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# Barriers to administering non-oral formulations in a paediatric population: A semi-structured interview study

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ABSTRACT

There is a paucity of research exploring barriers to non-oral medicines administration in paediatric patients; however, these undoubtedly influence medicines adherence. Studies conducted with healthcare professionals have identified various issues with the administration and acceptance of non-oral medicines and devices (Venables et al., 2012; Walsh et al., 2015). EMA (2014) guidelines specify that formulation teams should demonstrate 'acceptability' of paediatric formulations when developing pharmaceutical formulations.

Semi-structured interviews exploring barriers to administering non-oral medicines were conducted with young persons and the parents/legal guardians of children (0–17 years) with chronic conditions at the University Hospital of Coventry and Warwickshire, UK.

90 children prescribed a total of 148 non-oral medicines were recruited to the study; 88 barriers to administering non-oral medicines were reported. The most commonly reported barriers were: poor acceptance of face mask/difficulties with spacer for inhaled formulations (38% of reports); disliking parenteral/preferring alternative formulations (38% of reports); greasy texture of topical preparations; difficulty with administering an ocular ointment and the large dose volume of a nasal preparation.

Formulation teams should consider the use of child-friendly, age-appropriate designs to improve usability and acceptance, thus medicines adherence. These findings should be used to inform future development of non-oral formulations and devices, suitable in terms of safety, efficacy and acceptability to paediatric patients.



## 1. Introduction

Approximately 200 million prescriptions are issued annually for children and young people in the UK (Costello et al., 2004). It has been estimated that 5–10% of young people worldwide suffer from chronic health conditions (Newacheck et al., 2000).

Children with chronic conditions may be prescribed a variety of medicines and have complex regimes. There is evidence to suggest that adherence with prescribed medication is lower amongst adolescents and children than in adults (Staples and Bravender, 2002). Medication adherence rates between 11% and 93% in paediatric patients have been reported (Winnick et al., 2005).

Acceptability has previously been defined as the overall ability of a patient/caregiver to use a medicinal product as intended/authorised (Kozarewicz, 2014). Acceptability of a medicinal product has potential to significantly affect the patient's adherence and therefore is likely to influence its safety and efficacy (Kozarewicz, 2014). Usability has been used interchangeably with 'human factors' and defined as a 'multi-dimensional quality', which reflects human ability 'to interact easily and relatively error-free with a system or product.' This may be translated in medical device terms, as the measure of how well a device works to meet user expectation, thus administration without frustration (BSI, 2015).

Over the past two decades, trends in post-market adverse events related to design issues affecting usability of medical devices have been reported. These use-related design issues have resulted in problems with therapies (BSI, 2015).

There is a paucity of research exploring barriers to non-oral formulations and devices used in the administration of

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formulations to paediatric patients within a pragmatic environment. However, barriers to medicines administration undoubtedly influence medicines adherence. Studies conducted with healthcare professionals have identified various issues with the usability and child acceptance of non-oral formulations and devices, (Venables et al., 2012; Walsh et al., 2015). In order to improve formulations for children in the future, it is inevitable that one needs to understand barriers to administration, thus usability can inform future drug development work to improve the design of medicinal products and medical devices. Children have different sensory perceptions to adults and are therefore the most important participants for acceptability studies in paediatric patients; thus it was necessary to identify barriers to administration from their perspective to inform the design of future formulations and administration devices.

More information is needed to understand the factors that influence child and carers' attitudes to medicines adherence to inform future paediatric formulation design. Regulatory agencies have also noted the importance of acceptability of devices for the administration of non-oral formulations. EMA (2014) guidelines and guidance from BSI (2015) on 'user interface (UI) design/evaluation' support FDA (2011) draft guidance on optimizing medical device design, which outlines potential human factors and usability engineering (HFE/UE) analyses that should be conducted for medical devices, this includes formative evaluations of medical devices.

The aims of the present study were: (i) to establish the prevalence and nature of barriers to administering non-oral formulations to paediatric patients with chronic conditions (ii) to determine how frequently any factors identified with non-oral formulations (including devices used to administer formulations) are involved in compromising acceptability and refusal and (iii) to inform future paediatric (non-oral) medicines formulation and device design, the pharmaceutical industry and prescribers.

