LIFELAX – diet and LIFEstyle versus LAXatives in the management of chronic constipation in older people: randomised controlled trial

C Speed,[1] B Heaven,[2] A Adamson,[2,3] J Bond,[1,4] S Corbett,[5] AA Lake,[2,3] C May,[2] A Vanoli,[2] P McMeekin,[2] P Moynihan,[3,4,6] G Rubin,[7,8] IN Steen[2] and E McColl[1]*

[1]Newcastle Clinical Trials Unit, Institute of Health and Society, Newcastle University, Newcastle, UK
[2]Institute of Health and Society, Newcastle University, Newcastle, UK
[3]Human Nutrition Research Centre, Newcastle University, Newcastle, UK
[4]Institute for Ageing and Health, Newcastle University, Newcastle, UK
[5]North Tyneside General Hospital, Northumbria Healthcare Trust, North Shields, UK
[6]Dental School, Newcastle University, Newcastle, UK
[7]Department of Primary Care, University of Sunderland, Sunderland, UK
[8]Northern & Yorkshire Primary Care Research Network, Stockton-on-Tees, UK

*Corresponding author

Executive summary

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Executive summary

Background

The management of constipation in the over-55s is costly, generating far in excess of 450,000 general practitioner (GP) consultations per year in the UK, at an estimated cost of more than £4.5M per year. In older adults living in the community, approximately 20–25% have symptoms of constipation. The propensity to consult increases with age – for a GP with an average list size of 2000, approximately 16 patients aged 55 and over will consult about constipation each year (McCormick A, Fleming DF, Charlton J. *Morbidity statistics from general practice: fourth national study*. OPCS: London; 1995).

Though often trivialised as a medical problem, for people with chronic constipation the impact on quality of life (QoL) is considerable and the burden on health-care resources is substantial.

Objectives

To investigate the clinical effectiveness and cost-effectiveness of:

1. laxatives versus dietary and lifestyle advice
2. standardised versus personalised dietary and lifestyle advice.

Methods

Design

A prospective, pragmatic, three-armed cluster randomised trial with an economic evaluation.

Health technologies being assessed

1. Prescription of laxatives, with class of laxative and dose at the discretion of the GP and patient (standard care control arm).
2. Standardised, non-personalised dietary and lifestyle advice.
3. Personalised dietary and lifestyle advice, with reinforcement.

Setting

General practices in England and Scotland, UK.

Participants

People aged ≥ 55 years (lowered to 50 years during the course of the trial) with chronic constipation, living in private households. Participants were identified as those who had been prescribed laxatives three or more times in the previous 12 months, or with a recorded diagnosis of chronic functional constipation.

Outcome measures

The primary outcome was the constipation-specific Patient Assessment of Constipation-Symptoms (PAC-SYM)/Patient Assessment of Constipation-Quality of Life (PAC-QOL). Secondary outcomes comprised: European Quality of Life-5 Dimensions (EQ-5D), reported number of bowel movements per week; the presence/absence of the other Rome II criteria for constipation; and adverse effects of treatment; and relapse rates.

Intervention development

The content and mode of delivery of the two intervention arms was developed by working closely with patients and practice staff from two GP practices. The patient information underwent a series of revisions following extensive patient feedback using a range of cognitive interview techniques.

Results

Baseline data

The trial planned to recruit and retain 1425 patients from 57 practices (19 per arm); ultimately, 154 patients were recruited from 19 practices. Due to the low recruitment rates, we are not able to report the conventional trial findings. We report the baseline characteristics of our sample from data gathered from both the postal self-completion questionnaire and the face-to-face interview. These data suggest that our sample experienced very few symptoms of constipation (PAC-SYM – Frank

L, *et al.* Psychometric validation of a constipation symptom assessment questionnaire. *Scand J Gastroenterol* 1999;**34**:870–7) and the condition itself does not have a major impact upon their QoL (PAC-QOL – Marquis P, *et al.* Development and validation of patient assessment of constipation quality of life questionnaire. *Scand J Gastroenterol* 2005;**40**:540–51). The low level of symptoms of constipation is most likely explained by the fact that 90% of the sample had used a laxative in the previous week and thus were asymptomatic for constipation. Most people in our sample were satisfied with their laxatives in terms of the time they took to work and the effect they had on their stools. Levels of anxiety and depression were low in this group.

Fibre consumption can be classified as 'moderate' (Roe L, *et al.* Dietary intervention in primary care: validity of the DINE method for diet assessment. *Fam Pract* 1994;**11**:375–81). There was therefore scope for an intervention that focused on increasing dietary fibre to be effective. Characteristically in a sample of this age, average water consumption fell below the recommended guidelines**.**

Diary data

The daily diaries were analysed primarily in terms of overall response rate and item response rates. The diary was completed each day for a period of 6 months. The results show that the daily diary developed for the diet and LIFEstyle versus LAXatives in the management of chronic constipation in older people (LIFELAX) trial was an acceptable method of data collection for participants.

