Information for Children and Young People about reporting suspected adverse drug reactions

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# Abstract

## Background

When children and young people (CYP) report their own suspected adverse drug reactions (ADRs), different patterns of drugs and symptoms are noted. A new guide to reporting suspected ADRs using the Medicines and Healthcare Products Regulatory Agency (MHRA) Yellow Card scheme was developed by CYP, paediatric clinical pharmacology, Yellow Card Centres and the MHRA.

## Methods

An anonymous quality improvement project to assess the guide for CYP was undertaken (Sept 2020-Feb2021).

## Results

The survey was completed by 234 CYP age 13-18 years. Within respondents, 68/226 (30.1%) were using medicines, 209/225 (92.9%) had used medicines previously, and 211/225 (93.8%) had heard of side effects. 79/225 (35.1%) believed they had experienced a side effect, with some requiring hospitalisation. Only 8/221 (3.6%) respondents were aware of the MHRA Yellow Card scheme.

Overall, 182/196 (92.9%) of CYP both understood the guide and felt more knowledgeable about how to report suspected side effects. CYP comfortable to report their own suspected ADR increased from 179/222 (80.6%) before reading guide, to 189/196 (96.4%) after reading the new CYP guide. In addition, 156/196 (79.6%) believed they would report a side effect from a medicine used in future. Over 360 free text comments were also received, providing comments about what was good about the new guide, and areas for improvement that could be made.

## Conclusion

The new guide for CYP to inform them about how to report a suspected ADR to the MHRA was well received and increased the knowledge, and confidence to report, in those who responded.

What is already known on this topic?

* Under-reporting is a common problem for adverse drug reaction (ADR) spontaneous reporting schemes like the MHRA Yellow Card scheme.
* Young people are allowed to report suspected ADRs, but the number of reports is low
* When young people do report, the quality of reports is good, and the drugs and reactions differ from reports from adults about young people.

# What this study adds?

* Information developed with young people can increase understanding about, and willingness to, report suspected ADRs
* Young people were engaged with the process of document design and improvement, and contributed meaningfully to improve the content

# Introduction

The Medicines and Healthcare Regulatory Agency’s (MHRA) Yellow Card scheme (YCS) collects spontaneous reports about suspected adverse drug reactions (ADRs) from a range of stakeholders in the UK, including healthcare professionals, patients, parents, and carers. Spontaneous reports from patients are of similar quality to (1, 2), and identify additional information beyond, those from healthcare professionals (3, 4). The inclusion of patient and carer reports in spontaneous reporting schemes has increased worldwide (5). However, despite broadening the range of reporters for suspected ADRs, under reporting remains a problem (6).

Paediatric patients are affected by ADRs, with approximately 3% of all admissions to hospital of children and young people (CYP) directly related to an ADR (7). In addition, nearly one in five paediatric inpatient stays are complicated by an ADR (8). There are unique ADRs in children (e.g. interference with growth), and the effects can be lifelong. CYP may experience either different types of ADRs to adults for a particular drug, or different severity, or both (7, 8) and hence reporting them is particularly important.

While there is considerable literature about reports of suspected ADRs submitted by others about CYP (9-14), and clinical services are now being developed that promote paediatric pharmacovigilance activities (15), there is limited data on reports that CYP have submitted themselves. Within the UK, these data from suspected ADR reports to the MHRA YCS have been analysed; direct reports from CYP only comprise 2.3% of all reports about patients <19 years old; different medicines were reported; a range of important but previously uncommonly reported suspected ADRs were included (4).

Across the teenage years, a transition from dependence on parents/carers, to full independence across all aspects of life occurs, and this includes health. For healthcare professionals, this has historically focussed on ensuring continuity of disease management, such as stressing the importance of adherence to treatment (16-18), and transition to adult services (19). The current UK National Curriculum for secondary school age children specifically mentions that CYP should have “specific awareness of the dangers of drugs which are prescribed but still present serious health risks”(20), but does not include any specific guidance on what CYP should do in the event they are concerned about a suspected ADR. MHRA has worked with the Department of Education previously on the content of the Personal, Social, Health and Economic education (PSHE) curriculum, resulting in information being added about side effects at an age appropriate level for primary and secondary school children. For secondary school CYP, there is inclusion of the importance of discussing side effects with a GP or a pharmacist, reinforced with a link to the Yellow Card scheme for the reporting of side effects which they may choose to share with pupils. However, previous MHRA information was not specifically designed with CYP in mind. There is therefore a need for specific guidance aimed at CYP to inform, educate and empower them to self-report or at least be aware they can report their suspected ADRs. CYP have developed outline text for such a document previously (4), and since then this has been developed further by the MHRA pharmacovigilance team and paediatric clinical pharmacologists. This work details the quality improvement project undertaken to assess what CYP in the UK think of this updated information.

