

Potentially Inappropriate Prescribing in Children

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Background

There has been increasing focus on the quality of primary care for children with large scale population studies in the US and Australia reporting adherence to clinical guidelines of approximately 40 to 60%^{1,2}. In particular, there is limited evidence on the safety and effectiveness of prescribing for children². Medicines are generally considered appropriate in an adult population when they have a clear, evidence-based indication, are well tolerated in the majority of patients and are cost effective. Medicines or prescribing patterns that do not fit this description can be considered inappropriate or potentially inappropriate and may include misprescribing, over prescribing and underprescribing³. Potential consequences for children may be inadequate chronic disease management and unplanned hospital admissions and even rarely can result in preventable deaths⁴.

Optimal prescribing in children requires sufficient evidence on the safety and efficacy of medications in paediatric patients. However, studies show that for conditions with a high paediatric disease burden only a small proportion of clinical drug trials in these areas include paediatric patients⁵. Many drugs are unlicensed in children and are prescribed 'off label' and although not always inappropriate, the lack of a rigorous scientific basis for the prescription or dose can lead to side effects or adverse reactions. In 2007 the WHO launched a campaign to 'make medicines child size'. In an effort to address the issue of 'off label' prescribing, the European Medicines Agency and the US Food and Drug Administration now offer extensions to licenses to companies who provide evidence of safety and efficacy of a drug in a paediatric population. Current research highlights particular areas of concern for potentially inappropriate prescribing in asthma, antibiotics, anti histamines and amphetamines⁶.

Prescribing Indicators

The evaluation of whether medicines are prescribed rationally or appropriately is difficult. There has been insufficient research on developing validated tools to assess prescribing especially in children⁷. Prescribing indicators have been used to assess medication use in adult prescribing. Prescribing indicators or criteria can be defined as a measurable element of prescribing for which there is evidence or consensus that can be used to assess the quality of prescribing. Explicit prescribing indicators are specific statements of appropriateness of prescribing that are generally drug or diseases orientated and commonly focus on drugs to avoid. Drugs to avoid lists include medications that should be avoided in any circumstance, doses that should not be exceeded, and drugs that should be avoided

in patients with specific conditions or disorders³. These criterion based tools can be applied to large prescription or dispensing databases with little or no clinical information available regarding diagnosis or investigations⁸. Although the evidence base for developing explicit prescribing indicators is limited, combining expert professional opinion with consensus methodology can create quality indicators in areas where it would not otherwise be possible⁹. Explicit indicators such as the Screening Tool of Older Persons Prescriptions (STOPP) criteria enable the identification of potentially inappropriate prescribing while the Screening Tool to Alert doctors to Right i.e appropriate Treatment (START) criteria can be used to identify potentially appropriate medications that have been omitted¹⁰. Version 2 of these criteria, developed in 2015, include 114 criteria – 80 STOPP criteria and 34 START criteria¹⁰. Studies in older populations have been found the STOPP/ START criteria to be valid, reliable and generalizable across international primary care settings¹¹. Studies have highlighted that explicit prescribing indicators are not sufficient to assess whether prescribing is appropriate or not in the context of assessing daily prescribing practices on an individual patient level¹². However they can provide a means for comparing the prescribing practices of countries and can be used as outcomes to test whether interventions aimed at improving the safety and quality of prescribing have been effective¹³.

Ideally a prescribing indicator would be based on a thorough review of patient records with access to the full clinical and treatment history of the patient¹⁴, but this would be time consuming and could be extremely complex. A more realistic option is the development of prescribing quality indicators that can be applied to automated databases containing information on dispensed drugs. These databases are available in most developed countries; they generally lack detailed information about the patient or indication for the prescription but they allow process based prescribing indicators to be applied and to assess aspects of prescribing patterns, safety and cost effectiveness¹⁵.

Prescribing in Children with Asthma

The management of paediatric asthma, which is the most common chronic condition in childhood has been identified as an area of concern in the literature as it continues to cause death in people of all ages despite a number of preventable factors^{16,17}. Research in the UK has shown that adherence to international guidelines for example Scottish Intercollegiate Guidelines Network/ British Thoracic Society (SIGN/BTS) on pharmacological treatments is lacking in primary care¹⁸. European studies have also reported suboptimal treatment of asthma. In one Swedish study, 45% of children over seven years had at least one prescription of inhaled corticosteroids (ICS)

and only 10% had more than four prescriptions over a two year period¹⁹. Studies of adherence to asthma guidelines in primary care in the US have also identified the failure to prescribe daily maintenance medication (e.g. leukotriene receptor antagonists and ICS) in up to one third of patients with persistent asthma²⁰. In a previous study of Medicaid insured children with asthma in the USA, 73% were under-users of controller therapy with 49% reporting no controller use and 24% less than daily use²¹.