Economic data

With regard to the economic evaluation, all of the trial arms experienced a reduction in utility, as measured by EQ-5D. There was no statistical evidence to suggest that either the personalised intervention arm or the standardised intervention arm was associated with significant changes in utility at 3 months compared with the control arm. Data on related health-care costs show a cost saving of £13.34 for those in the personalised arm, compared with the control arm, and a smaller cost saving for the standardised arm. These savings primarily occurred because of reduced hospital costs, offset by a smaller increase in costs incurred through additional telephone consultations. As there was no significant change measured in utility, cost minimisation would suggest that the personalised arm would be the preferred course, as it produced the greatest cost savings. This finding is qualified by the fact that the statistically significant reduction in health-care costs was due to a relative small number of cases in this relatively small sample; confidence limits around all estimates are large.

Integrated qualitative process evaluation

Background

The randomised controlled trial (RCT) is the primary means by which clinically reliable knowledge and 'evidence' is constructed within the field of health technology assessment (HTA). The importance of the RCT lies not simply in its apparent methodological security, but in the social and political uses to which its results might be put. Evidence is a vital element of the politics of health care at the beginning of the twenty-first century: its production and application are politically contested both within the NHS and by specific interest groups, ranging from political parties to advocacy groups for particular groups of service users. Given the importance of the RCT in contemporary health care it is surprising that this crucial means of the social organisation and production of knowledge about health care has not been subject to sustained empirical attention in depth – but has instead been mainly the focus of macro-level analyses, such as that by Faulkner (Faulkner A. Strange bedfellows' in the laboratory of the NHS? An analysis of the new science of health technology assessment in the United Kingdom. In Elston MA, editor. *The sociology of medical science and technology*. Oxford: Blackwell; 1997. pp. 183–207). The process evaluation embedded within the LIFELAX RCT contributed toward addressing this gap, through the application of ethnographic research techniques to the empirical investigation of the social organisation, production, and effects, of the RCT in practice.

Objectives

The process evaluation addressed the following specific questions:

1. *Formation* How are ideas about the appropriateness of health technologies and their clinical applications formed and mobilised in practice; and how are the interests of consumers and other users defined and incorporated in the organisation of the trial?
2. *Integration* How are specific clinical and methodological problems within an RCT

identified and resolved within professional groups and networks; how is the trial integrated into the existing organisation of clinical service provision, and what professional and organisational dynamics are involved in this integration; and how is participation in the RCT negotiated and understood by subjects?

3. *Implementation* How is the production of results negotiated and organised within networks of researchers; how are its results mediated to the wider community and how is this negotiated and organised, both formally (through report writing and presentation); and, informally, how are the mechanisms and results of the trial understood by subjects?
4. *What lessons can be learned that will improve the organisation and conduct of HTA RCTs in the UK – and further afield?* This study has important implications for the organisation and conduct of HTA. It is important that its results can inform and develop both policy and practice.

Methods

Study group

Purposive sampling from three specific groups of participants in the trial: (1) project management and steering group ($n = 11$); (2) general practitioners (GPs), practice managers ($n = 6$) and nurses ($n = 9$) working to recruit and deliver patients to the trial and conduct the interventions; and (3) patients ($n = 23$) participating in the trial.

Data collection and analysis

A combination of qualitative research techniques were used, broadly following the precepts of Glaser and Strauss' (1967) model of constant comparison to develop first order analyses of the data. Throughout the contact period with each group a programme of semistructured interviews was undertaken. Some members of the trial team were interviewed iteratively across the life of the trial as new issues arose. All semistructured interviews were audio-taped with the respondent's consent, and transcripts formed the data subjected to formal analysis. The constant comparative method of qualitative analysis was carried out. Emerging themes were applied to the Normalisation Process Model (NPM) (May C. A rational model for assessing and evaluating complex interventions in health care. *BMC Health Serv Res* 2006;**6**:86).

Fieldwork commenced with initial mapping of the technical and social components of the trial. This mapping identified both the stakeholders and key structures of the system, from which a sample of both intervention situations and interviewees were chosen. Where observation was possible (e.g. at meetings or presentations), it involved the production of contemporaneous field notes from which analytic themes and categories were identified. It was important to observe routine and problematic applications of the trial, such as negotiations regarding the implementation of the protocol in busy primary care practices. Local documentary materials (e.g. protocols, correspondence, minutes of meetings, notices, leaflets, entries in newsletters) in which the trial was explained to professionals and subjects were analysed for comparison with themes emergent in the interview data, and with the wider literature concerning the particular form of intervention, and with HTA as a discrete field.

