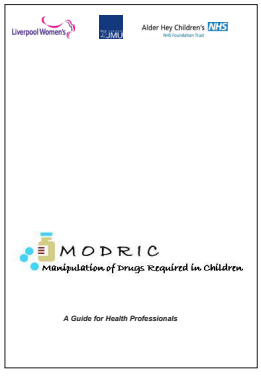
Guidance for modifying medicines for use in children

A guideline on the manipulation of drugs for administration to children has been developed by a team including staff from Liverpool John Moores University, Alder Hey Children's and Liverpool Women's Hospital NHS Foundation Trusts, and funded by the Research for Patient Benefit Programme from the National Institute for Health Research.

Manipulation of Drugs Required in Children (MODRIC): A Guide for Health Professionals is freely available for health professionals (www.alderhey.nhs.uk/wp-content/uploads/MODRIC_Guideline_FULL-DOCUMENT.pdf). It is intended for use by health-care professionals working in UK hospitals in neonatal and paediatric (birth to 18 years) inpatient settings.



'Manipulation of any medicinal product is not without risk,' commented team member Professor Jim Ford, from Liverpool John Moores University. He continued: 'For instance modifying the dosage form just before administration may result in an inaccurate or poorly reproducible dose, an altered product efficacy, or medication error. Use of the guideline should increase the numbers of babies and children who get the correct dose.'

The guideline draws attention to the lack of evidence relating to the correct manipulation of medicines to achieve a suitable dose for children, and asks the pharmaceutical industry to recognize that children may need a range of doses that require manipulation of adult dosage forms and to support practitioners who seek information around manipulations of medicines.

The guideline also highlighted the regulatory bodies who can work with the pharmaceutical industry to provide their known data for the benefit of children. The MODRIC group also suggests wider distribution of the guideline to hospital trusts so they are able to produce their own local guidance to support staff.

The guideline describes interventions that may avoid the need to manipulate medicines.

Where manipulation is considered necessary the guideline provides accessible, dosage form-specific guidance, for undertaking manipulations and provides guidance on avoiding manipulations (where possible) and medicines that should not be manipulated.

Effects of polypharmacy on hospital admission rates

Patients with a single illness who take many drugs have an increased risk of being admitted to hospital, but for patients with multiple conditions, taking many medicines is associated with a near-normal risk of admission, finds a new cohort analysis (Payne et al, 2013).

'The commonly-held assumption that polypharmacy is always hazardous and represents poor care is misleading,' says lead author Dr Rupert Payne, of the Cambridge Centre for Health Services Research, Cambridge. 'Our work shows that we need more sophisticated approaches to assessing the appropriateness of each patient's set of medicines.'

Working with colleagues in Nottingham and Glasgow, Dr Payne analysed Scottish NHS primary care data for 180 815 adults with long-term clinical conditions. They identified the numbers of regular medications each person was taking and linked this to whether or not the person was admitted to hospital in the following year.

For patients with only a single medical condition taking 10 or more medications was associated with a more than three-fold increase in the chance of having an unplanned hospitalization compared to patients who took only one to three medicines. However, patients with six or more medical conditions who used 10 or more medications only increased their chance of admission by 1.5 times compared to those taking one to three medicines.

Payne RA, Abel GA, Avery AJ, Mercer SW, Roland MO (2013) Is polypharmacy always hazardous? A retrospective cohort analysis using linked electronic health records from primary and secondary care. *Br J Clin Pharmacol* doi: 10.1111/bcp.12292

Long QT syndrome affects control of blood sugar levels

A study of 14 patients with congenital heart disease and 28 healthy control subjects has shown that patients with long QT syndrome produce twice the amount of insulin after consuming sugar than healthy subjects (Torekov et al, 2013). The patients' blood sugar decreases drastically a few hours after consuming sugar or food, compared to the healthy subjects who maintain a stable blood sugar.

Assistant Professor Signe Torekov and colleagues from the Department of Biomedical Sciences and The Novo Nordisk Foundation Center for Basic Metabolic Research at University of Copenhagen recruited patients from Aalborg and Gentofte hospitals with long QT syndrome.

'Until now, doctors thought that symptoms like fatigue and malaise in these heart patients were only caused by their arrhythmia, but the feelings of discomfort were also caused by their blood sugar being too low. With our discovery we can connect a specific potassium-ion channel to blood sugar levels, and this could benefit the diabetes patients of the future, because we will be able to gather more knowledge on the body's sugar metabolism,' concluded Dr Torekov.

