



King, S., Miani, C., Exley, J., Larkin, J., Kirtley, A., & Payne, R. (2018). The impact of issuing longer versus shorter duration prescriptions: a systematic review. *British Journal of General Practice*, 68(669), e286-e292. <https://doi.org/10.3399/bjgp18X695501>

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The impact of issuing longer versus shorter duration prescriptions: a systematic review

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TOTAL WORD COUNT: 2561

Abstract

Background

Long-term conditions place a substantial burden on primary care services, with drug therapy a core aspect of clinical management. The ideal frequency for issuing of repeat prescriptions for these medications is unknown.

Aim

To examine the impact of longer duration versus shorter (28-day) duration prescriptions.

Design and Setting

Systematic review of primary care studies (PROSPERO: CRD42015027042)

Method

Scientific and grey literature databases were searched from inception up to 21/10/2015. Eligible studies were randomised controlled trials (RCTs) and observational studies that assessed longer prescriptions (range 2 to 4 months) compared with shorter prescriptions (around 28 days), in patients with stable, chronic conditions being treated in primary care. Outcomes of interest were: health outcomes, adverse events, medication adherence, medication wastage, professional administration time, pharmacists' time/costs, patient experience, and patient out-of-pocket costs.

Results

Moderate quality evidence from nine studies suggested that longer prescriptions are associated with increased medication adherence. Evidence from six studies suggested longer prescriptions may increase medication waste, but results were not always statistically significant and were of very low quality. No eligible studies were identified that measured any of the other outcomes of interest, including health outcomes and adverse events.

Conclusion

There is insufficient evidence for the overall impact of differing prescription lengths on clinical and health service outcomes, although studies do suggest adherence may improve with longer prescriptions. Current UK recommendations to provide shorter prescriptions are not substantiated by the current evidence base.

How this fits in

Local guidance from many health service commissioners, as well as the UK's Pharmaceutical Services Negotiating Committee, encourages general practitioners (GPs) to issue shorter prescriptions, typically 28 days in length. This guidance is based on non-systematic review evidence, which was not substantiated by our systematic review. Longer prescriptions lengths for people with stable, chronic conditions could be potentially important to GPs in terms of reducing their workload. It also has the potential to have a positive impact

for patients, including improving adherence and thus medication effectiveness, and reducing time, cost and inconvenience.

Keywords

Prescription length, primary care, repeat prescribing, medication adherence, medication waste

Introduction

Long-term conditions place a substantial burden on health services, particularly in the primary care setting where they are commonly managed (1). For those patients with relatively stable conditions, drug therapy is usually managed using “repeat prescriptions”, where patients can request a further prescription for a long-term medication without requiring a further consultation with a clinician.

The UK Department of Health advises that the frequency of repeat prescriptions should “balance patient convenience with clinical appropriateness, cost-effectiveness and patient safety”, but does not specify a recommended period (2). However, local guidance from many health service commissioners, as well as the UK’s Pharmaceutical Services Negotiating Committee, encourages general practitioners (GPs) to issue shorter prescriptions, typically 28 days in length (3-6). This guidance is based on non-systematic review evidence of reductions in medicines waste and consequent cost savings (7, 8). One study has reported that shorter prescription lengths may benefit patients by providing better signalling to GPs for treatment discontinuations due to adverse events (9).

However, other work does not support the use of shorter prescriptions, with studies suggesting they may increase health service costs through increased GP administrative workload and pharmacist dispensing costs, increase patient-incurred costs through more frequent trips to the pharmacist (10, 11), and adversely impact upon medication adherence and patient satisfaction (12-14). Prescription lengths also vary considerably between and within countries. For example, the duration of thyroid prescriptions has been found to vary between 28 days in France and 6 months in Australia (15), and prescription durations across all therapeutic areas in the Canadian province of Quebec were approximately half the length of those in the rest of Canada (16).

Given the disparity in evidence and practice, a systematic review was undertaken to examine the impact of primary care physicians issuing longer (three month) versus shorter (28-day) duration prescriptions in patients with stable chronic conditions. The results of a cost analysis and decision analysis model are reported separately (see (17, 18)).

