

THE IMPACT OF
SMARTPHONE ENABLED
SUPPLY AND INTERVENTION
ON UNINTENTIONAL NON-
ADHERENCE TO MEDICINES
USING ECHO.

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ABSTRACT

The increasing ubiquity of smartphones and mobile applications offers new domains to extend patient support beyond the healthcare setting, and into the day-to-day. One notable example of where this opportunity lies is in reducing unintentional drivers of non-adherence.

This commentary presents a retrospective assessment of adherence in 8,481 patients over 12 months using the Echo mobile application. We specifically consider the potential impact of dosage prompts, supply prompts and direct supply to tackle unintentional non-adherence. In our review, we saw 75.24% adherence using the PDC>80% measure, and an average PDC of 88.05% for all medications for all patients.

Our objective in submitting this commentary is to contribute to, and urge furtherance of, more in-depth research around the role that mobile applications can play in improving medicines adherence and, as a consequence, health outcomes.

KEYWORDS

PHARMACY
ADHERENCE
SMARTPHONE
REMINDERS
TECHNOLOGY
HEALTH BEHAVIOUR

Medication non-adherence is a major source of waste in developed countries, with only 50% of patients who suffer from chronic diseases adhering to treatment recommendations [1]. Further research that has focused on adherence in specific classes of medication, has found variable adherence [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14]. For example, a study by Yeaw et al [15] found adherence in some medication classes to be as low as 35%.

It is widely agreed in the literature that good adherence to medication is associated with positive health outcomes [16], and that non-adherence increases the the risk of morbidity and mortality [17]. Finding new ways to support improved adherence should be a priority to health systems, and represents an opportunity to not just improve health outcomes, but also reduce direct and indirect costs within a financially stretched health economy.

Monitoring adherence is hampered by a number of systemic factors; data collection is fraught with difficulty and the inherent organisational fragmentation between pharmacy, hospital and general practice makes it unclear who is responsible for monitoring and intervention.

Medication non-adherence also has a complex aetiology which varies by disease and treatment. However, the causes of medication non-adherence can broadly be split into intentional (e.g. actively avoiding side-effects) and unintentional (e.g. forgetfulness) drivers [18]. Less research is available on the prevalence of individual causes of non-adherence.

However, a study by Barber et al [19], suggests that unintentional drivers account for 55% of medication non-adherence.

It is this combination of complex aetiology, delayed clinical impact and monitoring difficulties that make addressing medication non-adherence such a difficult problem. With smartphone penetration now over 85% [20] and Electronic Prescriptions available at 99.5% [21] of NHS England general practices, there is an unprecedented opportunity to reach millions of patients with targeted support, particularly with respect to unintentional non-adherence. However, in order to capitalise on this opportunity, we must overcome the issues around engagement. Smartphone-based reminder applications are not new [21] the reason they have not seen widespread adoption is that engagement is a difficult obstacle to overcome.

Realising that Echo had a unique opportunity to engage patients at population scale in 2016 we commissioned an independent online survey of 1029 members of the general public, which included 589 medication taking individuals. 52% reported never missing a medication dose, i.e. 48% consider themselves non-adherent, broadly agreeing with the literature.

Those reporting non-adherence were then prompted to attribute the main contributing factors. Unintentional drivers of non-adherence represented the three most common reasons where users simply forget to take it (69%), unintentionally run out of medication (29%), and are too busy to pick up medication from the chemist (14%). The other answers were all intentional citing wide effects (13%) not needing the medicine (8%), believe that the medication doesn't work (7%) and not knowing the reasons for medication being prescribed (2%).

The prominence of unintentional sources of poor adherence has implications for our preliminary research as it suggests that dose and resupply prompts, along with removing barriers to medication supply, could play a role in addressing non-adherence.

Our consequent hypothesis for retrospective review was that by reducing the main barriers to engagement such as set-up time, adoption rates and service awareness, smartphone-based dosage (taking the medicine) and supply (reordering the medicines) reminders can lower rates of unintentional non-adherence to medicines at a population level.

USING ECHO TO REVIEW ADHERENCE

Echo is a mobile application (commonly referred to as an app) that integrates multiple features that allow patients to request repeat medicines from their general practitioner (GP) and then receive direct supply via post to a chosen location (usually home). This is followed-up with patient-centric monitoring and prompts around dosage and resupply of medicines. Patients using the service for reasons of convenience around prescription ordering are auto-enrolled in dosage and resupply prompts. This eliminates the need for patient lead engagement whilst allowing patients to opt-out of adherence reminders.

