Changes in medication safety indicators in England throughout the COVID-19 pandemic: a federated analysis of 57 million patients' primary care records in situ using OpenSAFELY

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Abstract

Objective: To describe the impact of the COVID-19 pandemic on safe prescribing, using the PINCER prescribing indicators; to implement complex prescribing indicators at national scale using GP data.

Design: Population based cohort study, with the approval of NHS England using the OpenSAFELY platform.

Setting: Electronic health record data from 56.8 million NHS patients' general practice records.

Participants: All NHS patients registered at a GP practice using TPP or EMIS computer systems and recorded as at risk of at least one potentially hazardous PINCER indicator between September 2019 and September 2021.

Main outcome measure: Monthly trends and between-practice variation for compliance with 13 PINCER indicators between September 2019 and September 2021.

Results: The indicators were successfully implemented across GP data in OpenSAFELY. Hazardous prescribing remained largely unchanged during the COVID-19 pandemic, with no evidence of increases in indicators of harm as captured by the PINCER indicators. There were transient delays in blood test monitoring for some medications, particularly ACE inhibitors. All indicators exhibited substantial recovery by September 2021. We identified 1,813,058 patients (3.1%) at risk of at least one potentially hazardous prescribing event.

Conclusion: NHS GP data can be analysed at national scale to generate insights on service delivery. Potentially hazardous prescribing was largely unaffected by COVID-19 in a dataset of 57 million patients' full primary care health records in England.

Keywords: COVID-19, electronic health records, general practice, primary health care, medication errors, inappropriate prescribing

Summary box

What is already known on this topic

- Primary care services were substantially disrupted by the COVID-19 pandemic.
- Disruption to safe prescribing during the pandemic has not previously been evaluated.
- PINCER is an evidence-based, complex intervention to identify and correct hazardous prescribing in primary care. The intervention is pharmacist-led and has been rolled out nationally to GP practices in England.

What this study adds

- We were able to successfully generate data on PINCER indicators for almost the whole population of England in a single analysis.
- Our study is the most comprehensive assessment of medication safety during the COVID-19 pandemic in England, covering 95% of the population using well-validated indicators.
- Good performance was maintained across many PINCER indicators throughout the pandemic.
- Delays in delivering some medication-related blood test monitoring were evident though considerable recovery was made by the end of the study period.

How this study might affect research, practice, or policy

- Demonstrating the power of collaborative working with regards to openly sharing codelists and analytic code.
- Demonstrating the potential of federated analytics to provide near real-time reporting on important public health issues at a national level.

Introduction

The World Health Organisation (WHO) launched a patient safety challenge in 2017, Medication Without Harm [1], with an ambition to "*reduce severe avoidable medication related harm globally by 50% in the next 5 years*" [2]. The COVID-19 pandemic disrupted the delivery of primary care services within the National Health Service (NHS) in the UK from March 2020, with a 30% reduction in GP consultations; a 74% reduction in routine referrals and a 43% reduction in urgent cancer referrals [3,4]. The extent of disruption varied by clinical context [5–7], though most primary care services were restored by September 2020 [8,9]. It is possible that the disruption during this time will have contributed towards increased rates of medication related harm, with 34% of an estimated 66 million potentially clinically significant errors occurring in primary care prescribing in England annually as estimated using NHS dispensing statistics in 2015-16 [10].

As part of its response to the WHO challenge, PRIMIS at the University of Nottingham led on the national rollout of PINCER (pharmacist-led information technology intervention for medication errors) in collaboration with the Academic Health Science Networks [11]. The PINCER intervention (more information provided in Supplementary Text) is a proven programme of activities for reducing hazardous prescribing in general practices [12]. Briefly, it involves training pharmacists working in general practice to provide feedback, educational outreach and dedicated support, systematically focusing on patients identified to be at risk of harm from medications. These patients are identified using pre-specified and quality assured analytic indicators in the SNOMED-CT code classification system used by GP systems in England. PINCER includes 13 indicators of hazardous prescribing of high risk medications prescribed in primary care that: (1) can cause gastrointestinal (GI) bleeds; (2) are cautioned against in certain conditions (specifically heart failure, asthma and chronic renal failure); (3) require blood test monitoring (Box 1). These indicators have been developed in collaboration with academics from the University of Nottingham and made available to pharmacists in practices participating in the PINCER programme (see Supplementary Text).

OpenSAFELY is a new secure analytics platform for electronic patient records built by our group with the approval of NHS England to deliver urgent academic [13] and operational NHS service research [14,15] on the direct and indirect impacts of the pandemic: analyses can currently run across patients' full raw pseudonymised primary care records at 95% of English general practices (55% in practices using EMIS software, and 40% in practices using TPP software) with patient-level linkage to various sources of secondary care data; all code and analysis is shared openly for inspection and re-use.

