31 THE IMPACT OF PAEDIATRIC DOSE RANGE CHECKING SOFTWARE

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Dosing errors can cause significant harm in paediatric healthcare settings.

Our objective was to investigate the effects of paediatric dose range checking (DRC) clinical decision support (CDS) software on overdosing-related outcomes.

A before-after study and a semi-structured survey of prescribers was conducted across inpatient wards (excluding intensive care) in a regional children's hospital. DRC CDS software linked to a paediatric drug formulary was integrated into an existing electronic prescribing system.

The main outcome measures were; the proportion of prescriptions with overdosing errors; overdosing-related clinical incidents; severity of clinical incidents; and acceptability of the intervention.

The prescription overdosing error rate did not change significantly following the introduction of DRC CDS software: in the pre-intervention period 12/847 (1.4%) prescriptions resulted in prescription errors and in the post-intervention period there were 9/684 (1.3%) prescription overdosing errors (n=21, Pearson $\chi 2$ value=0.028, p=0.868).

However, there was a significant trend towards a reduction in the severity of harm associated with reported overdosing incidents (n=60, Mann-Whitney U value=301.0, p=0.012).

Prescribers reported that the intervention was beneficial and they were also able to identify factors that may have contributed to the persistence of overdosing errors.

DRC CDS software did not reduce the incidence of prescription overdosing errors in a paediatric hospital setting but the level of harm associated with the overdosing errors may have been reduced. Use of the software seemed to be safe and it was perceived to be beneficial by prescribers.

32 RAPID DROP IN MIDAZOLAM CONCENTRATION MAY BE LINKED TO PAEDIATRIC DELIRIUM IN CRITICALLY ILL CHILDREN – AN OBSERVATIONAL PILOT STUDY

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Introduction We sought to detect a relationship between midazolam concentration and development of new delirium in critically ill children who were on continuous midazolam administration.

Methods Delirium was detected using the Sophia Observation withdrawal Symptoms - Paediatric Delirium (SOS-PD) score and 104 left-over samples were available to measure midazolam concentrations.

Results Twenty-five percent of the included patients developed new delirium. Median cumulative midazolam dose was higher in patients who developed delirium compared to those without delirium but lower compared with the day preceding delirium detection, indicative of a rapid decline. Similar findings were made when active metabolites 1-hydroxymidazolam and 1-hydroxymidazolam glucuronide were considered.

Conclusions A sudden and significant reduction in midazolam concentration may contribute to the development of a delirium in critically ill children.

33 OFF-LABEL USE OF DRUGS IN PAEDIATRIC (SPECIALISED) OUTPATIENT CLINICS – WHAT HAS CHANGED BETWEEN 2009 AND 2019?

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Introduction Off-label use is still inevitable for paediatric drug treatment. The aim of this study was to analyse the licensing status of drug prescriptions in German paediatric (specialised) outpatient clinics and to determine changes over a 10-year time course.

Methods Cross-sectional, retrospective, monocentric studies were conducted in 2009 and 2019 to assess drug prescriptions regarding their licensing status in 10 (one general and nine specialised) outpatient clinics in Germany. Prevalence and relative frequency of off-label prescriptions were calculated, reasons for off-label prescribing analysed and logistic regression performed to determine influencing factors.

Results 751 prescriptions of 296 patients in 2009 and 1438 prescriptions of 786 patients in 2019 were examined and classified according to their licensing status. Relative frequency of off-label prescriptions was around 45% without significant change over that decade. Prevalence of off-label prescriptions was 60.1% in 2009 and 53.1% in 2019 and therefore significantly higher in 2009 (p=0.037). The number of prescriptions per patient was significantly higher in 2009 (2.5 ± 2.3 vs. 1.8 ± 1.5, p<0.000), too. Comparison revealed the same high-ranking reasons in every study: off-label use due to indication, overdosing and missing paediatric information.

Conclusions Off-label prescribing still plays an important role in clinical daily routine in paediatrics. Despite numerous regulatory efforts and incentives, no substantial reduction in off-label prescribing could be determined since 2009. Further efforts are needed to generate more evidence-based knowledge about paediatric pharmacotherapy and to treat children as best as possible.

34 ATTITUDES OF CHILDREN AND YOUNG PEOPLE AND THEIR PARENTS TOWARDS POLYPHARMACY – PILOT STUDY

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Introduction A recent survey of healthcare professionals found that healthcare professionals concerns about patient and family anxiety was the main barrier to deprescribing. However, the

attitudes of families, children and young people (CYP) have not previously been sought.