The functions described above arguably offer ways to support the hypothesis derived from the three main reasons for non-adherence. Reminders to reduce instances of patients forgetting to take medicines, supply prompts to reduce instances of patients unintentionally running out of medication, direct supply to reduce instances where patients too busy to pick up medication from the chemist. Whilst the direct impact of individual functions within Echo was not possible within this review, it is suggested that Echo would be suitable to consider the combined impact on the three main drivers of unintentional non-adherence.

COHORT SELECTION AND ANALYSIS METHODS

To gain insight into the potential impact the service may have at scale, we decided to conduct a review of adherence and compare this to the literature. We reviewed the data for all Echo patients with medication schedules falling between 1st May 2017 to the 30th April 2018, whose start date and calculated end dates of the medication regime were between those dates for all regularly dosed medication. Only first and second prescriptions were included to limit the effect of surplus medication that would not have been accounted for in the initial data.

Prescription data for contraceptives was not included as calculating adherence proves difficult given the variable schedule of administration, long reorder cycles which can exceed the length of our data collection period and the necessity for face-to-face consultation every other repeat prescription. "As required" medication was excluded as adherence to medication taken only as needed cannot be measured by our methods, given that we cannot monitor when patients need their as required medication. PDC was selected as the adherence measure due to its robustness to the effects of oversupply. PDC is the leading method used to calculate medication adherence at a population level [22].

A study by Zhu et al [23] explored how best to measure adherence, concluding that 'PDC . . . accurately reflects patient adherence behaviour, and . . . effectively handles drug switching and prescription overlaps', over other common adherence measures such as medical possession ratio (MPR).

The period of days covered (PDC) measure between first and second prescriptions was used to assess adherence levels, with adherence in an individual patient being deemed as having an average PDC across all medications of >80%. The following calculation was used: $PDC = (\text{Number of days in period covered} / \text{Number of days in period}) * 100\%$. The average PDC for a patient was calculated by finding the mean value of their PDCs for each individual medication.

RESULTS

Table 1

The criteria yielded a cohort of 8,481 eligible patient records, for whom average PDC was calculated individually. The cohort characteristics are provided for all patients, by age, and by the number of medicines, summarised below:

Summary of cohort characteristics

Total	# of patients	% patients (n=8481)	Adherence
All	8,481	100%	75.24%
Age	# of patients	% patients (n=8481)	Adherence
18-24	956	11.27%	71.44%
25-34	2696	31.79%	72.44%
35-44	2525	29.77%	75.80%
45-54	1604	18.91%	78.05%
55-64	488	5.75%	81.15%
65+	212	2.50%	86.32%
# of medicines	# of patients	% patients (n=8481)	Adherence
1	4334	51.10%	72.52%
2	2054	24.22%	75.66%
3	958	11.30%	77.45%
4	511	6.03%	83.37%
5	271	3.20%	82.29%
6+	353	4.16%	83.00%

Over three-quarters of Echo patients (75.24%) included in this analysis were found to be adherent to all of their medication using the PDC>80% measure. The average PDC for all medications for all patients included in this analysis was 88.05%. Age and polypharmacy did not, in our view, demonstrate more than weakly positive correlations.

The percentage of adherent patients taking medication from the BNF sub-chapters most commonly prescribed by Echo are outlined in Figure 2 below. Amitriptyline was excluded from the analysis for antidepressants as in recent years patients predominantly take it for clinical indications other than mood disturbance.