The PINCER indicators created by PRIMIS are typically implemented for single practices, or groups of practices, through a variety of technical methods (see Supplementary Materials) in different settings, to monitor compliance for practices that are participating in the PINCER programme. We set out to implement the full suite of PINCER codelists, methods and indicators in OpenSAFELY to permit monitoring of compliance on all prescribing safety indicators at a population-level; and to describe changes in compliance following the COVID-19 induced disruption to primary care services in England.

Box 1: The PINCER indicators

Indicators associated with gastrointestinal bleeding

- **Age ≥ 65 & NSAID**: prescription of an oral non-steroidal anti-inflammatory drug (NSAID), without co-prescription of an ulcer-healing drug, to a patient aged ≥65 years
- **PU & NSAID**: prescription of an oral NSAID, without co-prescription of an ulcer healing drug, to a patient with a history of peptic ulceration
- **PU & antiplatelet**: prescription of an antiplatelet drug without co-prescription of an ulcer-healing drug, to a patient with a history of peptic ulceration
- **Warfarin/DOAC & NSAID**: prescription of warfarin or DOAC in combination with an oral NSAID
- **Warfarin/DOAC & antiplatelet**: prescription of warfarin or DOAC and an antiplatelet drug in combination without coprescription of an ulcer-healing drug
- **Aspirin & other antiplatelet**: prescription of aspirin in combination with another antiplatelet drug (without coprescription of an ulcer-healing drug)

Indicators associated with cautioned medication in other conditions (including heart failure, asthma and acute kidney injury)

- **HF & NSAID**: prescription of an oral NSAID to a patient with heart failure
- **Asthma & beta-blocker**: prescription of a non-selective beta-blocker to a patient with asthma
- **CRF & NSAID**: prescription of an oral NSAID to a patient with eGFR <45

Indicators associated blood test monitoring

- **ACEI or loop diuretic, no blood tests**: patients aged 75 years and older who have been prescribed an angiotensin converting enzyme (ACE) inhibitor or a loop diuretic long term who have not had a computer-recorded check of their renal function and electrolytes in the previous 15 months
- Patients receiving methotrexate for at least 3 months who have not had a recorded:
    - Full blood count (FBC) within the previous 3 months (**Methotrexate and no FBC**)
    - Liver function test (LFT) within the previous 3 months (**Methotrexate and no LFT**)
- **Lithium and no level recording**: patients receiving lithium for at least 3 months who have not had a recorded check of their lithium concentrations in the previous 3 months
- **Amiodarone and no TFT**: patients receiving amiodarone for at least 6 months who have not had a thyroid function test (TFT) within the previous 6 months

Methods

Study design

We conducted a retrospective cohort study using general practice primary care electronic health record (EHR) data from all general practitioner (GP) practices in England supplied by the EHR vendors TPP and EMIS.

Data source

Primary care records managed by the GP software providers TPP and EMIS are available in OpenSAFELY, a data analytics platform created by our team with the approval of NHS England to address urgent COVID-19 research questions (https://opensafely.org). OpenSAFELY provides a secure software interface allowing the analysis of pseudonymized primary care patient records from England in near real-time within the EHR vendor's highly secure data centre, avoiding the need for large volumes of potentially disclosive pseudonymized patient data to be transferred off-site. This, in addition to other technical and organisational controls, minimises any risk of re-identification. Similarly pseudonymized datasets from other data providers are securely provided to the EHR vendor and linked to the primary care data. The TPP dataset analysed within OpenSAFELY (hereafter referred to as OpenSAFELY-TPP) is based on 24.2 million people currently registered with 2546 GP surgeries using TPP SystmOne software; the EMIS dataset analysed within OpenSAFELY (hereafter referred to as OpenSAFELY-EMIS) is based on 32.6 million people currently registered with 3821 GP surgeries using EMIS. These datasets contain pseudonymized data such as coded diagnoses and physiological parameters, including blood tests results requested by the practice. We make extensive use of EHR data regarding primary care prescriptions in the NHS in England. Briefly, health professionals able to write prescriptions in primary care in the NHS in England include GPs, as well as suitably qualified nurses, pharmacists, and physiotherapists. With very few exceptions, every prescription written by these prescribers is recorded within the patient's record in the GP clinical system. These prescriptions are then dispensed by an NHS-commissioned dispensing service, usually a community pharmacy or dispensing doctor in rural locations. No free text data are included. Further details on our information governance can be found in the information governance and ethical approval sections. More information about the OpenSAFELY platform is available on our website (https://opensafely.org/about and https://docs.opensafely.org); in our recent review for the UK Government, Department of Health and Social Care [16]; and in our previous publications, in particular [13].