Results

The trial team followed the guidelines set out by the Research Management and Governance framework (RM&G – Central Services Agency, 2008) for clinical trials in the UK. However, certain milestones proved difficult to attain. In particular, the experience of the trial team was that RM&G guidelines were subject to localised, and sometimes inflexible, interpretation by governance bodies implicated in the research, whereas the Multi-Centre Research Ethics Committee (MREC) stipulations were also difficult to negotiate in practice. As an example, observation of the trial team revealed that they had significant difficulty in implementing the multicentre RCT when a shared understanding of what constituted 'risk to patients' was lacking across sites. A great deal of the trial team's resources were therefore spent in developing creative and workable solutions to emerging practical problems of implementation. As demonstrated by a growing number of reports in the literature (e.g. Wald DS. Bureaucracy of ethics applications. *BMJ* 2004;**329**:282–4), the LIFELAX trial was not alone in experiencing these difficulties.

The LIFELAX trial depended on cooperation between the trial team and key individuals from a number of external organisations. To facilitate administrative work, the trial manager actively identified key contacts and developed working relationships with them through a sequence of telephone calls and/or written communication. In this regard the trial relied heavily upon the 'social aptitude' of the trial manager and his tactful approach in requesting additional resources. Social skills are infrequently identified as a key component of a trial manager's repertoire, yet they proved to be pivotal in the development of the LIFELAX trial, despite its early closure.

In following the research brief to assess the cost-effectiveness of diet and lifestyle interventions for the treatment of chronic constipation, the trial team developed nurse training packages based on Behaviour Change Counselling (BCC) techniques. Despite the time, expertise and financial resources spent on these interventions, the feedback from the interviewed primary care staff was that chronic constipation was a comparatively low priority issue for general practices. The perspective of practice staff can be summarised in three key points:

1. Chronic constipation was regarded as being successfully managed via laxatives.
2. Patients with chronic constipation typically saw their GP or a community nurse, therefore the practice nurses viewed the issue of constipation management as falling outside their remit of work
3. Some practice nurses described the BCC approaches as part of their current skill set, and therefore reported that the training interventions had little practical benefit for their routine patterns of work.

In this respect, the trial was perceived by some staff as giving nurses additional work, for a condition of low priority, and offering an intervention that, at best, was seen as relatively elementary to professional nursing practice. The participants interviewed through the process evaluation struggled to articulate whether they had benefitted from taking part in the research, while most of those attending practices randomised to the BCC arm did not view their consultation as differing from a routine nurse-led interaction.

Recommendations for research

A number of issues regarding the development and implementation of RCTs have been identified through the conduct of the process evaluation. The problem of the trial's topic, setting and training packages may have been identified had a prior feasibility study been conducted. At the time of the LIFELAX trial the HTA programme did not fund pilot studies of this nature, although the HTA have now changed their policy in this regard. However, numerous system-wide problems – such as the changing RM&G guidelines and research briefs that did not match General Medical Services contracts – also taxed the capacity of the trial to be successful. Following the results of the process evaluation, and the input of several of the reviewers of this report, we suggest the following:

1. Improved means and methods of communication are required between governance bodies, MRECs and researchers regarding the best way to conduct RCTs that are ethically, methodologically and practically sound.
2. There is a need for a clear and consistent means of applying for RM&G approval across Primary Care Trusts.
3. There is a clear need for pilot studies prior to the design and implementation of HTA RCTs:
   i. Pilot studies should assess the feasibility of all aspects of the intended research but, specifically, ensure that the assumptions underpinning the study are correct. These assumptions may be multiple but should ensure that: (1) there is an identified need for a technological intervention; (2) the intended beneficiaries also perceive a need for intervention and are in equipoise between the proposed interventions and control; and (3) the definition of the need or problem is commensurate between researchers, users and beneficiaries.
   ii. Pilot studies should assess whether the interventions will enable the intended users and/or beneficiaries to achieve relevant goals (such as *disposal* of symptoms).
   iii. Pilot studies should assess whether the intended interventions fit within existing patterns of work, and where they do not, assess the likely disruption and acceptability to intended users.
   iv. Pilot studies designed to assess the feasibility of the research should be conducted prior to any significant investment in the development of an RCT.

Trial registration

This trial is registered as ISRCTN73881345.

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Publication

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NIHR Health Technology Assessment programme

The Health Technology Assessment (HTA) programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA programme then commissions the research by competitive tender.

Second, the HTA programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

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Reports are published in the HTA journal series if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 01/10/04. The contractual start date was in June 2003. The draft report began editorial review in October 2009 and was accepted for publication in February 2010. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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