Clinical effectiveness and cost-effectiveness of issuing longer versus shorter duration (3-month vs. 28-day) prescriptions in patients with chronic conditions: systematic review and economic modelling

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Scientific summary

Identifying best practice for decommissioning health care

Scientific summary

Background

Patients with stable chronic conditions often require treatment with long-term medication. In England, an increasing number of NHS patients receive prescriptions for chronic conditions without a consultation in primary care. These repeat prescriptions are typically for 28 days' supply. The evidence base for this relatively short duration is uncertain.

Objective

The objective of this study was to assess whether 28-day versus 3-month prescription lengths, or shorter versus longer prescription lengths, in people with stable chronic conditions treated by general practitioners (GPs), have positive or negative impacts on a range of health outcomes, patient adherence, drug waste, dispensing costs, other NHS costs, and cost-effectiveness. There were three parts to this project:

1. a systematic review of the evidence on 28-day versus 3-month prescriptions in patients with chronic conditions treated in primary care, evaluating any relevant clinical outcomes as well as adherence to treatment, costs and cost-effectiveness
2. a cost analysis of medication waste associated with longer and shorter prescription lengths for five patient groups using the UK Clinical Practice Research Datalink (CPRD) over an 11-year period
3. the adaptation of three existing decision models to predict the costs and effects of differing adherence levels associated with 28-day versus 3-month prescription lengths in three clinical scenarios.

Methods

For the systematic review, databases searched included MEDLINE (PubMed) from inception to June 2016, and EMBASE, Cumulative Index to Nursing and Allied Health Literature, Web of Science and the Cochrane Central Register of Controlled Trials from inception to October 2015. Any comparative studies in patients with chronic conditions treated in primary care evaluating any relevant clinical outcomes as well as adherence to treatment, costs and cost-effectiveness were included. Standard systematic review methods were used, including duplicate screening for inclusion, data extraction and quality assessment. Risk of bias was assessed using the Risk Of Bias in Non-Randomized Studies – of Interventions (ROBINS-I tool). A meta-analysis was conducted in RevMan version 5.3. (RevMan, The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark). Dichotomous results were converted to continuous outcomes where necessary using methods recommended in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0).

The CPRD is a large, longitudinal primary care data set representing approximately 7% of the UK population. The cost analyses were based on five patient cohorts: (1) glucose control with oral therapy in type 2 diabetes mellitus (T2DM), (2) treatment of hypertension in T2DM, (3) treatment with statins (lipid management) in T2DM, (4) treatment for the secondary prevention of myocardial infarction and (5) treatment of depression. The analyses were run over an 11-year period and incorporated prescriptions from 250,000 patients in total. Treatment patterns were analysed in Stata® version 13.1 (Stata Corp LP, College Station, TX, USA).

The decision modelling took a NHS perspective. The three clinical scenarios were (1) medications for primary prevention of cardiovascular events in T2DM, (2) treatment of depression with selective serotonin reuptake inhibitors (SSRIs) and (3) medications for secondary prevention of cardiovascular events in people with hypertension. The three models chosen were adapted from models in relevant guidance issued by the

National Institute for Health and Care Excellence (NICE). Models were adapted using results from the systematic review on adherence, along with estimated dispensing fees (from NHS Drug Tariffs), prescriber time (from the CPRD analysis), costs of wastage (from the CPRD analysis) and data on the relationship between treatment and no treatment (from the NICE models or reports associated with them). The results were presented as costs per quality-adjusted life-year (QALY) and incremental cost-effectiveness ratios (ICERs). Modelling was conducted in Microsoft Excel® version 20.10 (Microsoft Corporation, Redmond, WA, USA).

