Scottish Government Health Directorates Chief Scientist Office

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# Child Medical Records for Safer Medicines (CHIMES)

## Researchers
Prof PJ Helms, Prof CM Bond, Dr JS McLay, Prof M Bennie, Dr C Black, Dr J Haughney, Dr YM Hopf, Dr B Kirby, Dr C Simpson, EE Scobie-Scott, Dr PC Sun, and Dr R Wood.

## Aim
**CHIMES** sought to assess the feasibility of a system for monitoring the safety of medicines for children based on linked routinely collected healthcare data. Three work packages (WP) investigated:
1. The acceptability to healthcare professionals, young people and parents/guardians; 2. Data completeness and their ability to reproduce well established patterns of disease and adverse drug reactions and 3. Novel methods for identifying potential adverse drug reactions in children.

## Project Outline/Methodology
In WP1 the acceptability of using linked health data was assessed in interviews, focus groups and questionnaires. In WP2 the completeness and validity of using linked Scottish NHS data was assessed by comparisons with established disease registries, disease prevalence, and adverse drug reactions. In WP3 unplanned discontinuation or drug switching was used to identify potential adverse drug reactions.

## Key Results
**WP1: Healthcare professionals** supported data linkage with appropriate safeguards, but wanted more information on the use of the data and the population health benefits. Presumed consent with the availability of individual 'opt out' was supported alongside clear legal and governance frameworks, sanctions for data misuse, effective dissemination of results and continuing public engagement.
**Young People and Parents/Guardians** assumed routine data were already used to monitor medicine safety. There was support for data linkage with appropriate data security and access controls. The NHS was the preferred data guardian and in contrast to the views of healthcare professionals individual consent with 'opt in' was preferred. Support was highest for studies with demonstrable health benefit and least for those sponsored by industry.
**WP2:** Scottish Prescribing Information System (PIS) data was shown to be sufficiently complete and accurate. Insulin prescribing in PIS were similar to published rates of Type 1 diabetes in Scottish and Swedish populations; prescribing patterns for asthma were comparable with an independent patient registry; and linked prescribing and hospital data reproduced published findings on hospitalisation for gastrointestinal complications in adults newly prescribed non-steroidal anti-inflammatory drugs.
**WP3**: Unplanned medication discontinuations or drug switching events identified a number of potential adverse reactions in children treated with the anti-obesity drug Orlistat and those using antidepressant medications.

## Conclusions
- Routinely collected prescribing data in Scotland is comprehensive and can be linked to other NHS data to identify potential adverse drug reactions in children.
- Data linkage is acceptable to healthcare professionals, young people and parents/guardians, although all groups have concerns that need to be addressed particularly individual opt-in and opt-out.

## What does this study add to the field?
- CHIMES developed techniques to monitor medicine safety using national routinely collected health data.
- A number of potentially novel adverse drug reactions were identified.

## Implications for Practice or Policy
- CHIMES provides an exemplar for the early detection of possible adverse drug reactions, with suggestions for how PIS could be improved for this purpose.
- CHIMES makes recommendations for building trust and support for data linkage research in Scotland among healthcare professionals and the public.

## Where to next?
Health and non-health datasets will be linked to investigate the impact of (i) prescribing multiple medications, and (ii) maternal medication on child health and development. Better publicising of the benefits of data linkage research is needed to develop and maintain the trust of the public, including young people.

**Further details from:** Dr Sharon Gordon, CHIMES Programme Manager (sharon.gordon@abdn.ac.uk).

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# Child Medical Records for Safer Medicines (CHIMES)
# Data Linkage for Paediatric Pharmacovigilance: Views of Healthcare Professionals

**Researchers**
Dr YM Hopf, Prof CM Bond, Prof J Francis, Dr J Haughney, and Prof PJ Helms.

## Aim
The aim was to explore the acceptability of linking routinely collected healthcare data to detect potential problems related to medication use (pharmacovigilance) in children. The main objectives were to: (1) describe the understanding of pharmacovigilance and knowledge of current systems amongst healthcare professionals in Scotland, (2) explore the views of healthcare professionals on the linkage of routinely collected NHS data for paediatric pharmacovigilance, and (3) make recommendations to address any issues or concerns raised.