Study population

We included all patients who were: alive; aged 18-120; registered with an OpenSAFELY-TPP or OpenSAFELY-EMIS practice; and recorded as at risk of at least one potentially hazardous prescribing indicator. A patient was considered as being "at risk" if they were found to belong to at least one of the PINCER indicator denominators as defined by the SNOMED-CT and NHS dictionary of medicines and devices (dm+d) codes and associated logic developed by PRIMIS for the PINCER programme (https://www.opencodelists.org/codelist/pincer/) between

September 2019 and September 2021. This time period was chosen to adequately cover both the period of service disruption onset and subsequent service recovery due to the COVID-19 pandemic in the UK.

Study measures

Definitions of the hazardous prescribing indicators are described in Box 1. The percentage for each indicator is formed of a numerator and denominator pair (see Supplementary Materials), where the numerator is the set of patients deemed by the indicator to be at risk of a potentially hazardous prescribing event, and the denominator is the set of patients for which assessment of the indicator is clinically meaningful. Higher indicator percentages represent potentially poorer performance on medication safety. Indicators belong to three groups: (1) those associated with gastrointestinal bleeds; (2) those associated with cautioned medications; and (3) those associated with blood test monitoring; these groups are used to summarise results.

Each indicator was specified in analytic code using PRIMIS SNOMED-CT codelists using the OpenSAFELY framework. We generated the numerator and denominator for each indicator per month between September 2019 and September 2021, and then calculated monthly percentages for each practice. For indicators assessing numeric values, only unambiguous results were used in the calculation of indicator percentages (for example, an eGFR value of ">30" was considered ambiguous for an indicator requiring the identification of patients with an eGFR value less than 45); note that this functionality was not available in OpenSAFELY-EMIS at the time of the study, so results for the *CRF & NSAID* indicator are reported for OpenSAFELY-TPP practices only.

The monthly indicator percentages were summarised as deciles and presented as decile charts across all practices each month. We also calculated the mean rate across practices in Q1 2020 and 2021 for each indicator as well as total counts of the numerator and denominator for each indicator across the two year period; note that in this cumulative data, repeated events will be counted for each month the event occurs (e.g., if a heart failure patient is prescribed an oral NSAID in two separate months (*HF & NSAID*), this is represented as two separate events). Across this period we also calculated the ratio of hazardous prescribing events to unique patients experiencing those events (to give an indication of the extent of repeated hazardous prescribing) and the number and percentage of practices with at least one instance of potentially hazardous prescribing at any point across the period.

Each blood test monitoring indicator has an associated monitoring window (e.g. lithium concentrations are required to be checked within 3 months). Should no action have been taken to rectify COVID-19 related delays, then 100% of patients will have been subject to delayed blood test monitoring by the end of the relevant monitoring window. For each blood test monitoring indicator, we have calculated this "projected date of maximum impact" from the onset of COVID-19 related disruption in March 2020. Each decile plot has been annotated to indicate when this projected date of maximum impact would have occurred.

Software and Reproducibility

Data management and analysis was performed using the OpenSAFELY software libraries and Python, both implemented using Python 3.8. A federated analysis involves carrying out patient-level analysis in multiple secure datasets, then later combining them: codelists and code for data management and data analysis were specified once using the OpenSAFELY tools; then transmitted securely to the OpenSAFELY-TPP platform within TPP's secure environment, and separately to the OpenSAFELY-EMIS platform within EMIS's secure environment, where they were each executed separately against local patient data; summary results were then reviewed for disclosiveness, released, and combined for the final outputs. All code for the OpenSAFELY platform for data management, analysis and secure code execution is shared for review and re-use under open licences at github.com/OpenSAFELY. Decile charts were drawn using Seaborn and matplotlib.

Patient and Public Involvement

We have developed a public website (https://opensafely.org/) which provides a detailed description of the platform in language suitable for a lay audience; we have participated in two citizen juries exploring public trust in OpenSAFELY [17]; we are currently co-developing an explainer video; we have 'expert by experience' patient representation on our OpenSAFELY Oversight Board; we have partnered with Understanding Patient Data to produce lay explainers on the importance of large datasets for research; we have presented at a number of online public engagement events to key communities (for example, Healthcare Excellence Through Technology (HETT); Faculty of Clinical Informatics annual conference; NHS Assembly; HDRUK symposium); and more. To ensure the patient voice is represented, we are working closely with appropriate medical research charities (for example, Association of Medical Research Charities).

We will share information and interpretation of our findings through press releases, social media channels, and plain language summaries.

