NICE National Institute for Health and Care Excellence

Surveillance report 2016 – Medicines adherence (2009) NICE guideline CG76

Surveillance report

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Contents

Surveillance decision

We will not update the guideline at this time.

We will transfer the guideline to the static list because:

- No evidence was identified that would impact on the current guidance and no major ongoing studies or research have been identified as due to be published in the near future (that is, within the next 3–5 years).

Reason for the decision

We found 115 studies through surveillance of this guideline.

This included new evidence on patient involvement in decisions about medicines, supporting adherence and reviewing medicines that supports current recommendations. We asked topic experts whether this new evidence would affect current recommendations on NICE guideline CG76. Generally, the topic experts thought that an update was not needed.

We did not find any new evidence on communication between health professionals.

None of the new evidence considered in surveillance of this guideline was thought to have an effect on current recommendations.

In addition, no major ongoing studies or research due to be published in the next 3–5 years was identified.

Other clinical areas

We did not find any new evidence in areas not covered by the original guideline.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all the new evidence and views of topic experts, we decided that no update is necessary for this guideline.

See how we made the decision for further information.

Commentary on selected new evidence

With advice from topic experts we selected 2 studies for further commentary.

Supporting adherence – interventions to increase adherence

We selected the randomised controlled trial (RCT) by Hedegaard et al. (2015) for a full commentary because the study covers the novel area of a pharmacist-led multicomponent intervention in secondary care.

We also selected the RCT by Lyons et al. (2016) for a full commentary because the study covers an emerging pharmacist-led intervention that has the potential to impact on NICE guideline CG76 recommendations in the future.

What the guideline recommends

NICE guideline CG76 states that no specific intervention can be recommended for all patients. It recommends that because evidence supporting interventions to increase adherence is inconclusive, interventions should only be used to overcome practical problems associated with non-adherence if a specific need is identified. Interventions should be targeted to the need.

Multifaceted pharmacist-led intervention

Methods

Hedegaard et al. (2015) conducted an RCT aiming to assess whether a multifaceted pharmacist-led intervention would improve medication adherence in patients with hypertension treated in secondary care.

Inclusion criteria

The inclusion criteria were for patients to be 18 years or older and prescribed 1 or more

antihypertensive drugs. Patients were excluded if they:

- lived in residential care
- received dose-dispensed medicine from a pharmacy
- had medicine dispensed by a home nurse
- had terminal illness
- had conditions that precluded patient interview
- lived outside the region of Southern Denmark
- were treated with more than 1 drug within a drug class.

Intervention

The intervention comprised:

- collaborative care
- medication review
- adherence counselling including motivational interviewing and telephone follow-ups with patients for up to 6 months.

The intervention group received the intervention and usual care. The control group received usual care only. This involved outpatient consultations with physicians or nurses between 2 and 4 times per year.

Outcomes

The primary outcome was overall adherence to antihypertensive and lipid-lowering drugs 12 months after inclusion, calculated using the medication possession ratio (MPR) measure. MPR was defined as the amount of drug available from refills during the follow-up period relative to the amount prescribed.

Secondary outcomes were:

- composite MPR at 3, 6 and 9 months

- adherence and persistence at 12 months to:
  - diuretics
  - calcium antagonists
  - beta-blockers
  - renin-angiotensin agents
  - lipid-lowering agents
- a 12-months combined end point of:
  - cardiovascular death
  - acute myocardial infarction or haemorrhagic or ischemic stroke
  - hospital admissions **and**
  - blood pressure and medication changes for antihypertensive and lipid-lowering drugs.

The definition of non-persistence was non-redemption of a prescription within the subsequent 90 days of the last date covered by the preceding prescription. This was estimated for medication prescribed at study entry.

Results

In total, 532 eligible patients were randomised to intervention (n=240) and control (n=292) groups.

Medication adherence and persistence

For the primary outcome of overall adherence:

- Median composite MPR was 0.91 (interquartile range [IQR] 0.76 to 0.98) in the control group, compared with 0.93 (IQR 0.82 to 0.99) in the intervention group (p=0.02).
- A significantly greater percentage of control group patients (30.2%) were non-adherent compared with intervention patients (20.3%) (p=0.01).

For the secondary outcomes:

- At 12 months, a greater proportion of control patients were classified as non-adherent for lipid-lowering agents (33.0% versus 23.4%; p=0.04) and plain renin-angiotensin agents (25.1% versus 16.2%; p=0.05).
- There were no statistically significant differences in 12-month adherence rates for the remaining drug classes analysed.
- There were no statistically significant differences in non-persistence for any of the drug classes.
- There were no statistically significant differences for any of the clinical outcomes.
- Physicians accepted 58 (64%) of 91 recommendations made by pharmacists on drug-related problems. However, there were no significant differences between the proportions of patients in each group with medication changes (49% of the intervention patients versus 46% of the control group [p=0.54]).