## 2. Materials and methods

### 2.1. Data collection tool

A semi-structured interview was selected for this study to obtain the qualitative data required and provide an appropriate balance in data collection and subsequent analysis (Malim and Birch, 1996). A multidisciplinary research team (Professor in Clinical Pharmacy, paediatric consultant and pharmacist) generated an outline of barriers to administering formulations to children; medicines administration issues were refined via four focus groups with healthcare professionals at the University Hospital Coventry and Warwickshire (UHCW) and Birmingham Children's Hospital (BCH). The data collected, in addition to self-report methodologies referenced in published studies (Medical Adherence Measure—MAM (Ingerski et al., 2010; Zelikovsky et al., 2008), Treatment Interview Protocol—TIP (Marhefka et al., 2004), Paediatric AIDS Clinical Trials Group PACTG questionnaire (NIAID, 2015) and Morisky Scales (Morisky et al., 2008, 1986) were used to inform the design of the self-report semi-structured interview tool. The Young Persons Advisory Group (YPAG) at Birmingham Children's Hospital ($n = 12$ members) reviewed the tool to ensure that it was age appropriate. The 13-item self-report tool used in the semi-structured interviews was designed to collect data exploring medicines acceptability and adherence. Open questions were used to elicit barriers to medicines administration and a closed question was used to identify rates of refusal. The tool used has been previously reported by Venables et al. (2015).

A semi-structured interview was conducted by a single researcher (not previously known to the patients) to minimise variation in approach and the responses were entered manually onto a structured data record during each interview. The interviews (maximum duration of 45 min) were conducted in a private area at the paediatric outpatients department at UHCW at times scheduled to coincide with routine clinical appointments.

Ethical approval was granted by the South Birmingham REC and informed consent was obtained from all participants.

### 2.2. Qualitative analysis

Thematic content analysis was conducted using a frame-work approach to form a coding spine (Pope et al., 2000). This analytical method was used to identify and group common themes arising from the qualitative data, relating to administering non-oral formulations.

### 2.3. Study setting and participants

A pragmatic approach was employed to identify and recruit participants, resulting in a total of 1559 study invitation letters being posted to patients (via their parent/carer) due to attend follow-up paediatric clinics (1448/1559) or handed out on the paediatric wards (111/1559) at UHCW. Study interviews were conducted with parents or carers (if legal guardians) of children or young people, or with young people directly. The opportunity to assent and participate alone was given to 12–16 years old, providing parent or carer consent was also obtained. Young people aged 16 to <18 years of age were permitted to consent alone and encouraged to discuss the study with a parent or legal guardian before providing consent. It was necessary to include young people (those over 12 years of age), where appropriate as this sub-population reported increased empowerment over medicines administration. Parents' and carers' views were more useful for younger children where they did not have the cognitive capability to participate alone or were not responsible for medicines administration.

Age-appropriate study information was provided to potential participants at least 24 h before asking for participation in the study. A total of 191 general and speciality outpatient clinics were targeted covering a wide range of chronic conditions (e.g., epilepsy, cystic fibrosis, neoplasms, cardiac disorders, endocrine disorders, tuberculosis, HIV, renal diseases, rheumatological diseases and survivors of neonatal intensive care). It should be noted that not all patients in clinics were prescribed medications; therefore not all patients were eligible for study inclusion. There was a scheduled approach to accessing patients at these clinics on a rotating basis to ensure wide coverage of the target patient population. UHCW is a teaching hospital with three age-banded paediatric wards. Inpatients from all three paediatric wards at UHCW were included at the recruitment phase to minimise the risk of missing eligible patients who were hospitalised during the study period.

### 2.4. Inclusion criteria

Children (aged 0 to <18 years) with chronic conditions and their parents/carers were recruited to the study. Patients were eligible for inclusion if they had been taking a prescribed medication for a chronic condition for at least one month prior to their outpatient appointment.

## 3. Results

A total of 280 participants consented to the FIND OUT study (Venables et al., 2015). In total, 90 participants were prescribed at least one non-oral formulation. Interviews exploring barriers to administering non-oral formulations were completed with