

performed independently by two reviewers. The quality of included studies was assessed using the Newcastle-Ottawa quality assessment scale for cohort and cross-sectional studies, and the National Institutes of Health quality assessment tool for case series. The review was conducted and reported in accordance with the PRISMA guidelines for systematic reviews³ and was registered on PROSPERO with registration number CRD42021221631.

Results In total 81 studies were included in the systematic review, with 18.5% (15/81) studies deemed of good quality, 24.7% (20/81) studies of fair quality, and 56.8% (46/81) studies of poor quality. Almost all of the studies (99%, 80/81) were on tocilizumab. Only one study investigated siltuximab and none were found for sarilumab. The total number of patients included in the identified studies was 211 (210-tocilizumab, 1 siltuximab). For tocilizumab, the most frequently reported clinical indication was the management of complications associated with hematopoietic stem cell transplantation (24.3%, 51/210) followed by its use in the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) (17.5%, 14/80).

Overall, tocilizumab was prescribed for 28 unlicensed indications, and the dose varied from 4 to 12 mg/kg. Dosing frequency was reported in 98.7% (79/80) of tocilizumab studies, with 'every two weeks' prescribed most often (53.2%, 72/79). Adverse events were reported in 20.4% (43/211) of patients of which 32.6% (14/43) experienced adverse events, e.g. respiratory tract infections (n=2) and low platelet counts (n=2). The clinical outcome of the off-label use of tocilizumab was described to be successful in 55% (44/80) of studies, with reported success in the treatment of SARS-COV-2 and uveitis (13.6%, 6/44, each). The article on siltuximab reported no clinical outcomes.

Conclusion This is the first systematic review of the off-label use of IL-6 directed therapies in children. The limited data suggest that tocilizumab may be effective in a number of off-label indications, but the quality of available evidence is low and there remains the need for adequately powered and well-designed studies to support its use in clinical practice. The findings of this review should be used as a basis to inform future clinical trials in paediatrics.

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PRIMARY PHARMACEUTICAL CARE AND YOUNG PEOPLE: EXPLORING YOUNG PEOPLE PERSPECTIVES

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Introduction According to recent literature, the prevalence and incidence of long-term illnesses such as asthma and diabetes in young people has substantially risen over the past 13 years.¹ Recent figures indicate that, in England, 4.1% of all prescriptions were prescribed for young people. More than 45 million prescriptions were dispensed for young people in 2017 by pharmacists.²

Aim The aim of this study was to investigate young people's perspectives of the pharmaceutical services that are provided from primary care pharmacists relating to medication.

Method A cross-sectional survey using both the online and paper-based tools was conducted from March to November 2019. The population for this survey was young people from age 18 to 24 years registered as students at one of the universities in the UK. The survey consisted of twenty-four questions and they were a mix of closed-ended questions such as multiple choice and Likert scale and open-ended questions. This research gained ethical approval from the Ethics Committee of the same University (ERN_17-1672).

Results A total of 210 survey responses were returned. Most of the participants were female (62.4%). The most frequent age was 18 years (35.2%). Among participants, 15.7% were diagnosed with long-term illnesses and the majority of them (33.3%) were diagnosed with respiratory disease all of which was reported as asthma. Pharmacists were not utilised as a source of information for young people whereas the majority (60.6%) obtained information from their doctors. Most of the participants (97%) had not taken part in an MUR or NMS and 78.8% of them had never been told about any services or support groups by their pharmacist.

Discussion and Conclusion There is a lack of provision of pharmaceutical services and support by primary care pharmacists to young people with long-term illnesses. Previous evidence shows that this could be due to a lack of confidence when dealing with young people, unwillingness of pharmacists to take on more responsibilities, or a lack of training and support.³ The results would be of benefit to the policymakers to assist in the further growth of the pharmacy services. Further research will enhance understanding of the perceptions of young people about the pharmaceutical services that are offered by primary care pharmacists with respect to medications.

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ASSESSING COMPLIANCE WITH OXYGEN PRESCRIBING IN PAEDIATRICS

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Aim The National Patient Safety Agency Rapid Response Report¹ and British Thoracic Society (BTS) guidelines² state that oxygen should be prescribed. Following the introduction of electronic prescribing in a specialist children's hospital, there was a reduction in the number of patients whose oxygen was prescribed. A series of audits were undertaken to determine how often oxygen administration was accompanied by a valid prescription and whether a variety of interventions affected prescribing.

Method Eight paediatric wards in a specialist children's hospital were included in the audit. Critical care and the Emergency Department were excluded. A total of 4 audits were

completed across 16 months. Each audit comprised of a pharmacist visiting each ward on a single day and asking nurses which patients were receiving oxygen. The electronic prescription for each patient was then reviewed to determine whether oxygen was prescribed or not. Data was recorded and then analysed using descriptive statistics. Medical and nursing staff on the wards at the time of data collection were also asked for their views about the prescribing of oxygen.