Strengths and limitations

Strengths

- The study was adequately powered to demonstrate significant differences between groups.
- The study enhanced the evidence base for multifaceted pharmacist interventions, including motivational interviewing, in the secondary care setting.
- The risk of bias was low due to appropriate randomisation, concealment, objective outcome measures and intention to treat analysis.
- The study included a 12-month follow-up period to assess sustained effects after the intervention had ended.
- The study used 5 extensively trained pharmacists at 3 different outpatient clinics.
- Objective and established measures of adherence were used.

Limitations

- Although data were obtained from 3 different outpatient clinics, the study was conducted at a single site in Denmark, and only patients from that specific region were eligible.
- Blinding of patients and pharmacists was not possible due to the nature of the intervention, but the risk of bias was reduced by the use of objective outcome measures.
- A longer-term follow-up study may be required to fully assess the prognostic impact on clinical outcomes.
- The study was focused on patients with hypertension. Larger studies across multiple conditions, which also include cost-effectiveness data, may be required to establish an impact on NICE guideline CG76.

Medicines advice services

Methods

Lyons et al. (2016) conducted an RCT aiming to assess the effectiveness of a pharmacist-led centralised advice service in patients already established on long-term medications for diabetes or lipid regulation, who use mail order pharmacy services. Patients were recruited through a UK NHS-contracted mail order and Internet pharmacy named 'Pharmacy2U', which includes more than 300,000 registered patients across England.

Inclusion criteria

The inclusion criteria were for patients to be prescribed 1 or more oral medicines for type 2 diabetes or lipid regulation. Patients were excluded if they:

- were under the age of 18 years
- lived outside of England
- had difficulty reading or understanding English or understanding the details of the study

- were prescribed drugs for dementia or showed signs of cognitive impairment
- had substantial hearing or sight impairment
- had medications ordered by a caregiver or family member
- received a first prescription of a medication included in the study.

Intervention

The intervention is an advice service led by pharmacists, with the flexibility to support patients taking prescribed medicines for any long-term condition. In this study, the intervention was focused on lipid-lowering and anti-diabetic medications. The conditions were targeted due to their high burden of disease and resource use, and reportedly poor medicines adherence.

There were 3 components of the intervention:

- Two tailored telephone consultations with a pharmacist, between 4 and 6 weeks apart. The first followed a semi-structured interview format and the second was to follow this up with a review and a discussion of any new or outstanding issues.
- A written summary of the discussion, following the first telephone consultation.
- A personalised medicines reminder chart setting out the patient's prescribed medications, including purpose of the medicine, dosage and timing.

The control group participants received standard care of the existing dispensing service, with medications delivered to their address following online or telephone orders.

Outcomes

The primary outcome was self-reported adherence to lipid-lowering or oral diabetes medicines, measured using a postal questionnaire adapted from the Diagnostic Adherence to Medication Scale. Data were collected at baseline, 4 weeks and 6 months following the second telephone consultation. Non-adherence was defined as less than 90% of medication taken in the past 7 days. An additional objective measure of refill adherence was also employed, using pharmacy dispensing data.

Secondary outcomes were:

- lipid and glycaemic control, measured by a self-administered finger prick test
- patient satisfaction, measured by 4-week follow-up self-report questionnaire.

Results

Out of 785 patients recruited to the study, 684 were eligible and 677 were randomised to the intervention (n=340) and control (n=337) groups.

For the primary outcome, at 6 months, 36 (10.6%) patients in the intervention group were non-adherent compared with 66 (19.6%) patients in the control group, a significant difference with an unadjusted odds ratio [OR] of 1.54 (95% confidence interval [CI] 1.11 to 2.15, p=0.01).

Pharmacy refill dispensing data also showed that significantly fewer patients in the intervention group (29.9%) were categorised as non-adherent (less than 90% of medication available) than in the control group (40.6%). This resulted in an odds ratio of 1.60 in favour of the intervention group (95% CI 1.14 to 2.24, p=0.006).

For the secondary outcomes:

- Glycaemic and lipid control test results did not differ significantly between groups (p=0.06 and p=0.24 respectively), although both tests showed a trend towards improvement in the intervention group.
- A total of 245 patients (reported as 92%, presumably of patients returning questionnaires) in the intervention group reported that they were satisfied with the service overall.