Results

We identified 1,813,058 (3.1% of 56.8 million) patients registered across 6,367 practices at risk of potentially hazardous prescribing as indicated by the PINCER indicators at any point between September 2019 and September 2021. Demographic characteristics for the 14,284,444 (25.1%) patients who were identified in at least one indicator denominator in the last month of the study period (September 2021) are provided in Table 1.

For each PINCER indicator, we show Q1 mean percentages for 2020 (which we use to represent a "pre-COVID-19 onset" period) and 2021 (which we use to represent a "post-COVID-19 onset" period) to enable comparison before and after the COVID-19 related service disruption (Table 2). Mean Q1 2020 percentages ranged from 1.11% (*Age ≥ 65 & NSAID*) to 36.20% (*Amiodarone and no TFT*), while Q1 2021 percentages ranged from 0.75% (*Age ≥ 65 & NSAID*) to 39.23% (*Amiodarone and no TFT*). The pre-/post-COVID-onset difference ranged from a reduction of 0.59% (*Warfarin/DOAC & antiplatelet*) to an increase of 6.98% (*ACEI or loop diuretic, no blood tests*).

Cumulative counts for each indicator are provided in Table 2. The percentage of patients identified as at risk of a potentially hazardous prescribing event in the study period ranged from 2.51% (36,927 of 1,470,315 patients; *Aspirin & other antiplatelet*) to 89.46% (40,664 of 45,456 patients; *Lithium and no level recording*). The ratio of hazardous events to patients ranged from 3.83 (*PU & NSAID*) to 10.90 (*PU & antiplatelet*). The percentage of practices with an event for each indicator ranged from 87.02% (*CRF & NSAID*) to 99.06% (*Asthma & beta-blocker*).

Indicators associated with gastrointestinal bleeding

The six indicators of potentially hazardous prescribing in relation to GI bleeds exhibit a decreasing trend across the study period with no evidence of an increase in hazardous prescribing as a result of COVID-19 induced service disruption (Figure 1a, OpenSAFELY-TPP only and OpenSAFELY-EMIS only decile charts are provided in Supplementary Figures 1a and 2a respectively). The mean percentage of *Warfarin/DOAC & NSAID* was 1.39% in Q1 2020; the equivalent rate in 2021 was 1.18%. Similarly, the percentage of *PU & antiplatelet* fell from 4.24% to 3.85% between Q1 2020 and Q1 2021 (Table 2). There were only marginal impacts on this improving trend during the months of most significant service disruption due to the COVID-19 pandemic. Some GI bleed indicators have lower incidence amongst practices than others; for example, the percentage of practices experiencing at least one hazardous prescribing event is 90.73% and 99.01% for the *Aspirin & other antiplatelet* and *Age ≥ 65 & NSAID* indicators respectively.

Table 1. Cohort description for any patients included in the denominator of at least one of the PINCER indicators at the end of the study period (September 2021), in OpenSAFELY-TPP and OpenSAFELY-EMIS. IMD=index of multiple deprivation.

Characteristic	Category	OpenSAFELY-TPP		OpenSAFELY-EMIS		Total	
		n	%	n	%	n	%
Total		5,998,805	100.00	8,285,639	100.00	14,284,444	100.00
Age	18-19	69,947	1.17	93,636	1.13	163,583	1.15
	20-29	473,181	7.89	679,780	8.20	1,152,961	8.07
	30-39	507,839	8.47	788,895	9.52	1,296,734	9.08
	40-49	468,532	7.81	689,394	8.32	1,157,926	8.11
	50-59	527,714	8.80	766,127	9.25	1,293,841	9.06
	60-69	1,217,103	20.29	1,647,347	19.88	2,864,450	20.05
	70-79	1,672,710	27.88	2,235,918	26.99	3,908,628	27.36
	80+	1,061,779	17.70	1,384,542	16.71	2,446,321	17.13
Sex	F	3,122,219	52.05	4,291,110	51.79	7,413,329	51.90
	M	2,876,586	47.95	3,994,529	48.21	6,871,115	48.10
Ethnicity	White	4,285,420	71.44	5,480,579	66.15	9,765,999	68.37
	South Asian	209,386	3.49	405,580	4.89	614,966	4.31
	Black	69,225	1.15	199,570	2.41	268,795	1.88
	Other	48,206	0.80	77,498	0.94	125,704	0.88
	Mixed	38,392	0.64	84,486	1.02	122,878	0.86
	Missing	1,348,176	22.47	2,037,926	24.60	3,386,102	23.70
IMD	Most deprived (1)	984,981	16.42	1,425,367	17.20	2,410,348	16.87
	2	1,094,257	18.24	1,569,287	18.94	2,663,544	18.65
	3	1,306,389	21.78	1,649,173	19.90	2,955,562	20.69
	4	1,283,629	21.40	1,741,211	21.01	3,024,840	21.18
	Least deprived (5)	1,227,902	20.47	1,875,295	22.63	3,103,197	21.72
	Missing	101,647	1.69	25,306	0.31	126,953	0.89
Region	East	1,337,146	22.29	343,151	4.14	1,680,297	11.76
	London	276,220	4.60	1,431,617	17.28	1,707,837	11.96
	Midlands[1]	1,282,238	21.37	1,494,269	18.03	2,776,507	19.44
	North East & Yorkshire[2]	1,548,534	25.81	702,833	8.48	2,251,367	15.76
	North West	94,912	1.58	1,693,016	20.43	1,787,928	12.52