Methods

We conducted a systematic review following standardised methodology and consistent with PRISMA guidance (19, 20). The protocol is published on the PROSPERO database (registration number CRD42015027042). The protocol and choice of outcomes was drawn up in consultation with lay patient representatives (21).

Data sources

We searched major scientific and grey literature databases from inception up to 21/10/2015, with no country or language restrictions. Search terms included combinations of the terms prescription, length, and duration, as well as specific time periods. Backward and forward citation searches were conducted. The databases searched and the full search terms are presented in Appendix 1. An updated search in PubMed in July 2017 identified no further articles.

Eligibility criteria

To be eligible, studies had to be randomised controlled trials (RCTs) or observational studies that compared longer duration prescriptions (including two to four months) with 28-day prescriptions (or around one month) in participants with relatively stable chronic conditions, for example, hypothyroidism, diabetes, cardiovascular disease, and depression. Studies were restricted to primary care settings in middle and high-income countries. Those conducted exclusively within secondary or tertiary care settings were excluded. The studies had to report on one or more of the following outcomes: health outcomes, adverse events, medication adherence, medication wastage, professional administration time, pharmacists' time/costs, patient experience and patient out-of-pocket costs.

Data extraction and synthesis

Two independent reviewers screened titles and abstracts identified by the searches, and screened full papers of potentially relevant studies. A third reviewer resolved disagreements. Relevant studies' characteristics were independently extracted by two reviewers, with a third reviewer checking and comparing the data extraction. An attempt was made to contact study authors for data missing from the identified papers.

Studies were analysed by outcome and by therapeutic area (e.g. lipid lowering medication, diabetic medication) as most of the included studies reported their results in this way. Studies varied in the nature and detail of the drug classification used; where necessary, we categorised medication categories (e.g. statins) into the corresponding therapeutic area (e.g. lipid lowering) to improve consistency across studies.

Within each study, we calculated effect sizes as odds ratios (OR) with 95% confidence intervals (CIs) for dichotomous outcomes, and mean difference (MD) with 95% CIs for continuous outcomes. Where appropriate, standard deviations (SDs) were imputed based on p values (19). Forest plots were generated using RevMan version 5.3. Meta-analyses were not conducted due to clinical heterogeneity between studies. The review was not designed to consider differences between therapeutic areas.

Risk of bias and quality of evidence

As only observational studies were identified, we assessed risk of bias using The Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool, although we also considered additional sources of bias (e.g. sample size) (22). Risk of bias was assessed by two reviewers independently, with discrepancies resolved through discussion. The GRADE criteria were used to assess the quality of evidence for each outcome (23).

Results

Our initial search identified 24,876 records across all databases. After duplicate removal, screening of titles and abstracts, and searching citations, 53 references were considered for full-text evaluation. Thirteen references representing 13 studies met the inclusion criteria (Appendix 2), although 4 were only reported in abstract form but were included because they presented clear outcome data (24-27).

Study characteristics are presented in Appendix 3. All the studies were conducted in the USA, and included nine retrospective cohorts (24-32), three cross-sectional analyses (33-35) and one retrospective before-and-after study (36). Three provided details of the healthcare setting, including a primary care clinic (28), patients seen in primary care, a mental health clinic, inpatient services and an integrated primary care mental health (30), and an internal medicine practice (33). Other studies did not explicitly report being conducted in primary care although we considered them unlikely to have been conducted exclusively in secondary or tertiary care settings (e.g. claims data from community pharmacies). Study populations included patients new to treatment (25-27, 30), patients receiving ongoing care (28, 29, 31), or both (35). Comparisons between prescription lengths were assessed for various therapeutic medication groups, including most commonly lipid-lowering, anti-hypertensive, diabetic, and anti-depressant medications (25-30, 32-36). Most studies compared a 30-day medication supply with a longer period: a 90-day supply (24-26, 29, 32, 35), a 60-day supply (28), or both 31-to-89 days or >90-day supplies (27, 31, 34). Other studies compared 100-day versus 34-day supplies (36), more or less than 90-day supplies (30), and a range of prescription lengths up to 90 days (33).

