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## Combining evidence from randomised controlled trials and non-randomised controlled studies with modified GRADE in the nocturnal enuresis guideline

Katrina Sparrow, Vanessa Nunes, Norma O'Flynn

*National Clinical Guidelines Centre for Acute and Chronic Conditions, Royal College of Physicians, London, United Kingdom*

**Background:** The National Institute for Health and Clinical Excellence (NICE) commissioned the National Clinical Guidelines Centre for Acute and Chronic Conditions (NCGC-ACC) to produce a guideline on the management of bedwetting in children. The bedwetting guideline is using a modified GRADE approach to analyse and present evidence. Nocturnal enuresis is a significant issue for several groups of children with disabilities – children with attention deficit disorder, and children with sickle cell disease for example. The guideline development group (GDG) requested the inclusion of both randomised controlled trials (RCTs) and non-randomised studies where RCT evidence was not available to ensure evidence from different population subgroups and safety aspects were considered in the guideline.

**Purpose:** To describe the analysis and presentation of combined RCT and non-randomised evidence for the bedwetting guideline,

**Method:** Currently NICE methodology states that guidelines should use modified GRADE to present evidence. To present the evidence, we will meta-analyse the RCTs and will conduct a separate meta-analysis of the non-randomised studies if the quality of the studies allows this.

**Results:** The initial sifting provisionally identified 40 non-randomised studies to be included in the evidence review. The following subgroups have been identified: children with monosymptomatic nocturnal enuresis, attention deficit hyperactivity disorder and sickle cell anaemia.

**Discussion:** With the more systematic use of modified GRADE across the NICE guidelines programme, the issues of combining different types of evidence are a core methodological issue for developers. It is not appropriate to combine RCT and non-RCT studies in a meta-analysis because of significant issues, such as increasing bias and heterogeneity. This posed problems for presenting the two types of evidence with modified GRADE. We will discuss the challenges which were found through two meta-analyses of RCTs and non-randomised studies and presenting these using modified GRADE, and how these were overcome.