Torekov SS, Iepsen E, Christiansen M et al (2013) KCNQ1 Long QT syndrome patients have hyperinsulinemia and symptomatic hypoglycemia. *Diabetes* doi: 10.2337/db13-1454 (Epub ahead of print 18 December 2013)

Continuing statin use reduces risk of delirium in intensive care patients

Continued use of statins may help prevent delirium in critically ill patients who received statins before hospital admission, according to a study of intensive care patients in the UK (Page et al, 2014).

'This is the first study using a validated delirium screening tool, the Confusion Assessment Method-ICU, to show that the administration of statins reduces delirium in these patients,' said lead author Dr Valerie J Page, of Watford General Hospital, Watford, UK. 'This benefit may be mediated by a reduction in systemic inflammation,' she added.

Of the 470 patients included in the study, 151 received statins. Statins were only given to patients who had received statins before admission.

Dr Valerie J Page, Watford General Hospital, Watford

After adjustment for age, sex and illness severity, administration of statins the previous evening was associated with a significantly lower risk of delirium and a concomitant reduction in serum C-reactive protein levels, a marker of systemic inflammation, the following day. The strength of the relationship between statin use and a lower risk of delirium was reduced when C-reactive protein was adjusted for.

'Although the pathogenesis of delirium is not fully understood, these data are consistent with a neuroinflammatory cause and suggest that the anti-inflammatory effects of statins may contribute to the effects of statin treatment on delirium,' said Dr Page. 'Our study on statin use and the risk of delirium in critically ill subjects included extensive data on a large, broadly representative population of consecutive intensive care patients, increasing its strength.'

Study limitations include the possibility that not all potential confounding factors were adjusted for and the limits of cognitive assessment tools in critically ill patients.

'Our findings suggest that statin treatment should be continued to help prevent delirium in critically ill patients who received statins before being admitted,' said Dr Page. 'The relationship between statin therapy and delirium and the mechanisms underlying this relationship are the subject of an ongoing randomized, placebo-controlled study in critically ill ventilated patients.'

Page VJ, Davis D, Zhao XB et al (2014) Statin use and risk of delirium in the critically ill. *Am J Respir Crit Care Med* Jan 13 (Epub ahead of print)

Predictors of access to care in patients with juvenile systemic lupus erythematosus

The UK JSLE Cohort Study study was undertaken to investigate factors that may influence the interval between symptom onset and diagnosis of juvenile systemic lupus erythematosus (JSLE).

Data from all patients recruited to the UK JSLE Cohort Study between 2006 and 2011 and meeting American College of Rheumatology criteria for lupus were analysed. Variables associated with time between symptom onset and diagnosis were identified using correlation tests. Linear regression was used to identify independent predictors of access to care.

A total of 257 children with JSLE were included in the analysis (216 females, 41 males, ratio 5.3:1). The median time from symptom onset to diagnosis was 0.4 years (range 0.0–14.1 years, interquartile range 0.2–1.4). A linear regression model identified being of African or Caribbean origin (P = 0.006), Asian (P = 0.045), referred by a paediatrician (P = 0.047) or having nephritis (P = 0.045) at presentation as independent predictors of shorter time to diagnosis.

Within this national UK cohort, ethnic origin, initial source of referral and having lupus nephritis at presentation were strong predictors of the interval to establishing a diagnosis of JSLE.

Smith EMD, Foster HE, Gray WK, Taylor-Robinson D, Beresford MW on behalf of the UK JSLE Study Group (2013) Predictors of access to care in juvenile systemic lupus erythematosus: evidence from the UK JSLE Cohort Study. *Rheumatology* doi: 10.1093/rheumatology/ket402 (Epub before print 5 December 2013)

Once-daily treatment for lower urinary tract symptoms

Vesomni, a new, once-daily fixed-dose combination of solifenacin 6 mg and tamsulosin 0.4 mg, is now available in the UK for the treatment of lower urinary tract symptoms in men with moderate to severe storage and voiding symptoms associated with benign prostatic hyperplasia that do not respond adequately to monotherapy.

Intensity-modulated radiation therapy safe and beneficial in head and neck cancer

Analysis of survival data for patients in the USA treated for head and neck cancer has shown that 84.1% of patients treated with intensity-modulated radiation therapy had not died from cancer, compared with 66.0% of patients treated with traditional radiation.

Once-daily ICS/LABA treatment for asthma and COPD

Fluticasone furoate/vilanterol (Relvar Ellipta) is the first inhaled corticosteroid/long acting beta2-agonist (ICS/LABA) combination to provide continuous 24-hour efficacy for the treatment of asthma and chronic obstructive pulmonary disease (COPD) in a practical once-daily dose.