# Methods

The Quality Improvement project was registered at Alder Hey Children’s Hospital (audit ref 6145) in August 2020, and was carried out and reported in line with SQUIRE 2.0 guidance (21).

Using the form of words about how to inform and empower CYP to report suspected ADRs previously developed by 300 CYP working across five iterative phases (4), an ad-hoc working group at the MHRA was convened. This group included regulatory experts, pharmacovigilance experts, paediatric clinical pharmacologists, as well as contribution from regional Yellow Card Centres. This team used the form of words created previously (4) and adapted this into a guide for CYP (Figure 1). The team then proceeded to undertake the larger scale survey.No patient identifiable information was collected.

The format of the online survey was structured as follows:

* Age, and experience of medicines and side effects
* Review of updated information
* Feedback about this information

The exact wording of the questions in the survey is shown in the supplementary data section, along with the possible answers (format and options) available to the respondents.

The online information and survey was developed using the Surveymonkey platform ([www.surveymonkey.co.uk](http://www.surveymonkey.co.uk)) and designed by MHRA. Members of the MHRA ad-hoc working group undertook pilot testing of the survey initially, followed by a small cohort of CYP known to the authors, and the responses reviewed to ensure that both the new guide and the survey questions had been understood. These pilot responses were not included in the final dataset of responses presented in the results section.

Following this pilot phase, the finalised questionnaire was approved by the MHRA ad-hoc group, and the questionnaire was released. It was promoted by the MHRA team, its ad-hoc working group, through established groups, and engaging with new CYP stakeholders e.g. sharing with other government departments to promote (Department for Education and Department for Digital, Culture, Media & Sport through their Civil Society and Youth Directorate), and promoted using the MHRA’s Twitter channel on social media. Online responses were accepted between September 2020 and February 2021. Groups of CYP who had previously contributed to the development of the text were not included in the promotion of the survey. In order to be compliant with GDPR legislation, the age range accepted for respondents was limited to 13-18 years.

Data were analysed using descriptive statistics (Microsoft Excel)

# Results

Two hundred and thirty-four young people completed some or all of the survey. The demographic information about this population is shown in table 1. Feedback was received between September 2020 and February 2021.

The demographics, and experience with medicines and side effects, are detailed in table 1. Respondents were aged between 13-18 years, with the most common age 14 years. Less than a third were taking medicines, but more than 90% had experience of taking/receiving medicines. There was a high level of knowledge about the existence of side effects, with 211 (93.8%) respondents having heard of them. Overall, 79 (35.1%) CYP who responded believed they had had experienced a side effect. Contained within this unselected population, there were four reports of suspected side effects severe enough to send the young person to hospital (Table 1).

Young people who responded that they had experienced a side effect were provided with a free text field to provide additional details if they wanted to. Forty-five young people provided responses. Despite having not read the updated guide at this point in the survey, and therefore with no information to guide them about what was required in a response, 21 provided suspected drug(s) and reaction(s) pairs such that 22 Yellow Cards could have been completed (Table 2) and those that were valid were uploaded to the Yellow Card scheme database. Clinically serious suspected adverse drug reactions were present, including suicidal ideation and meningitis (Table 2).

Eight of the 221 respondents (3.6%) had heard of the MHRA Yellow Card scheme, while 213/221 (96.4%) had not. Only 1/222 (0.45%) had reported a Yellow Card.

The final question prior to review of the draft guide was about who a CYP would tell if they thought they had experienced a side effect. The CYP were offered multiple options, and could select multiple responses. The most common responses were “parents” or “someone who cares for you” (see table 3).

The final form of words that was then presented to the CYP for review is shown in figure 1. The first question after the guide was presented was “Do you understand the guide”, and of the 196 responses to this question, 182 (92.9%) reported that they understood the guide, while 14 (7.1%) did not.

* The subsequent questions used free text responses to further understand “What did you like about this guide”. One hundred and fifty-nine written comments were provided in response to the question, complete feedback provided by CYP is shown in the supplementary data section. Common themes included: Easy to read
* Clear
* Informative
* Well structured/ Divided into sections
* Organised
* Easy to understand
* Use of the QR code.

