions for initial analysis.

In order to try to decide the best way to group them, we looked at other systematic reviews and qualitative evidence syntheses (QES) on children's chronic pain to see how they grouped studies by conditions for subgroup analyses:

- Of 7 recent Cochrane effectiveness reviews on children's chronic pain, only 2 were able to perform subgroup analyses – they grouped trials into **headache** versus **non-headache chronic pain** (all other pain conditions) based only on the numbers of trials rather than any other criteria.

- In the past, individual Cochrane reviews were done for **recurrent abdominal pain** and for **sickle cell disease (SCD) pain** in children, so those were pulled out as important pain condition ‘groupings’.
- A 2021 WHO review of management of children’s chronic pain by Fisher et al categorised trials by pain condition, **according to the ICD-11 classification**.
- The only 2 QES we know of in the field did not group studies by condition since one focused solely on juvenile idiopathic arthritis (JIA) and the other had only 8 studies.

We have explored using ICD-11 to classify and group studies but the level of detail our qualitative studies give on pain conditions is poor - for some/most studies it won’t be clear which ICD-11 pain category they fit under. Also, we do want to integrate our findings with the prior Cochrane effectiveness reviews.

Based on the above reviews, we think that we should most probably have separate groupings on SCD, headache, and recurrent abdominal pain. We also think we should have a group for JIA, given that its treatment is distinct from other musculoskeletal pain conditions. We will need a ‘mixed conditions’ category for studies which focus on 2+ conditions. We have then tried to group the rest of the studies in a logical way as shown in the table below. So far we propose 10 potential groupings.

**Table 1. Proposed grouping of our 42 studies**

<b>Groups</b>	<b>Number of studies</b>	<b>Conditions</b>
<b>Group 1 - Musculoskeletal pain</b>	3	Any type of joint or muscle pain. A few examples are back pain, neck pain and shoulder pain.
<b>Group 2 - Sickle Cell Disease</b>	6	Sickle Cell Disease
<b>Group 3 – Abdominal pain</b>	2	This included colitis, IBS, Chron’s disease

<b>Group 4 – Complex Regional Pain Syndrome</b>	2	Complex Regional Pain Syndrome
<b>Group 5 – Headache/migraine</b>	1	Migraine
<b>Group 6 – Juvenile Idiopathic Arthritis</b>	6	Juvenile Idiopathic Arthritis
<b>Group 7 – Dysmenorrhea</b>	1	Dysmenorrhea
<b>Group 8 – Skin conditions</b>	1	Epidermolysis Bullosa
<b>Group 9 – Neurological conditions</b>	4	<p><i>Study 1</i> - Cerebral Palsy</p> <p><i>Study 2</i> - Children with cognitive impairment from brain damage/cerebral palsy with pain from different sources (Four children had pain related to spasms associated with feeding and bowels).</p> <p><i>Study 3</i> - Children with special needs - All the children had limited physical and cognitive abilities from a wide range of diagnoses including cerebral palsy and degenerative brain disorders/syndromes. The children had different types of pain sources, which included:</p> <ul style="list-style-type: none"> <li>*Pain related to spasticity including muscle spasms, dislocation and fractures (commonly relating to hips, legs, spine and shoulders).</li> <li>*Gastro-intestinal pains including reflux, vomiting, gastrostomy problems, constipation and ‘wind’ (MSB - very common in cerebral palsy – from medication, alteration on peristaltic movements)</li> <li>*Other pains were associated with sore ears (which were often described as being problematic pressure points), toothache, and pain that resulted from handling, moving and finding a comfortable position for the child. The positioning-related pains were exacerbated if the child was wearing splints or supports of any kind.</li> </ul> <p><i>Study 4</i> - Severe Neurological Impairment - static encephalopathies (which included cerebral palsy, spastic quadriplegia following</p>

		<p>infection or trauma (2) and cerebral malformations), progressive encephalopathy (adrenoleukodystrophy, Hallervorden Spatz, Sanfilippo Rett), a variant of late infantile batten’s disease, and undiagnosed degenerative conditions).</p> <p>Sources of Pain:</p> <ul style="list-style-type: none"> <li>* Pains associated with alterations in gut motility such as gastro-oesophageal reflux, wind and constipation.</li> <li>* Pains related to musculoskeletal problems, particularly muscle spasm, dislocated hip, joint and back pain and pain generally associated with the child’s immobility.</li> <li>* Co-incidental pains that can also occur in otherwise well children, for instance, ear and tooth ache.</li> <li>* Pain related to poorly fitting aids and equipment.</li> </ul>
<p><b>Group 10 – Mixed conditions</b></p>	<p>15</p>	<p><i>Study 1</i> - Complex Regional Pain Syndrome and extreme muscle pain.</p> <p><i>Study 2</i> - headache, abdominal pain, back pain, hand pain, foot pain, and facial pain and total body pain.</p> <p><i>Study 3</i> - headache, neck pain, shoulder pain, abdominal pain, and widespread pain</p> <p><i>Study 4</i> - This study included participants under Palliative care with the following conditions: epidermolysis bullosa; osteogenesis imperfecta; xeroderma pigmentosum; human T-cell lymphotropic virus (HTLV)/hereditary spastic paraparesis.</p> <p><i>Study 5</i> – not diagnosed, fibromyalgia, reflex sympathetic dystrophy (also called Complex regional pain syndrome).</p> <p><i>Study 6</i> - complex regional pain syndrome, headaches/migraines, stomach migraines, constipation, chronic pain, nephroptosis, costochondritis and no diagnosis.</p> <p><i>Study 7</i> – headaches/migraine, chronic ear infections, physical deconditioning, dizziness, amplified pain syndrome, lower back</p>

pain, wrist and ankle pain, abdominal pain, tethered cord syndrome, chronic leg pain, Complex regional pain syndrome.

*Study 8* – knee pain, abdominal pain, back pain

*Study 9* - abdominal pain, headaches, bone pain and back pain

*Study 10* - musculoskeletal pain, neuropathic pain (all complex regional pain syndrome type I).

*Study 11* - Diffuse idiopathic pain syndrome, Localised idiopathic pain syndrome, Complex Regional Pain Syndrome Type 1, Inflammatory disorders (*Note that complex regional pain syndrome is under localised pain syndrome and fibromyalgia under diffuse idiopathic pain syndrome*).

*Study 12* - localised idiopathic pain syndrome, diffuse idiopathic pain syndrome, complex regional pain syndrome type 1, and arthritis.

*Study 13* -Localised Idiopathic Pain Syndrome, Diffuse Idiopathic Pain Syndrome and Chronic Regional Pain Syndrome Type 1.

*Study 14* -musculoskeletal pain and neuropathic pain (all complex regional pain syndrome type I).

*Study 15* - knee pain, migraine, neuropathic pain, back pain, abdominal pain, unknown, neck pain, chest pain, arm pain, hip pain, spine and shoulder pain

We wanted to ask you two important questions about these groups:

1. Do you have any other suggestions on how to group the studies by condition?
2. What do you think of the current groupings of studies in Table 1, e.g.,
  - Do you think that the neurological group 9 is valid considering that the sources of pain are a mix of different things?
  - Do you have any suggestions on how we could improve the mixed conditions group 10? For example, should we split these into 2+ groups, or organise the conditions in a different way?

There may be no right or wrong answers in terms of how we group studies but we need to have a clear rationale for our decisions.

Please let us know if you have any suggestions or questions.