Results

In the systematic review, from 15,257 unique citations, 54 full-text papers were reviewed and 16 studies were included, most of which were rated as having a moderate to serious risk of bias. For five of the 16 studies, only an abstract was available, and for a sixth study only an extended conference abstract was available. None was a randomised controlled trial (RCT); 11 were retrospective cohort studies, three were cross-sectional surveys and two were cost studies. A variety of patient groups were included, all studies were carried out in the USA and all were conducted in a variety of primary care settings. Adherence was based on indirect estimates of pharmacy refill claims, and was reported in a variety of ways including the proportion of days covered and the medication possession ratio. Drug waste was also reported in several ways, including the proportion of days' supply wasted and the mean number of days' supply wasted. No information on health outcomes was available. One study reported on achievement of target cholesterol levels and found that longer prescription lengths were associated with statistically significantly lower final mean serum cholesterol values {185.3 mg/dl [standard deviation (SD) 46.2] vs. 191.5 mg/dl [SD 52.6]}. Nine studies reported on adherence, and all nine reported better adherence with longer prescription lengths. An exploratory meta-analysis of adherence results from six retrospective cohort studies suggested that adherence was lower with a 28-day supply (standardised mean difference –0.45, 95% confidence interval –0.65 to –0.26). From the six studies reporting on drug wastage, the trend was for more wastage with longer prescription lengths. Five studies gave some information on costs, and four of these suggested that total costs were lower with longer prescription lengths.

The cost analysis of CPRD data corroborated the review findings that although longer prescription lengths (≥ 60 days) were associated with greater medication waste per prescription than shorter prescription lengths (< 60 days), once the additional dispensing fees and prescriber time required to issue a prescription were taken into account, longer prescription lengths resulted in a net cost saving. This finding was consistent across all five conditions studied, and savings ranged from £6.33 to £9.07 per prescription when total unnecessary costs (TUCs) were standardised to a common 90-day time period. The biggest impact on the cost savings was prescribers' time costs. The largest differences in the mean cost of wastage per prescription for the two prescription lengths were observed in the lipid management of the T2DM cohort, and the smallest differences were observed in the depression cohort.

The decision modelling suggested that longer prescription lengths were associated with lower costs and higher QALYs than shorter prescriptions for all three clinical scenarios (primary prevention of cardiovascular events in T2DM, medications for secondary prevention of cardiovascular events in people with hypertension and treatment of depression with SSRIs).

Limitations

The available evidence base is rated as being at a moderate to serious risk of bias, and there is no good evidence on the impact of prescription length on patient outcomes. All of the studies identified were conducted in the USA, which has a distinctly different health-care system from that in the UK, with very different (and generally higher) costs. This raises concerns over the generalisability of this evidence to the UK setting.

The cost analyses study could investigate only prescriptions issued and not patient adherence. In addition, the cost analyses were based on products issued only and did not account for underlying patient diagnoses. Lack of good-quality evidence affected the decision modelling strategy. The modelling was based on existing models, and no probabilistic sensitivity analysis was available.

Conclusions

The current evidence suggests that 90-day prescription lengths are associated with better adherence than 28-day prescription lengths in patients with stable chronic conditions being treated in primary care. No evidence was found of a direct impact of prescription length on health outcomes. This study found evidence suggesting that longer prescriptions resulted in net cost savings owing to reductions in costs associated with dispensing fees and prescriber time, which outweighed wastage costs.

Future work

One potential research priority is a cluster RCT to establish much more robust evidence for the most appropriate prescription length in patients with a variety of chronic conditions treated in general practice. The priority for future research should be to identify patients with particular conditions or characteristics who should receive shorter or longer prescriptions. Primary care patients with chronic conditions should be randomised to several prescription lengths including 28-day and 3-month prescriptions, and followed up to establish all relevant clinical outcomes including health status, adherence, quality of life, patient experience and patient costs. Drug waste and NHS costs should also be collected to derive more robust estimates of the cost-effectiveness of differing prescription lengths in different conditions.

Further decision modelling could run probabilistic sensitivity analyses, which would enable an expected value of perfect information analysis. This would help to determine the value of carrying out a RCT.

Standard methods for reporting of adherence and drug waste need to be established so that future studies with these outcomes can be compared more easily.

Study registration

This study is registered as PROSPERO CRD42015027042.

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