	South East	502,990	8.38	1,905,796	23.00	2,408,786	16.86
	South West	956,765	15.95	714,957	8.63	1,671,722	11.70

[1] Comprised of *East Midlands* and *West Midlands* in OpenSAFELY-TPP
[2] Comprised of *Yorkshire and the Humber* and *North East* in OpenSAFELY-TPP

Table 2. Indicator rates for PINCER hazardous prescribing indicators: Q1 2020/2021 percentages and cumulative results between September 2019 and September 2021. Mean values are calculated at the practice-level. Rates for CRF & NSAID (italicised) are calculated across 2546 OpenSAFELY-TPP practices; all other indicator rates are calculated across all 6367 practices (2546 OpenSAFELY-TPP + 3821 OpenSAFELY-EMIS practices). Tables for OpenSAFELY-TPP and OpenSAFELY-EMIS separately are available in Supplementary Tables 1-2.

Indicator	**Q1 mean percentage 2020**	**Q1 mean percentage 2021**	**Cumulative counts**			
			Denominator	Numerator (% of denominator)	Ratio of hazardous prescribing events to unique patients experiencing an event	Number of practices with at least one hazardous prescribing event (% of total number of practices)
Gastrointestinal bleeding	-	-	10,881,675	551,844 (5.07%)	5.53	6335 (99.50%)
Age ≥ 65 & NSAID	1.11	0.75	9,207,007	334,487 (3.63%)	4.54	6304 (99.01%)
PU & NSAID	1.32	1.07	678,218	32,089 (4.73%)	3.83	5801 (91.11%)
PU & antiplatelet	4.24	3.85	678,218	41,414 (6.11%)	10.90	5943 (93.34%)
Warfarin/DOAC & NSAID	1.39	1.18	1,915,117	84,101 (4.39%)	4.57	6193 (97.27%)
Warfarin/DOAC & antiplatelet	2.26	1.67	1,249,865	52,575 (4.21%)	5.86	6068 (95.30%)
Aspirin & other antiplatelet	1.67	1.20	1,470,315	36,927 (2.51%)	7.15	5777 (90.73%)
Cautioned medications	-	-	7,594,687	228,587 (3.01%)	9.43	6321 (99.28%)
HF & NSAID	1.71	1.43	735,781	31,034 (4.22%)	6.09	5622 (88.30%)
Asthma & beta-blocker	1.27	1.29	6,646,586	185,289 (2.79%)	10.24	6307 (99.06%)
CRF & NSAID	*1.27*	*1.12*	*476,925*	*14,558 (3.05%)*	*4.70*	*2217 (87.08%)*
Blood test monitoring	-	-	3,358,954	1,102,209 (32.81%)	6.59	6329 (99.40%)
ACEI or loop diuretic, no blood tests	5.16	12.14	3,095,595	850,587 (27.48%)	5.89	6303 (98.99%)

Methotrexate and no FBC	18.64	22.73	238,042	164,502 (69.11%)	5.05	6278 (98.60%)
Methotrexate and no LFT	19.62	23.27	238,042	166,484 (69.94%)	5.14	6278 (98.60%)
Lithium and no level recording	31.47	38.44	45,456	40,664 (89.46%)	6.93	5912 (92.85%)
Amiodarone and no TFT	36.20	39.23	59,925	46,268 (77.21%)	6.22	5993 (94.13%)

Indicators associated with cautioned medications

Time trends and variation for all three “cautioned medication” indicators are presented in Figure 1b (OpenSAFELY-TPP only and OpenSAFELY-EMIS only decile charts are provided in Supplementary Figures 1b and 2b respectively): there is no evidence that the COVID-19 related disruption to service delivery had any substantial impact on compliance for all indicators. The *CRF & NSAID* and *HF & NSAID* indicators have notably lower incidence amongst practices, with 87.08% and 88.30% of practices experiencing at least one hazardous prescribing event respectively, in comparison with the *Asthma & beta-blocker* indicator, for which 99.06% of practices experience at least one hazardous prescribing event.