## Project Outline/Methodology
A mixed methods study was conducted which included interviews with professional stakeholders, focus groups with frontline healthcare professionals, and a three-round Delphi survey with nurses, pharmacists and doctors with an interest in paediatric medicines use in Scotland. The survey was structured using the Theoretical Domains Framework of Behaviour Change and the results were triangulated across the three arms of the study.

## Key Results
**Interviews:** Pharmacovigilance was perceived as important by healthcare professionals. Participants (n=23) were aware of current pharmacovigilance systems and their limitations. A number of issues with using data linkage for pharmacovigilance were identified including data security, anonymisation, and legal constraints that should be addressed prior to implementation. Recommendations included: clear and accessible legal and governance frameworks; acquisition of Caldicott Guardian and Research Ethics approvals; the use of anonymised aggregate data where possible; only linking data when absolutely essential; strict access control to linked data with independent vetting of applications; imposing meaningful sanctions for misuse; an 'opt-out' mechanism for patients; and provision of more information on the available data and its uses, and greater involvement of the public.

**Focus Groups:** In addition to issues raised in the interviews participants (n=22, 6 groups) were concerned that funding to support the use of routine data might be diverted from already hard pressed "front line" services.

**Delphi Survey**: 121 participants consented to take part and 27 participants completed all three rounds. Consensus was established on the need for professional standards, requirements for linkage, and the use and format of feedback. Data linkage for paediatric pharmacovigilance was strongly supported in view of its potential benefits.

Triangulation of all results identified the main areas to consider prior to full implementation, namely: practical/technical and regulatory; and provided lists of what were regarded as essential and preferable requirements.

## Conclusions
- Data linkage for paediatric pharmacovigilance has support from healthcare professionals in Scotland; in view of the current knowledge gap in this area.
- Support by front line healthcare professionals would be enhanced if they received more feedback on the uses of linked data for health gain and implications for their own practice.

## What does this study add to the field?
Healthcare professionals in Scotland support linked health data for paediatric pharmacovigilance; as long as clear and accessible guidance on safeguards are in place and regular feedback on the benefits are made available to them.

## Implications for Practice or Policy
Front line health care professionals should be more actively engaged in policies and practice relevant to the acquisition and uses of linked health data.

## Where to next?
These findings will be compared to a parallel study exploring the views of young people and parents/guardians. Recommendations on data linkage for pharmacovigilance should be drawn from both frontline healthcare professionals as data collectors and the public as data providers.

**Further details from:** Dr Sharon Gordon, CHIMES Programme Manager (sharon.gordon@abdn.ac.uk).

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# Child Medical Records for Safer Medicines (CHIMES)
# Data linkage for paediatric pharmacovigilance: Views of young people, parents/guardians.

**Researchers**
EE Scobie-Scott, Prof C Bond, Dr D Shaw and Prof PJ Helms.

**Aim**
To identify the acceptability to young people and parents/guardians of linked routinely held NHS health data for enhanced medicines safety in children (paediatric pharmacovigilance).

**Project Outline/Methodology**
A mixed methods study was conducted including interviews with 17 key stakeholders (Young peoples' representatives, national child patient support groups and child focused public bodies); 4 focus groups with young people parents/guardians; and a national survey of young people (N=132) and parents/guardians (N=145) recruited from an on line panel.

**Key Results**
- The expectation was that routine data were already being used to monitor the safety of medicines.
- The use of linked health data for enhanced medicine safety and health gain was supported by the majority.
- Individual 'opt in' rather than 'opt out' was the preferred method for signalling consent, particularly for young people.
- Protection of data was seen as key to gaining and retaining public trust hence the need for a robust legal ethical and data guardianship framework.
- The NHS was identified as the preferred organisation to assume the role of data guardian.
- Research undertaken by the NHS or academic organisations for health gain was more acceptable to participants, than research undertaken by industry.

