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Outcomes guarantee for lipid-lowering drugs: results from a novel approach to risk sharing in primary care

STEPHEN CHAPMAN, ELLY REEVE, DAVID PRICE, GIRI RAJARATNAM, RICHARD NEARY

Abstract

An 'outcomes guarantee' was established between North Staffordshire Health Authority, North Staffordshire Hospital National Health Service (NHS) Trust, Parke-Davis (now Pfizer Ltd), and Keele University. The agreement was that if atorvastatin failed to reduce low-density lipoprotein cholesterol (LDL-C) to ≤ 3 mmol/L among a specified percentage of the patient population, Pfizer would reimburse the healthcare provider for wasted resources. An audit and intervention programme was developed, approval was obtained from the scientific merit and ethics committee and 27 practices were recruited from Central and North Stoke primary care groups. General practitioners were free to prescribe any statin. Any financial rebate was to be determined at the study end, based on the cost differential between different doses of atorvastatin. Of 1,408 patients identified as being at risk of heart disease, 877 were prescribed statins and 669 were still taking them on completion of the study. Of these, 402 patients met LDL-C targets. All patients whose dose was titrated according to the outcomes guarantee matrix achieved target, so no refund was due. An outcomes guarantee offers an open and transparent process to work with the pharmaceutical industry on an NHS agenda.

Key words: outcomes guarantee, risk sharing, statins, coronary heart disease.

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Department of Medicines Management, Keele University, Keele, Staffordshire, ST5 5BG.
Stephen Chapman, Professor of Prescribing Studies
Elly Reeve, Business Manager

82 Gravelly Bank, Lightwood, Stoke-on-Trent, ST3 7EF.
David Price, General Practitioner

North and South Stoke Primary Care Trusts, Heron House, Great Fenton Business Park, Grove Road, Stoke-on-Trent, ST4 4LX.
Giri Rajaratnam, Director of Public Health

University Hospital of North Staffordshire, Pathology Directorate, Central Pathology Laboratory, Hartshill Road, Stoke-on-Trent, ST4 7PA.
Richard Neary, Consultant in Medical Biochemistry

Correspondence to: Professor Stephen Chapman
(email: s.r.chapman@keele.ac.uk)

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Introduction

After changes in the organisation of the National Health Service (NHS), primary care organisations are now responsible for supporting general practitioners in the implementation of evidence-based medicine. This includes implementation of the recommendations and central guidance from the National Institute for Clinical Excellence (NICE) and those laid out in the government's National Service Framework (NSF) for coronary heart disease (CHD).[1,2] The challenge in primary care is to identify and monitor drug use in 'at-risk' populations. Routine prescribing data from the prescription pricing authority give information only on prescribing cost and volume,[3] so some form of audit is required.

The problem with audit is that it is resource-intensive, so primary care organisations have been looking at ways of involving all members of the healthcare team.[4] Historically, pharmaceutical companies have offered sponsored nurses to help with audit in areas of chronic disease, where this has been aligned with company objectives. An outcomes guarantee is a novel approach to company-sponsored audit. One benefit is that it directs audit activity to a healthcare organisation's agreed agenda and ensures that treatment is targeted to the highest-priority patients.

The cost pressures from increased drug use make it imperative for primary care organisations to ensure that drugs are targeted appropriately and used effectively. An outcomes guarantee provides a framework to achieve this. The sponsoring company underwrites the key benefit that it is claiming for its product – if the product does not perform according to its claims, then the company refunds the wasted resource.

Lipid-lowering therapy was chosen for the pilot project on the following grounds: high-priority treatment; objective and measurable outcome; rapid growth in prescribing and burden on healthcare resources; consensus on recommended practice and clear guidelines.[2,5-7]

The design of the outcomes guarantee matrix and the terms and conditions of supply have already been published.[8] This paper provides details of the structure of the audit and the results.

Materials and methods

After obtaining ethical approval, we sent letters to all 39 practices in the two North Staffordshire primary care groups (Central and North Stoke) that had agreed to participate, informing them of the project. They were asked to return a reply slip, indicating whether the individual practice wished to participate in the project. The letters, sent out in March 2000,

Table 1. Inclusion and exclusion criteria for the 'at risk' cohort

Inclusion	Exclusion
Already receiving a statin but not at target LDL cholesterol level, or no cholesterol measurement in past 12 months	Already receiving a statin and at target LDL cholesterol level
Secondary prevention patient not on a statin and not at LDL cholesterol target	Not receiving a statin but at LDL cholesterol target
Secondary prevention patient not on a statin and with no cholesterol measurement in past 12 months	

Key: LDL = low-density lipoprotein

were signed by representatives from the primary care groups, the health authority, and Keele University. Follow-up letters were sent out in April 2000 to non-responders in Central Stoke, at the primary care group's request.