Indicators associated with blood test monitoring

All blood test monitoring indicators exhibited an increase in delayed monitoring immediately following the onset of COVID-19 (May-July 2020; Figure 2).These increased rates showed considerable recovery by August-September 2020, in the case of *Lithium and no level recording* (31.47% Q1 2020 vs 38.44% Q1 2021), *Methotrexate and no FBC* (18.64% Q1 2020 vs 22.73% Q1 2021) and *Methotrexate and no LFT* (19.62% Q1 2020 vs 23.27% Q1 2021). The *Amiodarone and no TFT* indicator behaved similarly (36.20% Q1 2020 vs 39.23% Q1 2021), though the initial post-COVID-onset recovery period extended into October-November 2020 (Table 2). As with the other groups of indicators, the incidence amongst practices is high though this varies by indicator: incidence varies from 92.85% (*Lithium and no level recording*) to 98.99% (*ACEI or loop diuretic, no blood tests*).

The “*ACEI or loop diuretic, no blood tests”* indicator exhibited a noticeably different COVID-19 response pattern than the other blood test monitoring indicators. Here, the monitoring worsened steadily over a longer period of time, increasing from a mean of 5.16% to 12.14% between Q1 2020 and Q1 2021, beginning to recover in June 2021. The assessment window for this indicator is significantly wider than the windows for the other blood test monitoring indicators: within 15 months of prescription compared to three (lithium and methotrexate) or six (amiodarone) months.

Discussion

Summary

Despite substantial barriers to the delivery of primary care during the COVID-19 pandemic, good performance was maintained across a diverse range of widely evaluated and nationally adopted indicators of safe prescribing. There were evident delays in delivering some medication-related blood test monitoring within the time-window specified in the safety measure; especially for those blood tests where the time-window for compliance is itself already very long, and tests infrequent. However all indicators exhibited considerable recovery by the end of the study period.

Strengths and limitations

This study has a range of strengths. Compared to other routes of access to primary care data, OpenSAFELY offers more complete coverage of more patients with greater controls on security and complete transparency in terms of methodology and reproducibility. Previous audits for compliance with PINCER or similar measures and indicators in primary care rely on manual audit within a practice, or analyses on data downloaded from a group of practices. By contrast OpenSAFELY executes analyses in a secure environment inside the EHR provider data centre, across the full set of all structured data in the GP record including all tests, prescriptions, diagnostic codes and referrals. In addition, although the underlying GP data is stored in two very different settings (TPP and EMIS), it was possible to describe PINCER indicators for almost all GP practices (~99%) in England for the first time using a single analysis in OpenSAFELY: the necessary variables and analyses were defined once, then executed in each setting identically, with the outputs aggregated afterwards, in a process known as “federated analytics”. Overall this represents a unique, national platform able to capture the patient journey for 57 million people in England whilst prioritising patient privacy.

A second strength is the transparency and reproducibility of the analysis: as with all OpenSAFELY analyses, the complete set of all code for the platform and for all data curation and analysis for every study from raw data to completed output is shared openly on GitHub in standard formats for scientific review and efficient re-use under open licences by all.

A third strength is the robustness of the indicators for each safety behaviour: all eligible patients and targeted clinical safety behaviours were developed for the national PINCER medication safety programme which has been extensively peer reviewed and evaluated throughout the NHS over many years with strong support from clinicians and commissioners.

We also note some limitations. Firstly, our results as presented here are only descriptive in nature: we have not attempted to statistically assess the extent to which indicator rates changed during the period of service disruption following the onset of COVID, or the extent to which pre-pandemic rates were recovered. Furthermore, our study period does not allow for consideration of a pre-pandemic period in which variation in indicator rates over time could inform such statistical hypothesis testing. Finally, we acknowledge that our data will only include prescriptions and test results carried out in primary care, or those in secondary care that are returned to GPs as structured data: this may therefore not include test results communicated by letter or phone (such as tests requested while a person is in hospital, or other settings like psychiatric outpatients). However this is in line with the methodology

already used in the national PINCER programme to evaluate compliance with the targeted safety behaviours using primary care data alone.