Strengths and limitations

Strengths

- An additional objective measure of adherence was used to reduce the risk of bias inherent in the subjective measure of self-reported adherence.
- Incomplete outcome data was explained by the reasons for withdrawal and addressed by intention to treat analysis.

- The study built on earlier research that led to the development of the New Medicines Service (NMS), by focusing on established medicines over a longer period.
- The study was reported to be the first of its kind to investigate the impact of a pharmacist-led intervention in mail order pharmacy.

Limitations

- In view of the chronic nature of the conditions, the follow-up for 6 months was too short to assess fully the clinical impact on symptoms.
- Blinding of participants and pharmacists was not possible, although the risk of performance bias was lessened by presenting the intervention to participants as an opportunity to access advice from a pharmacist, without mentioning adherence.
- The authors acknowledged that the study would have benefitted from a pilot and feasibility stage, which may have helped to improve the initial response rate of invited participants.
- A single mail-order pharmacy was used for recruiting participants. It is possible that the results may not be generalisable to the whole UK setting, where patients are able to obtain prescriptions from any pharmacy.
- A single pharmacist was used to deliver the intervention.
- Cost-effectiveness data were not included in the analysis.
- The number of respondents completing the satisfaction questionnaire was not clearly reported.
- A total of 128 (37.6%) patients in the intervention group either did not receive the intervention or were lost to follow-up. Only 64 (19%) patients in the control group were lost to follow-up. Although intention to treat analysis was employed to address this imbalance, the authors did not discuss the impact of the high attrition rate.

Impact on guideline

The NICE guideline CG76 committee highlighted the difficulty in interpreting studies that do not assess a single intervention but include multicomponent interventions. This means it is not possible to assess the constituent interventions in isolation. The committee also

concluded that there is conflicting evidence to suggest that multicomponent interventions mainly based on motivational principles increase adherence. This led to the recommendation that although adherence can be improved, no specific intervention can be recommended for all patients. Interventions to increase adherence should be tailored to the specific difficulties with adherence the patient is experiencing.

Multifaceted pharmacist-led interventions

The new evidence has enhanced the evidence base for multifaceted pharmacist-led interventions, including motivational interviewing, in the secondary care setting. Further larger studies, which also cover cost effectiveness, may be needed to assess whether the improvement in adherence can be translated into better clinical outcomes. The study is therefore unlikely to impact on NICE guideline CG76.

Medicines advice services

Topic expert feedback highlighted the emergence of the NMS, delivered by community pharmacists for newly prescribed medicines and now funded throughout England. The new evidence has enhanced the earlier research that led to the development of the NMS. It has adapted this emerging intervention to improve adherence to more established medicines over a longer period. This is particularly pertinent to long-term conditions, where the vast majority of prescriptions are well established and would not be eligible for the NMS. Further research, including cost-effectiveness data, may be required to establish an impact on NICE guideline CG76.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 8 years after the publication of medicines adherence (2009) NICE guideline CG76.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual'.

Previous surveillance update decisions for the guideline are on our website.

New evidence

We found 63 new studies in a search for randomised controlled trials and systematic reviews published between 18 December 2014 and 11 July 2016.

Evidence identified in previous surveillance 6 years after publication of the guideline was also considered. This included 52 studies identified by search.

From all sources, 115 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: summary of new evidence from surveillance and references for all new evidence considered.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

Views of stakeholders

Stakeholders commented on the decision not to update the guideline. Overall, 6 stakeholders commented. See appendix B for stakeholders' comments and our responses.

Eight stakeholders commented on the proposal not to update the guideline: 3 disagreed with the decision, 3 agreed with the decision and 2 noted that they had no comments on the proposals. Eight stakeholders commented on the proposal to put the guideline on the static list: 3 disagreed with the decision, 3 agreed with the decision and 2 noted that they had no comments on the proposals.

One stakeholder suggested an amendment to the wording of recommendations in section 1.1 relating to patient beliefs. This will be considered when the guideline is next updated.

Several comments suggested changes to make to review questions. A stakeholder suggested amending the definition of adherence and incorporating phases of adherence. Another stakeholder suggested that the Accessible Information Standard be incorporated into the guideline recommendations. Finally, another stakeholder suggested that the polypill, for improving adherence in the secondary prevention of cardiovascular diseases, be incorporated into the guideline recommendations. However, surveillance includes all new evidence relevant to the scope and no evidence to address the suggested questions was identified. No new ongoing or relevant published studies were identified by the consultees.

See ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual' for more details on our consultation processes.

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