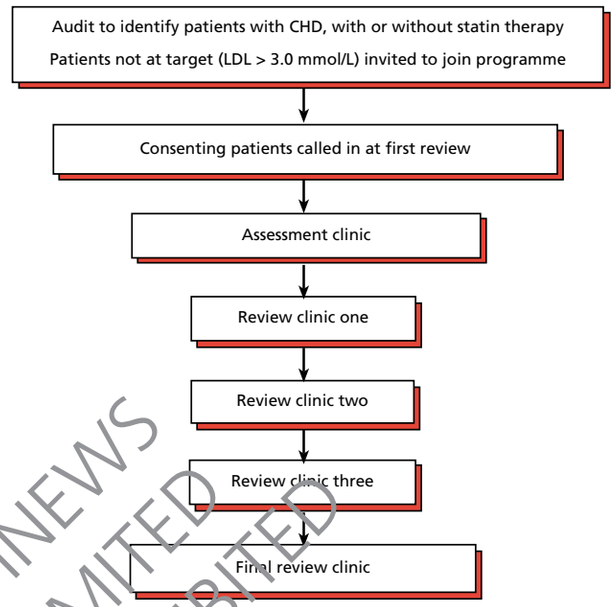
Two agency nurses were recruited, provided with materials and protocols, and trained in case finding and audit of patients at risk of cardiovascular disease. These nurses were responsible for gaining formal commitment from practices and holding introductory meetings. They then trained individual practice nurses or, in the case of single-handed practices with no practice nurse, took direct responsibility for implementation of the programme. After training, the practice nurses undertook case finding and audit of practice medical referrals to identify a cohort of at-risk patients who were invited to attend an 'at risk clinic'. The inclusion and exclusion criteria for this cohort are listed in table 1.

Patients who attended the nurse-led clinic were invited to participate in the programme of review clinics and were also asked to consent to data collection. Both consenting and non-consenting patients were able to participate in the quarterly clinics and final review (after 12 months), but only data from consenting patients were analysed.

At the clinics, nurses measured total and low density lipoprotein (LDL) cholesterol using a Cholestech™ machine, and patients were referred to their general practitioner for modifications to treatment or for assessment of other factors, such as high blood pressure. General practitioners remained free to prescribe the statin of their choice. Concordance rates were measured in order to assess whether the 20% adjustment for non-concordance, assumed within the atorvastatin guarantee matrix, was an over-or under-estimate. Nurses were guided by a semi-structured questionnaire on the data collection form to ask whether patients were taking the medicines as prescribed and whether they had taken at least six out of the seven tablets in the last week. This was used as a measure of concordance. The patient intervention flow is shown in figure 1.

Data from consenting patients were anonymised and coded and sent to Keele University for analysis. Interim reports on the status of the patients were fed back to the practices, and a final progress report indicated the number of at-risk patients who had been treated. The coded information was then analysed against the criteria of the outcomes guarantee matrix to determine whether a refund was due.[8] The percentage of patients on atorvastatin whose LDL cholesterol levels were at government targets was compared with the percentage guaranteed by the sponsor (Parke-Davis/Pfizer). If the actual percentage was lower than the guaranteed percentage, then the sponsor agreed to refund the cost of unsuccessful treatment to the primary care organisations.

Figure 1. Patient intervention flow



Key: CHD = coronary heart disease; LDL = low-density lipoprotein

Table 2. Patients participating in the study (n=1,408)

	Start of study	Dropped out	Did not attend	End of study
Pre-existing statin	503	54	70	379
New statin during study	375	20	21	334
Lifestyle advice only	530	123	80	327
Total	1,408	197	171	1,040

Results

Of the 39 practices that were contacted (representing a population of about 174,000 patients), 30 expressed an interest in participating (i.e., 77% of practices, representing a population of about 129,000). Three practices (7%) stated that they did not wish to participate and six (15%) did not respond. Central Stoke had higher rates of practice interest than North Stoke,

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Table 3a. Patients receiving a statin* during the study (n=878)

	Start of study	End, on statin	End, not on statin	Dropped out	Did not attend	Compliance rate
Pre-existing statin	503	362	17	54	70	72%
New statin during study	375	307	27	20	21	82%
Total	878	669	44	74	91	76%

* Patients could be on any statin, as directed by the GP

Table 3b. Patients never receiving a statin during the study (n=530)

	Start of study	Attended final clinic	At LDL target	Not at LDL target	Dropped out	Did not attend	Compliance rate
Lifestyle advice only	530	327	165	162	123	80	62%

Key: LDL = low-density lipoprotein

possibly because they had been actively involved in the development of the project and more proactive in the recruitment of practices: all 21 of the Central Stoke practices responded, and 19 (90%) expressed an interest in participating in the project.