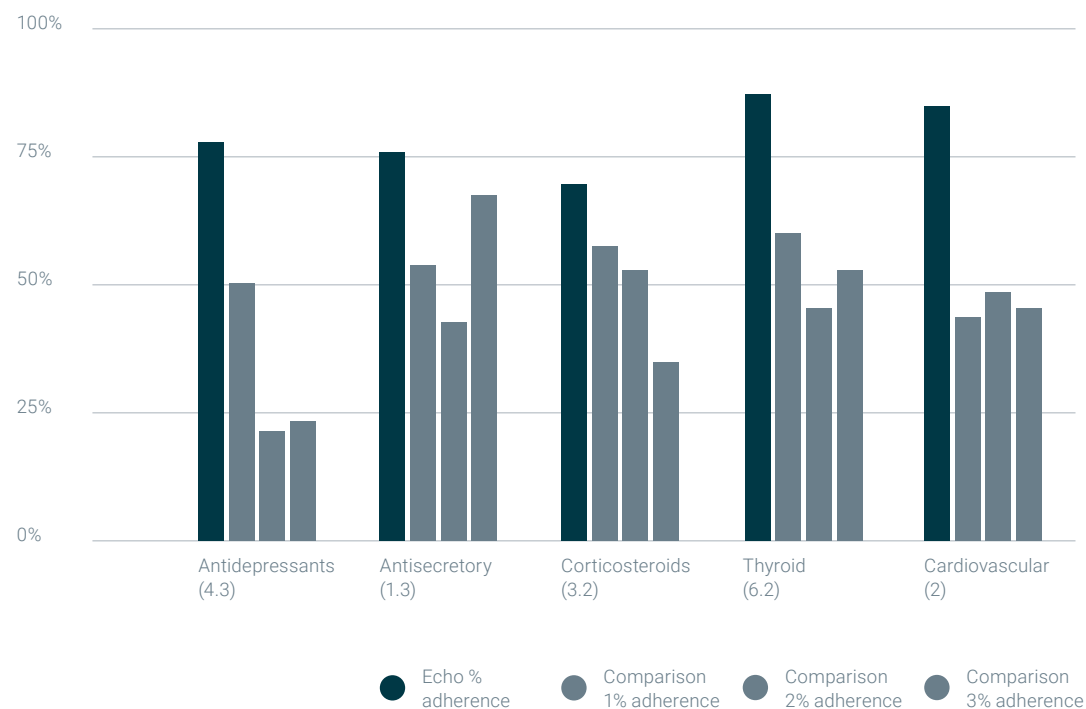
To measure continued engagement with the adherence-promoting functionality, we reviewed the number of patients disabling dosage and supply notifications separately. We found that 9.6% of patients opted out of dosage reminders, e.g. 90.4% of patients continued to receive these notifications. 14.3% of patients opted out of supply notifications meaning 85.7% of patients continued to receive supply prompts.

ANALYSIS

The percentage of adherent patients taking medication from the BNF sub-chapters most commonly prescribed by Echo were compared with equivalent statistics from the literature [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14], as summarised in Table 2. Those marked with an asterisk used MPR as a measure of adherence, with varying thresholds for what was considered adherent. MPR gives higher percentage estimates for adherence than our measure (PDC), so comparing our lower PDC percentage estimates to MPR is deemed appropriate.

As so many prescribed drugs overlap within the sub-chapters of 'Cardiovascular System' (chapter 2), we have considered the whole chapter and its corresponding figure of 83.14% adherent patients, rather than considering 'Hypertension and heart failure' (chapter 2.5).

Figure 2 Adherence in commonly prescribed BNF sub-chapters against comparators



We observed a weakly positive correlation between age and polypharmacy, and adherence differs from a large proportion of prior research in this area, however, may be reflective of some of the limitations discussed below.

The low opt-out rates for the adherence functionality could be attributed to various factors. Firstly patients had already downloaded the app, and have therefore actively engaged, and secondly, that since users are attracted to the delivery service provision, adherence prompts support and enhance a function which offers a direct, tangible benefit.

SUMMARY AND RECOMMENDATIONS

Whilst our analysis sought to be robust, it was not originally intended for the purpose of publication or constructed around a central hypothesis, but to support internal strategy and design of adherence-promoting application features. Therefore the findings are solely provided to provide early insight and recommend further research. It is also recognised that there were a number of limitations when comparing adherence to general population studies, which should factor into any conclusions:

- The results of our study are skewed to the demographics of the cohort, which differs from the general population in many respects. The cohort is younger than the general population, especially given our ageing population.
- There is selection bias within our cohort as Echo users are arguably more adherent to their medication, given that they have taken the initiative to download and use Echo in the first place.
- We excluded as required medication, and contraceptives, due to the complexity of regimes and monitoring.
- Whilst our data around patients who actively opted out of prompts enabled us to understand active disengagement, we were unable to measure passive engagement (i.e. those who allowed prompts but ignored them).
- It was not possible to identify and exclude any patients who use other pharmacy services in between two supplies dispensed by Echo.

Despite the above limitations, our preliminary findings show a consistently high level of adherence when compared to numerous different studies in varying disease groups. Furthermore, the opt-out model suggests a high engagement with the adherence-supporting features. Given these early findings, and the minimal costs of scaling the underlying adherence technology, this new approach could represent a cost-effective delivery mechanism for an adherence promoting intervention. Therefore it is suggested our approach merits further, more robust research.

It is Echo's intention to further this research and work with interested academic institutions to robustly review adherence across a much wider dataset, and to include further behavioural support functions within the Echo app.

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