No eligible studies were identified that measured health outcomes or adverse events. Only one retrospective cohort study measured a risk factor for a health outcome (serum cholesterol was lower in the 60-day compared to 30-day prescription group at 3-years, mean 4.8 [standard deviation 1.2] mmol/l vs. 5.0 [1.4] mmol/l respectively; $p=0.003$) (28). No eligible studies reported professional administration time, pharmacists' time/costs, patient experience or out-of-pocket costs other than prescription costs. The most common reported outcomes were medication adherence and wastage.

Medication adherence

Nine studies reported medication adherence, indirectly estimated using pharmacy claims refill data (Appendix 4) (25, 26, 28, 30-34, 36). Commonly used measures of adherence were the proportion of days covered (PDC = number of days in a given time period "covered" by prescription claims for a particular drug, divided by the number of days in the time period), or the medication possession ratio (MPR = total number of days supplied for all refills of a particular drug in a given time period, divided by the number of days in the time period). We elected not to separate these measures in our analyses (although PDC has been found to provide a more conservative estimate of adherence than the MPR (37)). PDC and MPR were expressed either as the proportion of patients achieving a particular threshold (generally >80%), or the average (mean) value.

Consistent findings were found across all studies. Three cohort studies found prescription lengths shorter than 90 days were associated with poorer adherence across a range of therapeutic areas (including lipid-lowering therapy, antihypertensives, diabetes medication and antidepressants), based on both adherence <80% threshold (odds ratios 0.21 to 0.65, Figure 1) (25, 28, 30). A further three cohort studies found similar associations, based on mean reduction in adherence (mean decrease 0.12 to 0.30, Figure 2) (26, 31, 32). A

controlled before-and-after study found shortening of antihypertensive, diabetic and lipid-lowering prescription length from 100 to 34 days was significantly associated ($p < 0.01$) with a 5.3% to 13.2% reduction in those time periods where PDC was $\geq 80\%$, and a mean decrease in PDC of 0.034 to 0.080 (no differences were observed for seizure medication or anti-psychotics) (36). In a further cross-sectional study, prescriptions of >90 days were associated with greater adherence (PDC $>80\%$) compared with prescriptions of ≤ 30 days for drugs affecting the renin-angiotensin system, statins and oral diabetes medications (relative risk 1.61, $p < 0.001$ for each) (34). A second cross-sectional study found each 30-day increment in prescription length (up to 90 days maximum) was associated with a 5.7% increase in mean adherence ($p < 0.0001$), diabetes, anti-hypertensive and lipid-lowering medications (33).

Medication wastage

Medication wastage was reported in six of the included studies (see Appendix 5) (24, 26, 27, 29, 32). All measures of wastage were indirect, estimated based on pharmacy claims refill data. The majority of these studies defined wastage in a similar manner, such as a 'switch in medication type within the same clinical class or to the same medication but with a different strength, occurring before the expected refill date' (29). One study also included discontinuation within its definition (24). Waste was expressed as percentage of days' supply wasted, percentage of patients with wasted medication, or mean number of days' supply wasted.

Two retrospective cohort studies assessed percentage of days' supply wasted, finding only small differences ($\leq 1.5\%$) between different prescription lengths, but neither study reported raw data or statistical comparisons, and additional information could not be obtained from the authors (24, 27).

Three studies evaluated the percentage of patients that wasted medication (27, 32, 35). Odds ratios could be calculated for one retrospective cohort and one cross-sectional study (32, 35). In general, there was non-significant trend for longer prescriptions (90 days vs. 30 days) to be associated with higher proportions of patients with wasted medication; this was statistically significant for lipid-lowering drugs for the study by Taitel only (OR 0.84, 95% CI 0.72-0.98) (32). A third cohort study reported varying patterns across therapeutic areas, but with no statistical analysis and insufficient data to calculate effect sizes (27).

Four studies reported the mean number of days' supply wasted over one year (26, 29, 32, 35). Effect sizes could not be calculated for one study in which it was unclear if days wasted was standardised between the two prescription groups (35). The remaining studies found evidence that shorter (30 days vs. 90 days) prescriptions were significantly associated with a mean reduction in waste days. Across a range of therapeutic areas, Taitel reported a reduction of between 3.5 and 6.9 days over a 1-year study period (32), and Murphy found a reduction of 0.03 to 0.13 days over a 30-day period (26, 29); Jiang found a mean reduction of -0.1 days averaged for all therapeutic areas (26).