Of the 30 practices that expressed an interest and were therefore invited to participate in the project, 27 practices started and 26 practices completed the project, representing a practice population of around 104,000.

From these 26 practices, some 1,408 patients attended the assessment clinic and consented to join the programme (see table 2). At this stage, 503 of these patients were taking a statin but had either not had a cholesterol measurement for 12 months or were not at target. The remaining 905 patients were not receiving a statin. Of these, 375 were prescribed a statin during the project. At the end of the project, 669 patients were taking statins (see table 3a), 327 did not receive statin treatment (see table 3b), and the remainder had dropped out of the project or did not attend the final review clinic.

Of the 669 patients who completed the project and were still taking a statin, 581 had both LDL and total cholesterol readings: of these, 402 (69%) met the targets specified in the NSF for CHD.

Of the 378 patients on atorvastatin, 162 were at target and entered into the matrix (table 4), while 76 were still having their dose titrated towards target. All of the atorvastatin-treated patients whose dose had been titrated up to 80 mg met target, so no refund was due under the terms of the guarantee. Table 5 shows the outcomes guarantee matrix and table 6 is the populated outcomes guarantee matrix.

Table 4. Patients on atorvastatin at final review clinic of the study

Patients on atorvastatin	Number
Total on atorvastatin at final clinic	378
In the outcomes guarantee matrix	162
Not in the matrix because not at target and statin dose being titrated	76
Not in the matrix because no adequate baseline data	114
Not in the matrix because no end LDL reading	25
Not in the matrix because baseline LDL > 6.5 mmol/L (treated to target with 10 mg statin)	1

Key: LDL = low-density lipoprotein

Discussion

It is important to emphasise that this was a project to test a process, not a comparative measure of the performance of statins. Structured audit data were collected and reported back to the practices. The outcomes guarantee project ensured that, within 26 practices, a total of 1,408 patients who were at risk of heart disease were brought in and reviewed with minimum disruption to the general practitioners' workload. The outcomes guarantee matrix, which was generated before the project was started, and the accompanying protocol, ensured that only patients agreed by all parties to have, or to be at high risk of, heart disease were called in for review. This has enabled the practices to meet relevant targets set out in the NSF for CHD: to have an up-to-date register of patients with heart disease, and to have a system closely aligned to the recently issued NICE guidelines on audit of patients after myocardial infarction.[1] An independent qualitative evaluation of the stakeholders' perceptions of the project is being reported separately.

Previous attempts at establishing risk management programmes have failed, for reasons including lack of interest from potential stakeholders and lack of definable markers of efficacy. The Department of Health recently initiated a shared-risk policy for β-interferon in the treatment of multiple sclerosis, raising awareness of the potential for such schemes. We believe that the present outcomes guarantee project was successful because we were able to generate widespread interest for the scheme and buy-in from stakeholders and, in targeting

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Table 5. Outcomes guarantee matrix for the study

	Baseline LDL cholesterol (mmol/L)							
	Mild 3.0–4.8		Moderate 4.8–5.6		Severe 5.6–6.0		Complex 6.0–6.5	
Atorvastatin dose	Predicted	Guaranteed*	Predicted	Guaranteed	Predicted	Guaranteed	Predicted	Guaranteed
10 mg	89	71	36	29	14	11	8	7
20 mg	98	78	69	55	37	30	23	18
40 mg	99	79	81	65	60	48	45	37
80 mg	100	80	90	72	73	58	60	48

*The 'guaranteed' figure is the predicted figure adjusted by a pre-agreed figure of 20% to allow for patient non-concordance.

For example, the matrix predicted that 89% of patients classified as having a mild baseline LDL cholesterol should achieve the required reduction in LDL cholesterol if they took atorvastatin 10 mg. This figure is then adjusted for non-concordance by a pre-agreed figure of 20%, giving a guaranteed figure of 71% for the matrix

Table 6. Populated outcomes guarantee matrix for the study

	Baseline LDL cholesterol (mmol/L)											
	Mild 3.0–4.8 (n=144)			Moderate 4.8–5.6 (n=14)			Severe 5.6–6.0 (n=2)			Complex 6.0–6.5 (n=2)		
Atorvastatin dose	Predicted	Guaranteed	Actual	Predicted	Guaranteed	Actual	Predicted	Guaranteed	Actual	Predicted	Guaranteed	Actual
10 mg	129	102	127	5	4	9	0	0	2	0	0	2
20 mg	142	113	141	9	7	13	0	0		0	0	
40 mg	143	114	143	11	9	14	1	0		0	0	
80 mg	145	116	144	12	10	1	1	1		1	0	

n=number of patients entered into matrix

The 162 patients included in table 6 are those eligible for the outcomes guarantee because they have had recorded baseline data. Of the 144 patients classified as mild, we guaranteed that 71% (102 patients) would reach target on a 10 mg dose after adjusting for concordance. The actual number who achieved target at 10 mg was 127