Prescribing of a long acting beta agonist (LABA) without an ICS, referred to as LABA monotherapy, has been used as an indicator of the quality of asthma care in adults in a number of studies^{22,8}. A recent Cochrane review found that LABA monotherapy in children was associated with an increased risk of serious non-fatal adverse events which were statistically significant for formoterol but not for salmeterol²³. In clinical practice, ICS/LABA combination inhalers are widely prescribed reducing the risk of inadvertent prescribing of LABA monotherapy and these combination inhalers were not included in the PIPc indicator list. Low but persistent rates of LABA monotherapy have been found in European studies and UK studies^{18,24}.

The clinical significance of poor adherence to guidelines in asthma is highlighted in a US study in which an organized disease management program delivered to patients in primary care resulted in increased adherence to guidelines in addition to a 35% reduction in hospitalization rates, a 27% decrease in Emergency department presentations and a 19% decrease in outpatient visits²¹. Barriers to physician adherence to guidelines identified in the literature include lack of awareness, familiarity and agreement with guidelines in addition to lack of self efficacy, lack of outcome expectancy and inertia of previous practice²⁵.

Antibiotic Prescribing

A large multinational cohort study in primary care in 2010 found that the most commonly prescribed drugs in children are anti-infectives, dermatological agents and respiratory drugs. The prevalence of the most commonly prescribed drugs was highest in children under 2 years²⁶. Many of these prescriptions may be inappropriate and it has been estimated that nearly 50% of antibiotic prescriptions for children given by primary care physicians are unnecessary²⁷. For example, in the UK there are around six million antibiotic prescriptions for children each year, the majority of which are for upper respiratory infections, most of which likely have a viral aetiology²⁸. The large scale population study of quality of care in Australia identified the overuse of antibiotics in eczema, croup, otitis media and tonsillitis as areas of concern with the use of antibiotics in tonsillitis as the only indicator with an estimated adherence of less than 50%¹. Inappropriate prescribing of antibiotics

The following table presents the agreed PIPc Indicators:

Table 1. PIPc Indicators by system.

Respiratory System	
1	Intranasal beclometasone should not be prescribed to children under 6 years
2	Carbocysteine should not be prescribed to children
3	An inhaled short acting beta-2 agonist should be prescribed to all children who are prescribed two or more inhaled corticosteroids
4	An inhaled short acting beta-2 agonist should be prescribed to children under 5 years who are prescribed a leukotriene receptor antagonist
5	An inhaled corticosteroid should be prescribed to children aged 5-15 years who are prescribed a long acting beta-2 agonist
6	Children under 12 years who are prescribed a pressurised metered-dose inhaler should also be prescribed a spacer device at least every 12 months
Gastrointestinal System	
7	Loperamide should not be used in the treatment of diarrhoea in children under 4 years.
8	Domperidone should not be prescribed concomitantly with erythromycin
Dermatological System	
9	Children prescribed greater than one topical corticosteroid in a year should also be prescribed an emollient
10	Tetracyclines should not be prescribed to children under 12 years
Neurological System	
11	Codeine/Dihydrocodeine medications should not be prescribed to children under 12 years
12	Sedating antihistamines should not be prescribed to children under 2 years

is, in turn, linked to increasing antibiotic resistance at both a population and individual level. A systematic review and meta-analysis, which included 11 studies on children, found that individuals prescribed an antibiotic in primary care for a respiratory or urinary infection developed bacterial resistance to that antibiotic and that this effect is greatest in the month immediately after treatment but may persist for up to 12 months²⁹. The authors concluded that this effect not only increases the population carriage of organisms resistant to first-line antibiotics but also creates the conditions for increased use of second line antibiotics in the community²⁹. On a positive note, a more recent study from the US of over 38,000 children has demonstrated a reduction in antibiotic use in children and adolescents from 8.4% to 4.5% from 1999/2002 to 2011/14 with the largest decrease in children under 2 years³⁰.

Measuring PIP in Children

We developed a set of 12 prescribing indicators using a Delphi consensus methodology to support prescribing for children in primary care³¹. The Delphi consensus method allowed an estimate of an overall group opinion to be reached by improving agreement between a panel of international experts through two rounds of an on-line questionnaire. The PIPc indicators developed related to commonly prescribed medications in Ireland and focused on indicators that could be applied in the absence of clinical information.

We are currently working on the application of these indicators to a primary care dispensing database to identify the prevalence of potentially inappropriate prescribing in children in primary care in Ireland.

Conclusion

The identification and measurement of potentially inappropriate prescribing in children remains a difficult and challenging task. Overall trends in prescribing rates are showing a slight reduction in the prescribing of some medications such as antibiotics but not in others such as amphetamines. Adherence to clinical guidelines by prescribing doctors could be improved, particularly for common chronic conditions like asthma. More research is required to provide clarity on the appropriateness and safety of prescribing in children.

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