Comparison of existing literature

A recent systematic review of healthcare usage during the pandemic, encompassing 81 studies across 20 countries found that healthcare utilisation (including visits, admissions, diagnostics and therapeutics) reduced by 37% during the pandemic, highlighting a substantial reduction in April-May 2020 [18]. The WHO also identified significant disruption to countries' healthcare capacity for non-communicable diseases in a rapid assessment in May 2020 [19]. A population cohort-based study conducted using the OpenSAFELY platform reported that clinical activity in relation to blood tests declined in the months following COVID-19 onset, but also reported recovery of these same tests by September 2020 [8]. These findings are in line with our observations of the blood test monitoring indicators, where substantial delays were experienced in the same period of time. Interrupted service delivery leading to reduced NSAID prescriptions following acute presentations may also explain the temporary reduction of the first GI bleed indicator (*prescription of an oral NSAID, without co-prescription of an ulcer-healing drug, to a patient aged ≥65 years*) in April-July 2020; this is supported by data for this period in OpenPrescribing [20] and lower than predicted rates of prescribing for naproxen and ibuprofen in this period [21]. Elsewhere we have found evidence of prioritisation of anticoagulant services, with blood tests to manage high-risk anticoagulants being prioritised during the initial stages of the COVID-19 pandemic [8]; data from the current study also suggests that prescribing in relation to anticoagulants is a priority, with all GI bleed indicators being unaffected, and continuing to decline, following COVID-19 onset.

In the early stages of the pandemic, in recognition of the increased risk of medication related harm during the COVID-19 pandemic, NHS England and local Clinical Commissioning Groups (CCGs) revised guidance regarding blood test monitoring, extending the recommended monitoring window for some patient populations (e.g., in relation to lithium [22] and methotrexate [23]) or advising that blood monitoring for lower risk medications should be carried out “if possible” (e.g., ACE inhibitors [24]), if clinically safe to do so. There is some evidence in our data that practices did adopt this revised guidance, with post-recovery blood test monitoring often falling just short of pre-pandemic levels (particularly in the case of methotrexate and lithium).

Implications for policy and research

The variation in service recovery observed in the blood test monitoring indicators may in part be due to the assessment window for each indicator, and clinicians prioritising urgent work during the pandemic. For example, it is possible that the protracted recovery of the ACE inhibitor monitoring was due to primary care services proactively prioritising monitoring of higher risk prescriptions such as methotrexate so as to minimise the impact of service disruption on patient care. It is also likely that the systems put in place around the monitoring of high risk drugs (e.g., clinical system alerts) contributed towards expedited recovery of the other blood test monitoring indicators, particularly in the case of lithium and methotrexate. The decile chart for this indicator starts to plateau well before the ‘worst case scenario’ timepoint, suggesting that the majority of primary care providers successfully implemented recovery programmes in this clinical domain. Further areas for research include using innovative change detection methodologies [25] to ascertain practice-level features that influence

recovery and resilience in the context of service disruption to inform WHO and NHS England's recommendations to "build back better".

The potential impact of this analysis for data usage in the NHS is considerable. Historically, due to practical and privacy challenges around accessing GP data at scale, each practice participating in the PINCER programme has been required to manually execute the necessary computerised searches before individually uploading their results for central oversight; in some centres data for a group of practices and patients can be downloaded and analysed in larger volumes. This manual approach introduces delays and increases the resource cost of monitoring safety. Using the OpenSAFELY framework we were able to execute a single analysis for almost the entire population of England in near-real-time, while leaving data in situ. This approach is efficient: analyses can be easily updated, and expanded, because they are executed in a single framework from re-executable code. It also preserves patient trust: OpenSAFELY was the single most highly trusted COVID-19 data project in a rigorous Citizens Jury sponsored by the NHS and the National Data Guardian [17]. Furthermore, the additional data also securely accessible through the OpenSAFELY tools can be used to describe PINCER indicators in fine-grained demographic or clinical sub-populations. These tools can facilitate near real-time audit and feedback in the context of rapidly evolving pressures on the health service and are readily extendable to other clinical and challenges.

More broadly this analysis demonstrates the power of collaborative working with shared open source code in the NHS: it built upon the work of PRIMIS in establishing and then publicly releasing the full code for a set of rigorously tested medication safety indicators; and then implemented the open code from PINCER in the open source framework of OpenSAFELY, to assess a critical public health question on a national scale. Open working as demonstrated here is strongly supported by senior stakeholders in multiple sectors [16,26,27] and can bring substantial benefits: it facilitates efficient re-use of prior technical work; it ensures fidelity through the consistent implementation of data curation and analysis across all organisations; it supports complete reproducibility; it enables error-checking by all interested parties; and it facilitates public and professional trust.

Conclusion

NHS GP data can be analysed at national scale to generate insights on service delivery. Potentially hazardous prescribing was largely unaffected by COVID-19 in a dataset of 57 million patients' full primary care health records in England.

Administrative

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Conflicts of Interest

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare the following: B.G. has received research funding from the Laura and John Arnold Foundation, the NHS National Institute for Health Research (NIHR), the NIHR School of Primary Care Research, the NIHR Oxford Biomedical Research Centre, the Mohn-Westlake Foundation, NIHR Applied Research Collaboration Oxford and Thames Valley, the Wellcome Trust, the Good Thinking Foundation, Health Data Research UK, the Health Foundation, the World Health Organisation, UKRI, Asthma UK, the British Lung Foundation, and the Longitudinal Health and Wellbeing strand of the National Core Studies programme; he also receives personal income from speaking and writing for lay audiences on the misuse of science.