Risk of bias and quality of evidence

Lack of methodological detail prevented assessment of risk of bias for the four studies presented as abstracts (24-27). One study was classified as having a serious risk of bias due to a small sample size (31) and another was similarly classified as a cut-off point of 84 days was used with no justification provided for this decision (32). The remaining seven

studies were considered to have a moderate risk of bias (Appendix 6) (28-30, 33-36). In nine studies, the authors did not explicitly report taking measures to control for selection bias.

In terms of GRADE assessment, the evidence was determined to be of very low quality for all outcomes except adherence outcomes, which were considered to be of moderate quality.

Discussion

Summary

This is the first systematic review of evidence comparing the impact of shorter and longer prescriptions on clinical and health service outcomes. We found some evidence from six studies that longer prescriptions are associated with increased medication waste, but the results were not always statistically significant and are of very low quality. We found moderate quality evidence to suggest that longer prescriptions are associated with better adherence. If medication adherence is positively correlated with health outcomes, as seems to be suggested by the wider literature (38, 39), there may be benefits to increasing the length of repeat prescriptions for patients with chronic conditions. However, we found no direct evidence assessing the association between different prescription lengths and health outcomes (including adverse events). Furthermore, although it is important to minimise medication waste, this needs to be balanced against the needs of patients and clinicians' workloads. However, we found no direct evidence comparing different prescription lengths with differences in health professionals' administrative time, pharmacists' time or patient experience.

Strengths and limitations

Although we followed rigorous methodology, there are limitations to this systematic review. It is possible that some of the studies are not truly representative of primary care, although the findings are generally consistent regardless of setting. Moreover, all of the eligible studies were conducted in the USA and their applicability to UK settings could be limited given differences in health care systems. We may also have missed evidence where prescription lengths were considerably different to our inclusion criteria. Some of the studies differentiated patients receiving new versus existing prescriptions, but we did not consider this in the protocol and not enough studies reported this information to allow a post hoc subgroup analysis. Finally, it was not possible to make comparisons of effect sizes between different therapeutic areas. We have recently conducted an analysis within routine UK primary care health records, not included in this systematic review, which addresses some of these concerns (17).

A key issue with all of the studies was their use of indirect, proxy measures for both adherence and waste, based on administrative prescription refill data. The two key adherence measures used were PDC and MPR, which may introduce bias in favour of longer prescriptions as well as underestimating true adherence (40, 41). Similar concerns can be raised about the estimation of waste. Nevertheless, a review of such approaches has determined that indirect measures still have value (42).

None of the studies explored why adherence may differ between prescription lengths. Reasons for medication nonadherence are often complex, and can be both intentional and unintentional (43). Longer prescription lengths may overcome barriers to unintentional adherence, such as enabling patients to follow a regular medicine regimen or reducing logistical barriers such as visits to the pharmacy (28, 31, 33). However, given the observational nature of the studies, there is a risk of systematic differences, with longer prescriptions issued to patients considered more adherent by the prescriber, those having more stable illness (30), or those of non-white ethnicity (44).

We identified only one study that showed a beneficial association between longer prescriptions and improved clinical outcome (28). There was a lack of research examining the association between prescription duration and other outcomes, although some non-comparative evidence exists for shorter prescriptions being considered inconvenient and disempowering, and causing patient dissatisfaction and anxiety (13, 14),(45).

Implications for research and practice

This review has found that medication adherence may be associated with longer prescription durations, which in theory may translate to clinical benefit. The evidence that such prescriptions also lead to increased waste is, however, very weak. Current UK policy recommending the provision of shorter prescriptions is not substantiated by the current evidence base, and further research is required to evaluate the clinical, health service and economic impact of differing prescription lengths.

This research was funded by the NIHR HTA contract number: 14/159/07.

All work was conducted and analysed independently of the funder. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Ethical approval was not required for this research.

Competing interests: None declared. *All authors have completed the unified competing interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author).*

Acknowledgments

We would like to thank the following people who made invaluable suggestions during the review process: Catherine Meads, Anthony Avery, Molly Morgan Jones, and Adam Martin. We would also like to thank the peer reviewers for their comments on this paper.

Figure 1 Medication adherence

Figure 2 Wasted medication

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