One hundred and thirty-seven written comments were provided for the question “what could be improved?”. Themes and full responses are shown in the supplementary data section, but are summarised here:

Nothing could be improved/I don’t know (n=31, 22.6%)

Improved graphic design/how it looks (n=41, 29.9%)

Altering the content/text (including comments about being too long) (n=48, 35.0%)

Creation of other versions for younger readers (n=4, 2.9%)

Requests for specific information about drugs and their side effects (n=6, 4.4%)

Suggestions to promote the Yellow Card scheme more (n=3, 2.2%)

Other (including technical issues with the QR code) (n=4, 2.9%)

After reading the guide, in response to the question “Do you know more now about how to report a side effect than before?”, 182/196 (92.9%) answered yes. CYP comfortable to report their own suspected ADR increased from 179/222 (80.6%) before reading guide, to 189/196 (96.4%) after reading the new CYP guide. Conversely the percentage of CYP who would not be comfortable to report their own suspected ADR decreased from 43/222 (19.4%) to 7/196 (3.6%) (Figure 2).

Of the 196 responses to “Would your report a side effect from a medicine you use in future?”, 156 (79.6%) replied “Yes”, 8 (4.1%) replied “No”, and 32 (16.3%) replied “Not Sure” (Figure 2A).

The survey concluded with a question asking “Do you have any additional comments or thoughts?” which was answered by 83 CYP. Sixty-five (78.3%) responses were that there was nothing they wanted to add. The remaining comments are shown in the supplementary data section.

# Discussion

This quality improvement project has collected the views of 232 CYP about an updated guide from the MHRA about reporting suspected ADRs. In combination with the 300 CYP who previously helped develop the original form of words, this represents a genuinely inclusive and collaborative effort with CYP to improve the reporting of suspected ADRs.

While the survey was anonymous, and no patient identifiable data were collected, it is reassuring how the background medicine information broadly aligns with the general population. Of 16-24 year olds in the UK, 19% take a medicine at least weekly (22), compared to 30% amongst our respondents. There was a good level of knowledge about the existence of side effects which is consistent with the presence of this subject in the UK national PHSE curriculum.

The feedback on the updated guide was mostly very positive, which supports the ongoing development of this guide. With the licensing and approval of COVID-19 vaccine use in those age 12-17, a specific vaccine related guide has been prepared based on the feedback reported here to help provide additional information at this time based on this CYP guide, which is now live (<https://coronavirus-yellowcard.mhra.gov.uk/resources>).

An additional positive in the information provided was the quantity and quality of suspected ADRs spontaneously provided by CYP who completed the survey. Nationally there are in the region of 200 Yellow Card reports from CYP per year (4). This project suggests that while the reporting is low, this may be due to lack of awareness (evidenced by the lack of knowledge of the MHRA Yellow Card scheme) rather than a lack of willingness to report, and aligns with the altruism previously described in CYP when it comes to clinical trials (23).

However, we are mindful that the responses were not all positive, and that over 1/3 of children were not satisfied with the guide in its current form. While use of professional graphic design will alleviate some of the most common complaints, continued consideration of feedback from CYP using the guide will be needed to make sure it is fit for purpose. We do particularly note detailed individual responses such as the one highlighting perceived discrepancies in the age targeted, or the need for several copies for different ages. These shows both the benefit of getting CYP to comment, but also the need the need to continue the iterative development of guides such as this. In addition, response from CYP have highlighted areas where other guides or information may be required, such as how to fill in the actual Yellow Card.

An important limitation was that, as this was undertaken as a quality improvement project, we could not ask for personal identifiable information nor include those aged less than 13 for GDPR regulatory reasons. Therefore we do not know if the respondents are a representative sample compared to the general population.

An additional limitation relates to the wording of the questions. Within the guide, it directs CYP to report any suspected ADR to “Someone who cares for you”, but the possible responses included parents separately. The responses putting “someone who cares for you” increased following reading the guide, but parents reduced (Table 3). The guide was phrased this way to ensure that children in care, in foster homes, and other situations where a parent is not able to contribute were not excluded, but we can see how this could have affected the replies. More pleasingly, however, was noting that the proportion who would not be comfortable reporting a suspected ADR themselves decreased more than five-fold, which strongly supports the underlying premise of creating a guide specifically for CYP.

Once a guide is finalised, the method of disseminating this information to CYP needs to be considered. As suspected ADRs could occur in any CYP who uses medicines, we think that discussing with the Department for Education the possibility of modifying the existing school PHSE curriculum to include this information is one way to proceed, reaching approximately 700,000 CYP per year. .