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B.G. (guarantor) attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

B.G. (guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Information governance

NHS England is the data controller for OpenSAFELY-EMIS and OpenSAFELY-TPP; EMIS and TPP are the data processors; all study authors using OpenSAFELY have the approval of NHS England. This implementation of OpenSAFELY is hosted within the EMIS and TPP environments which are accredited to the ISO 27001 information security standard and are NHS IG Toolkit compliant.[28]

Patient data has been pseudonymised for analysis and linkage using industry standard cryptographic hashing techniques; all pseudonymised datasets transmitted for linkage onto OpenSAFELY are encrypted; access to the platform is via a virtual private network (VPN) connection, restricted to a small group of researchers; the researchers hold contracts with NHS England and only access the platform to initiate database queries and statistical models; all database activity is logged; only aggregate statistical outputs leave the platform environment following best practice for anonymisation of results such as statistical disclosure control for low cell counts.[29]

The OpenSAFELY research platform adheres to the obligations of the UK General Data Protection Regulation (GDPR) and the Data Protection Act 2018. In March 2020, the Secretary of State for Health and Social Care used powers under the UK Health Service (Control of Patient Information) Regulations 2002 (COPI) to require organisations to process confidential patient information for the purposes of protecting public health, providing healthcare services to the public and monitoring and managing the COVID-19 outbreak and incidents of exposure; this sets aside the requirement for patient consent.[30] This was extended in November 2022 for the NHS England OpenSAFELY COVID-19 research platform.[31] In some cases of data sharing, the common law duty of confidence is met using, for example, patient consent or support from the Health Research Authority Confidentiality Advisory Group.[32]

Taken together, these provide the legal bases to link patient datasets on the OpenSAFELY platform. GP practices, from which the primary care data are obtained, are required to share relevant health information to support the public health response to the pandemic, and have been informed of the OpenSAFELY analytics platform.

Ethical Approval

This study was approved by the Health Research Authority (REC reference 20/LO/0651) and by the LSHTM Ethics Board (reference 21863).

As noted in the Information Governance section, OpenSAFELY operates under existing COPI guidance, setting aside the need for patient consent.

Data sharing

All data were linked, stored and analysed securely within the OpenSAFELY platform (https://opensafely.org/). Data include pseudonymised data such as coded diagnoses, drugs, and physiological parameters. No free text data are included. Detailed pseudonymised patient data are potentially reidentifiable and therefore not shared.

All code is shared openly for review and reuse under MIT open license (https://github.com/opensafely/pincer-measures). All codelists used are openly available at OpenSAFELY Codelists (https://www.opencodelists.org/codelist/pincer/). Results are available as an online report https://reports.opensafely.org/reports/changes-in-pincer-measures-throughout-the-covid-19-pandemic/.

Provenance and peer review

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Figure legends

Figure 1 - Practice level decile plots for PINCER prescribing indicators, specifically in relation to (a) GI bleeding and (b) cautioned medications. The percentage of patients identified as at risk of potentially hazardous prescribing as measured by each indicator is reported for the period September 2019 to September 2021 (inclusive). The median percentage is displayed as a thick blue line and deciles are indicated by dashed blue lines. The month of national lockdown in England as a response to the onset of COVID-19 (March 2020) is highlighted with an orange dashed vertical line. Deciles for CRF & NSAID are calculated across 2546 OpenSAFELY-TPP practices; all other deciles are calculated across 6367 practices (2546 OpenSAFELY-TPP + 3821 OpenSAFELY-EMIS practices). Decile plots for these same indicators, in OpenSAFELY-TPP and OpenSAFELY-EMIS separately, are available in Supplementary Figures 1 and 2 respectively.

Figure 2 - Practice level decile plots for PINCER blood test monitoring indicators. The percentage of patients identified as at risk of potentially hazardous prescribing as measured by each indicator is reported for the period September 2019 to September 2021 (inclusive). The median percentage is displayed as a thick blue line and deciles are indicated by dashed blue lines. The month of national lockdown in England as a response to the onset of COVID-19 (March 2020) is highlighted with an orange dashed vertical line. The project date of maximum impact, as measured from the onset of COVID-19, for each indicator is shown by a green dashed vertical line. All deciles are calculated across 6367 practices (2546 OpenSAFELY-TPP + 3821 OpenSAFELY-EMIS practices). Decile plots for these same indicators, in OpenSAFELY-TPP and OpenSAFELY-EMIS separately, are available in Supplementary Figures 3 and 4 respectively.