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cholesterol management, we had an objective surrogate measure of health outcome that was easily monitored using near-patient testing. The fact that lipid-lowering interventions are congruent with national policy and have a strong evidence base probably made it considerably easier to recruit and retain general practices on this programme. We believe that the informed consent process and the structured interview time with the nurse at each clinic had a beneficial effect, ensuring that patients had a full understanding of risks and benefits and helping the nurses understand the reasons why non-concordant patients were not taking their medicines as prescribed.

Even with strong reasons for participating, patients did not always attend the clinics – in the case of the elderly, patients became housebound, were admitted to hospital or suffered non-cardiac illness such as severe chest infections over the winter (see tables 7 and 8). This reflects the reality of general practice and shows how, even with intensive resources, NSF and new GP contract targets can still be challenging. Nonetheless, of the 878 patients treated with a statin, 669 were still taking them at the final review clinic, giving a compliance rate of 76%. If the pilot were replicated, we suggest that participating primary care organisations place high emphasis on the importance of patient follow-up.

According to criteria applied by the nurses, 95% of the patients who were taking statins at the end of the project were concordant with their medication. For the cohort of patients who were eligible to be included in the atorvastatin matrix, the actual reported non-concordance rate was 4%, compared with a prospectively assumed non-concordance rate of 20%.

Our project has demonstrated that it is possible for academia and the NHS to have an open and transparent relationship with a commercial partner, and to identify and treat at-risk patients with little effect on general practitioner workload. Although our project focused on lipid-lowering interventions, and on one lipid-lowering agent in particular (atorvastatin), it is tempting to wonder whether the concept could be applied more widely, especially for drugs or devices that are new to the market.

Immediately after launch, there is most shared risk between the purchaser and the manufacturing company – the drug has been tested only on a carefully selected cohort of patients in randomised clinical trials, usually in a hospital setting; as soon as the drug is available in general practice, the cohort of patients that might be treated expands massively. Disseminating the drug within the terms of an outcomes guarantee means that the drug is more likely to be targeted to the patients who are likely to ben-

Table 7. Reasons for patients' non-attendance at final clinic

Reason	Number
On holiday	25
Unwell	30
DNA	76
No reason recorded	40
Total	171

Table 8. Reasons for patients dropping out of project

Reason	Number
Adverse event	2
Housebound	20
Hospital	40
Left the practice	50
Refused	24
Nursing home	4
Died	40
Joined SEARCH trial	12
Unwell	1
Unknown	40
Total	197

Key: SEARCH = Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine

efit most, such as those with characteristics most similar to the participants in the clinical trials. Thus, both the healthcare provider and the pharmaceutical company gain by getting the drug to the patients who benefit most.

In reality, not all drugs are likely to be eligible or appropriate for an outcomes guarantee arrangement; the prerequisites for success include the following:

- A clear and objective proxy marker of health gain
- The ability to measure this marker simply, preferably using near-patient testing
- A clearly identified health need in the local population
- A strong evidence base for the drug's use
- Congruence with local priorities and strategies.

While prescribers remain free to prescribe the drug of their choice, there are no particular implications for the pharmaceutical price regulation scheme – the unit price of the drug purchased has not changed, and the company resources to support it are similar to those that would be used for other marketing activities, such as sponsored nurse audits.

Outcomes guarantee is in essence a simple concept, effectively marshalling commercial resource to a health service agenda while being open and transparent in advance. Thus, it negates the ambiguity that often arises when companies fund primary care projects. This appears to us to be a more intelligent way of working with the industry for mutual benefit. The alternatives are to capitulate to commercial programmes without strategic input or to take an ostrich-like approach, pretend that they are not there and forego the potential benefits. Neither of these options appears tenable in the 21st century.

Key messages

- Cost pressures from increased drug use make it imperative for primary care organisations to ensure that drugs are targeted appropriately and used effectively
- An outcomes guarantee arrangement with a pharmaceutical company ensures a refund to the NHS if the drug does not work under defined circumstances. This helps reduce financial risk
- An outcome guarantee assists healthcare organisations in undertaking necessary audits and ensures that treatment is targeted at the highest-priority patients. In this pilot project, 1,408 patients who were at risk of heart disease were identified and reviewed with minimal disruption to the general practitioners' workload
- In patients receiving atorvastatin under the terms of the outcomes guarantee, treatment outperformed predictions, so no refund was needed, because resource was not wasted

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Acknowledgements/conflict of interest

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