**Conclusions**
Young people and parents/guardians were supportive of research using routinely collected anonymised NHS healthcare data if managed within a robust, transparent legal and ethical framework and with the ability to signal consent for the use of their data by individual 'opt in' rather than 'opt out'. Young people, parents and guardians need more information on the guardianship of their personal data and the benefits of data linkage research in order to address their concerns about privacy and their desire to be more actively involved in signalling consent.

**What does this study add to the field?**
Although young people and parents/guardians strongly support the use of linked health data to enhance medicines safety and health gain there is less support for research for commercial gain. The desire to signal consent by individual 'opt in' runs counter to the widely held assumption that an 'opt out' option would address any concerns and be an acceptable method to signal approval at the population level. Young people and children are well able to engage in discussion about the uses to which their health data are put.

**Implications for Practice or Policy**
The study offers suggestions as to how public trust and support of data linkage could be developed and maintained by building on the established trust in the NHS. The research community and those responsible for maintaining healthcare records should not conclude that support is universal, and should engage with the public, including with young people and children, in decisions and policies relevant to the linkage and use of NHS health care data.
Although there is strong public support for use of linked health data for enhanced medicines safety the preference for individual 'opt in' rather than assumed consent with an 'opt out' option points to an urgent need to provide more information on the governance processes involved in gaining access to the data and the benefits of conducting population level health research on linked health data.

**Where to next?**
Public awareness of health data linkage and its uses needs to be increased, with information made available as to how and why research using such data can benefit medicines safety and contribute to individual and population health gain. Engagement of young people and children in such discussions would strengthen support for such research.

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# Child Medical Records for Safer Medicines (CHIMES): Data Linkage for Pharmacovigilance Using Routine Health Data.

**Researchers**
Dr B Kirby, Dr JS McLay, Dr C Simpson, Prof M Bennie, and Prof PJ Helms.

## Aim
To explore the completeness, data validity and ability of the Scottish Prescribing Information System (PIS) to link with other national Scottish health data in support of a routine mechanism for improving the safety of medicines for children (paediatric pharmacovigilance).

## Project Outline/Methodology
The first stage was to establish the completeness of the Community Health Index number (CHI) in the relevant data sets in order to link them using this unique patient identifier. This was followed by an assessment of the extent to which well-established disease prevalence and incidence, and associations between medicines and adverse events, could be reproduced using the linked data. With CHI as a key a 'Pharmacovigilance Development Platform', was developed by linking PIS data with the Acute, Cancer, Deaths and Mental Health (ACaDMe) data mart, and the Maternity (SMR02) and Hospital Episode data (SMR01). PIS and SMR02 linked data was further linked to a well established Birth Cohort, the Aberdeen Study of Eczema and Asthma To Observe the Influence of Nutrition (SEATON).

## Key Results
- CHI was present on over 90% of dispensed items from January 2010, with current (2012-13) levels reaching 95%.
- Insulin prescriptions in PIS were identified for 96% of patients with a hospital admission for Type 1 diabetes recorded in SMR01.
- Rates of newly prescribed insulin were consistent with previously published incidence rates for Type 1 (insulin dependent) diabetes in the Scottish, and Swedish populations.
- Prescribing of asthma medications from the PIS data was complete and accurate when compared with self-reported medicine use at the same time as the 10 year follow up of the SEATON birth cohort.
- Asthma status (inferred by prescription of asthma medications in PIS) was identified for 86% of SEATON birth cohort patients who were subsequently lost to follow up.
- PIS linked to hospital episode data (SMR01) reproduced published findings on the likelihood of hospitalisation for gastrointestinal complications in adult patients newly prescribed non-steroidal anti-inflammatory drugs.

## Conclusions
- Data held in the Scottish Prescribing Information System data is sufficiently complete and accurate, for medicines prescribed in general practice and dispensed in the community, and can be reliably linked to other NHS datasets using the Scottish Community Health Index number.