Methods A questionnaire was designed to assess the attitudes of CYP and their parents towards polypharmacy and deprescribing based on a previously validated adult questionnaire (rPATD). Initial review and modification took place following input from a young person patient and public involvement group and a content evaluation panel of experts. Ethics approval was obtained, and a maximum of 22 participants (10% of the total study population) were to be recruited for the pilot. Inclusion criteria were CYP taking >2 for 28 days or more. The questionnaire was completed online using Microsoft Forms. Descriptive analysis was undertaken.

Results Twenty participants completed the piloting process (12 parents, 5 CYP aged 10–15 years and 3 CYP aged 16–17 years), as saturation was achieved. The mean number of medicines taken was six. Most parents (67%) thought their children were taking many medicines, whereas only 38% of CYP agreed with this. Only one CYP in the 10–15yrs stated they wanted to be involved in decisions about their medicines, whereas all of the CYP in the 16–17yrs cohort, and 92% of parents, said they liked to be involved. Overall, 83% of parents and 63% of CYP stated they would like to try stopping one of their medicines if it was advised by a doctor.

Conclusions The pilot data would suggest that CYP and their parents would be happy to consider stopping one of their medicines if advised to do so but data from the full study, which is currently recruiting, and statistically powered is awaited.

35 WHAT IS KNOWN ABOUT THE PHARMACOLOGY OF INTRAMUSCULAR THERAPEUTICS IN DUCHENNE MUSCULAR DYSTROPHY? A SYSTEMATIC REVIEW

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Introduction In 2018 the Centers for Disease Control published updated Standards of Care for Duchenne Muscular Dystrophy – newly included was the recommendation for all patients with DMD who received steroids to receive prescriptions for intramuscular (IM) hydrocortisone for emergency administration at home.

The aim of this systematic review was to assess the current understanding of the pharmacodynamics and kinetics of intramuscular therapies in patients affected by DMD.

Methods A systematic review was conducted according to Cochrane methodology. Medline, EMBASE and PubMed databases were searched. Two independent reviewers reviewed the abstract of each identified paper. Where there was any discrepancy in the decision to include or exclude a paper, a third reviewer arbitrated.

Results The search returned a total of 98 papers. 96 papers were excluded: 61 described animal or in-vitro studies, whilst the remaining studies did not study an intramuscular pharmacological intervention or were review articles.

Of the two included articles, one compared the immunogenicity of intramuscular and subcutaneous administration of influenza vaccination, and the other studied ten patients with DMD who were injected with two different doses of plasmidic DNA. Neither study reported on the pharmacodynamics or kinetics of the interventions.

Conclusions There is very limited evidence into the pharmacokinetics and -dynamics of IM therapies for children affected by muscular dystrophy. Given the recognised changes in the muscle structure and function, studies to explore if this causes clinically significant changes in boys with DMD are required.

36 MAPPING VARIATION BETWEEN NATIONAL AND LOCAL CLINICAL PRACTICE GUIDELINES FOR ACUTE PAEDIATRIC ASTHMA FROM THE UNITED KINGDOM AND THE NETHERLANDS

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Introduction Increasingly, hospitals rely on local clinical practice guidelines (CPGs) alongside national guidance to standardise clinical care. This study examines variation between national and local CPGs, using the example of acute paediatric asthma (APA) CPGs from the United Kingdom and the Netherlands.

Methods Fifteen British and Dutch local CPGs were collected with the matching national guidance for the management of APA. The drug sequences, routes and methods of administration recommended for patients with severe APA were represented. Deviations from national guidance were measured. Variation in recommended doses of intravenous salbutamol was examined. CPG quality was assessed using the AGREE II instrument.

Results British and Dutch national CPGs differed in the recommended drug choices, sequences, routes and methods of administration for severe APA. Local British CPGs diverged from national guidance for 23% of their recommended interventions compared to 8% for Dutch local CPGs. Variation in second-line recommendations was greater than for first-line recommendations across local CPGs from both countries. Recommended starting doses for salbutamol infusions varied by more than tenfold. The quality of the sampled local CPGs was low across five out of six AGREE domains (<60%).

Conclusions Local CPGs for the management of severe APA featured substantial variation and frequently diverged from national guidance. Their methodological quality was low. Although limited to one condition, this study suggests that unmeasured variation across local CPGs may contribute to variation of care more broadly, potentially undermining healthcare quality.

37 DEPRESCRIBING LONG ACTING BETA2 AGONISTS IN CHILDREN AND ADOLESCENTS WITH STABLE ASTHMA: A SYSTEMATIC REVIEW

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