We do also note that this survey, and the associated guide, are only currently available in English, and online, so future work will be needed to reach out to those who are either non-English speakers or who struggle with internet access. The team remain actively engaged with the MHRA about how best to continue the implementation phase of this work.

In conclusion, the updated guide for CYP succeeded in informing them about how to report a suspected ADR was well received, and increased the knowledge and confidence to report a spontaneous adverse drug reaction report amongst those who responded. The guide can be a useful tool to raise awareness about using the Yellow Card scheme with CYP and the importance of reporting suspected side effects.

# Acknowledgement

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| --- | --- |
|  **Demographics** | **Count (%)** |
| Age (years) | 13 | 48 (20.5%) |
| 14 | 52 (22.2%) |
| 15 | 49 (20.9%) |
| 16 | 41 (17.5%) |
| 17 | 24 (10.2%) |
| 18 | 20 (8.5%) |
| Using medicines currently? | Yes  | 68 (30.1%) |
| No | 155 (68.6%) |
| Unsure | 3 (1.3%) |
| Taken (or been given) medicines before? | Yes | 209 (92.9%) |
| No | 13 (5.8%) |
| Unsure | 3 (1.3%) |
| Have you heard of side effects | Yes | 211 (93.8%) |
| No | 9 (4.0%) |
| Don’t Know | 5 (2.2%) |
| Do you think you have ever had a side effect? | Yes | 79 (35.1%) |
| No | 96 (42.7%) |
| Don’t Know | 50 (22.2%) |
| How serious was the side effect? | Very serious - bad enough to go to hospital | 4 (4.9%) |
| Somewhat serious - to see a healthcare professional like a doctor or pharmacist | 10 (12.2%) |
| Was bad enough to affect what you do everyday | 14 (17.1%) |
| Mild or uncomfortable | 25 (30.5%) |
| Very mild or slightly uncomfortable | 13 (15.9%) |
| Not serious | 15 (18.3%) |
| I don't know | 1 (1.2%) |

Table 1: Demographics and baseline experience of medicines and side effects of Young People who answered the survey

|  |  |
| --- | --- |
| **Drug suspected of causing ADR** | **Suspected ADRs (verbatim from the form)** |
| Adapalene | Redness and Itchiness on face |
| Amitriptyline | Dry mouth, headaches, increased heart rate and hot flushes |
| Aspirin | Mild lightheadedness |
| Beta Blocker | Dizzy and tired |
| Beta Blocker | Heart rate too slow |
| Cephalosporin | Full body rash |
| Doxycycline | Change in appetite |
| Fluoxetine | Suicidal Thoughts |
| Ibuprofen | Headache |
| Insulin | Allergic to the adhesive |
| Insulin | Hypoglycaemia |
| IVIG | Meningitis |
| Metformin | Stomach ache |
| Methotrexate | Threw up every day for a week |
| Olanzapine | Extreme fatigue |
| Oral Contraceptive | Upset all the time |
| Oral Contraceptive | 50 day period |
| Penicillin | Rashes and temperature |
| Pregabalin | Weight gain |
| Roaccutane | Really bad hormonal imbalance |
| Sumatriptan | Lose my appetite |
| Topiramate | Tiredness |

Table 2: Drug and reaction pairs from all suspected adverse drug reactions reported by Young People who answered the survey

|  |  |  |
| --- | --- | --- |
| **Who would you tell if you thought you had a side effect to a medicine?** | **Before reviewing updated MHRA information n (%)** | **After reviewing the updated MHRA information n (%)** |
| Someone who cares for you (e.g. your parents, family or carer) | 114 (50.7%) | 166 (84.7%) |
| Your parents | 178 (79.1%) | 7 (3.6%) |
| Your doctor, nurse or pharmacist | 107 (47.6%) | 113 (57.7%) |
| A teacher | 21 (9.3%) | 33 (16.8%) |
| I would report a Yellow Card myself | 16 (7.1%) | 83 (42.4%) |
| I don't know | 8 (3.6%) | 4 (2.0%) |
| Other (please specify) | 4 (1.8%) | 8 (4.1%) |

Table 3: Respondents views on who they would inform about a suspected adverse drug reaction before and after reviewing the updated MHRA information

## Figure legends

**Figure 1: Updated information leaflet about CYP reporting their own suspected adverse drug reactions (ADRs) that CYP were providing feedback about**

**Figure 2 A: Percentage of young people who would be comfortable reporting a suspected adverse drug reaction (ADR) before and after reading the guide. B: Percentage of young people willing to report a suspected ADR following reading the guide.**