## What does this study add to the field?
The high degree of patient identifier (CHI) completeness across national health data sets supports the development of a platform for improved medicines safety in children and in adults.

## Implications for Practice or Policy
Large scale routinely collected health databases offer new opportunities to study medicine safety in a 'real world' environment and could be used to improve the monitoring of medicines prescribed to children in Scotland. The utility of PIS for pharmacovigilance would be improved if data such as the specific date and time of dispensing, reason for the prescription, and drug dose and frequency information were included.

## Where to next?
The recommended improvements in PIS, and the ability to establish a pharmacovigilance platform, should inform the design of national routine systems for medicine surveillance, and the early detection of potential adverse drug reactions. Linked routine health data could contribute to the conduct of clinical trials and offers opportunities to improve post marketing surveillance in pursuit of the safe use of medicines not just for children but for all age groups.

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# Child Medical Records for Safer Medicines (CHIMES)
# Paediatric pharmacovigilance: Utility of routinely acquired healthcare data.

**Researchers**
Dr PC Sun, Dr JS McLay, Dr C Black, Prof M Bennie, Dr B Kirby, Dr C Simpson, and Prof PJ Helms.

## Aim
To assess the utility of routinely collected healthcare data to identify potential adverse drug reactions (ADRs) in children and more specifically to test the hypothesis that an early unplanned medication discontinuation or drug switching (within 4 months) could 'signal' a possible ADR.

## Project Outline/Methodology
A pilot study was undertaken using the Primary Care Clinical Informatics Unit-Research (PCCIU-R) database. The usefulness of the prescribing information in PCCIU-R for pharmacovigilance was assessed using exemplar drugs prescribed to children about which there are continuing safety concerns namely antidepressants and Orlistat - an anti-obesity medication.

Children <17 years old receiving a first prescription of any of these drugs during the three year study period (1 Jan 2006 – 31 Nov 2009) were identified and any early unplanned medication discontinuations or drug switching noted. Clinical diagnostic codes and any free text in the PCCIU-R GP records 3 months prior to and following a drug discontinuation or switching were used for "signal enhancement".

The study was then extended to the whole Scottish population from 1 April 2010 – 31 March 2011 by linking the Prescribing Information System (PIS) data to hospital admission data held in Scottish Morbidity Records (SMR01). Co-prescribed medication in PIS and the reasons for hospitalisation recorded in SMR01 were used for signal enhancement.

## Key Results
- Prescribing patterns for the medicines of interest were similar in the primary care database and the national dispensing database (PIS) and both data sets produced discontinuation rates similar to previously published data.
- High rates of unplanned medication discontinuations were found for children prescribed Orlistat and those prescribed antidepressants.
- In the primary care data a potentially novel adverse symptom of urinary retention was identified around the time of unplanned Orlistat discontinuation.
- Among antidepressants selective serotonin reuptake inhibitors (SSRIs) were more likely to be associated with a hospital admission for overdose or self-harm than in those children treated with Tricyclic Antidepressants.

## Conclusions
- Unplanned medication discontinuation or drug switching with signal enhancement can be used to identify potential ADRs in children.
- Routinely collected healthcare data generated both expected and novel pharmacovigilance signals.

## What does this study add to the field
Whole population data based on routinely acquired health data has potential to identify unusual side effects, as noted for the drug Orlistat, and to follow larger numbers of children exposed to medicines of interest than are possible in post marketing studies.

## Implications for Practice or Policy
Modest additions to the current PIS data extracts to include fields such as indication, exact dispensing date and dosing schedule should be considered. Prescribers of medicines to children should be encouraged to enter reasons for unplanned medication discontinuations or switching in the electronic record in order to enhance early identification of potential ADRs.

## Where to next?
Using the approaches outlined here the introduction of the national primary care database with linkage to Out-patient, Accident and Emergency and Death registry would further enhance the study of medicines safety. Linking health with non-health datasets, such as education, would also allow investigation of the effects of exposure in pregnancy on subsequent child health and development.

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