Following the baseline audit, a variety of actions were introduced in order to improve the rate of prescribing including: a) Circulation of a hospital-wide Patient Safety Alert b) Highlighting oxygen prescribing at Ward Managers Meetings and Doctor Handovers c) Reminding all new doctors, nurses and pharmacists that oxygen must be prescribed and that prescribers should be challenged when oxygen isn't prescribed d) Inclusion of oxygen prescribing in the Trust's Medication Safety mandatory training

Results The baseline audit (November 2019) found 4.9% compliance with oxygen prescribed. At this point doctors described oxygen prescribing as 'unnecessary work'. Junior nurses knew oxygen should be prescribed but did not believe it was their responsibility to chase prescribers. Following the introduction of remedial action (February 2020) compliance with oxygen increased to 39.1%. Repeat audits (December 2020 and April 2021) found compliance to be 53.8% and 42.1% respectively.

Conclusion Whilst compliance with oxygen prescribing has improved since the baseline audit, the Trust has not achieved the target of 80% compliance with oxygen prescribing. Contributing factors to this are the rapid turnover of medical and nursing staff and an apparent culture change is required to highlight the importance of oxygen prescribing amongst multi-disciplinary teams.

If an impactful change is to be made, it needs to be made clear to all groups that this is an important task. The key seems to be continual communication so that oxygen prescribing becomes routine across the Trust.

Action to be taken includes ensuring all relevant staff are aware of the need to prescribe oxygen; regular re-audit and sharing of the results with senior nursing, medical and pharmacy staff. The process for prescribing oxygen is now demonstrated during the introduction to electronic prescribing and we have started a Quality Improvement Project in conjunction with senior nurses on the ward who performed the worst across our audits.

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COULD THE FORMULATION AND/OR METHOD OF ADMINISTRATION OF ORAL NADOLOL HAVE A CLINICALLY SIGNIFICANT IMPACT ON THE DOSE DELIVERED TO THE PATIENT

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3-year-old girl requiring oral nadolol 100mg twice daily. The only UK licensed formulation available was 80mg tablets. Family had been instructed by another hospital to disperse 2 x 80mg nadolol tablets in 10ml water and administer 6.25ml. However, tablets did not disperse well with concerns about dose accuracy and consistency. Possible alternative formulations were an 'in-house' extemporaneous suspension (10mg in 5ml) or an unlicensed 'special' suspension (40mg in 5ml). Latter sourced and supplied. However, the family subsequently reported an increase in ectopy and child reverted to use of dispersed tablets. Could the change in formulation have a clinically significant effect? How accurate is the dose delivered via these formulations?

Method We asked regional QC to investigate (using Corgard (R) 80mg tablets):

- Accuracy and uniformity of nadolol tablet breaking
- Uniformity of nadolol distribution within the tablets
- Nadolol assay by HPLC of
 - nadolol 80mg and 160mg in 10ml distilled water
 - nadolol 40mg and 20mg segments (of 80mg tablets)
 - nadolol 10mg in 5ml suspension ('in-house' extemporaneous suspension)
 - nadolol 40mg in 5ml suspension (unlicensed special)

Results Whilst the distribution of nadolol in Corgard(R) 80mg tablets was demonstrated to be uniform, the process of breaking Corgard(R) 80mg tablets into halves and quarters demonstrated variability with segment weights.

Nadolol formulations of dispersed tablets in water 80mg in 10ml and 160mg in 10ml suggest nadolol is not fully soluble as supernatant assay concentration was lower than the initial concentration (after initial dilution and shaking) for both strengths. The solubility limit of nadolol in water estimated to be ~8mg/ml.

Nadolol 10mg in 5ml suspension assay concentration was 112% of the expected concentration demonstrating a suitable manufacturing process for the 'in-house' 10mg in 5ml extemporaneous formulation.

Nadolol 40mg in 5ml (unlicensed special) assay concentration was only 79.9% of the expected concentration. However, the low assay result could have been due to the analytical method used for analysis which may require further validation for testing of this suspension type. Of note, only a single sample was tested.

Conclusion In this case, the patient was complex and unstable, and her clinical condition may well have contributed to the increase in ectopy experienced. However, the work done by regional QC identified the risk of inaccuracy and/or variation in the dose of nadolol delivered using different formulations and/or methods of administration.

The solubility limit of nadolol in water is estimated to be ~8mg/ml. Dispersed oral solutions must be thoroughly mixed prior to patient use especially if a proportional dose is required. Inconsistency of the dose of nadolol delivered should be considered when using this method.

Further, the change in formulation to the oral suspension could, unintentionally, have resulted in a difference in the dose delivered to the patient.

A consistent method for administration should be followed and, if a change in formulation is considered necessary, the patient monitored for any sign of reduction in efficacy and/or increase in adverse effects.