Does point-of-care testing lead to the same or better adherence to medication? A randomised controlled trial: the PoCT in General Practice Trial

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ABSTRACT

Objective: To compare the clinical effectiveness of point-of-care testing (PoCT) with that of pathology laboratory testing, as measured by patients' adherence to medication.

Design: Multicentre, cluster randomised controlled trial using non-inferiority analysis. Medication adherence was assessed twice (in April 2006 and January 2007) by a self-administered questionnaire using the five-item Medication Adherence Report Scale (MARS-5).

Setting: 53 Australian general practices in urban, rural and remote areas across three Australian states, September 2005 to February 2007.

Participants: 4968 patients with established type 1 or type 2 diabetes, established hyperlipidaemia, or requiring anticoagulant therapy were recruited to the study. Of these, 4381 were included in the analysis (2585 in the intervention group and 1796 in the control group).

Intervention: The intervention group (3010 patients in 30 practices) had blood and urine samples tested using PoCT devices within their general practices. The control group (1958 patients in 23 practices) had samples tested by their usual pathology laboratories.

Main outcome measures: The proportion of questionnaire responses indicating medication adherence overall and by condition.

Results: PoCT was non-inferior to pathology laboratory testing in relation to the proportion of questionnaire responses indicating medication adherence (39.3% v 37.0%) (difference, 2.3% [90% CL, –0.1%, 4.6%]; $P < 0.001$). Non-inferiority could also be concluded separately for patients with diabetes (38.5% v 37.3%) (difference, 1.2% [90% CL, –2.5%, 5.0%]; $P = 0.01$); hyperlipidaemia (38.3% v 37.3%) (difference, 1.0% [90% CL, –1.5%, 3.5%]; $P < 0.001$) and for patients requiring anticoagulant therapy (44.5% v 41.4%) (difference, 3.1% [90% CL, –2.1%, 8.3%]; $P = 0.01$).

Conclusions: Having access to immediate test results through PoCT is associated with the same or better medication adherence compared with having test results provided by a pathology laboratory. PoCT used in general practice can provide general practitioners and patients with timely and complete clinical information, facilitating important self-management behaviours such as medication adherence.

Trial registration: Australian Clinical Trials Registry ACTRN 12605000272695.

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The prevalence of chronic disease, including diabetes, cardiovascular disease, cancer and obesity, is increasing worldwide. The World Health Organization has estimated that, by 2020, chronic disease will be responsible for three-quarters of all deaths.[1]

Chronic disease is a common presentation in general practice. General practitioners play a key role in implementing management and preventing complications of disease. However, improvements in health outcomes will not be achieved unless patients consistently act upon medical advice.

Improving long-term medication adherence is crucial to improving chronic disease outcomes. The overwhelming evidence from large-scale randomised controlled trials (RCTs) is that medication adherence is suboptimal[2-5] and is influenced by many variables, including number and cost of medications, duration of disease, age, and patient attitudes, beliefs and perceptions relating to illness.[6,7] Factors that positively influence patients' outcomes include active patient involvement in decision-making processes affecting their care, good communication, and providing patients with education and quality information about their disease.[8,9]

Point-of-care testing (PoCT) produces an immediate test result, thus enabling immediate decisions and discussion about patient treatment, and has the potential to engage patients in their own care. A systematic review of PoCT by Delaney and colleagues suggested that PoCT could be valuable in managing patients with chronic conditions in general practice.[10] The intention would be for PoCT to provide an alternative method of testing, rather than to replace traditional pathology laboratory testing, so it is essential for GPs to be confident that PoCT would not have a negative effect on clinical outcomes, including medication adherence. Our aim in this trial was to determine whether patients' medication adherence was non-inferior (the same or better) when PoCT was used compared to when pathology laboratory testing was used.

METHODS

Study design

The PoCT in General Practice Trial was an Australian Government-funded, multicentre, cluster RCT comparing PoCT with pathology laboratory testing. The purpose of the trial was to determine the safety, clinical effectiveness, cost-effectiveness and satisfactoriness of PoCT in a general practice setting. The trial was designed to evaluate the impact of PoCT under "real-world" conditions rather than to measure efficacy and did not specify how practices should integrate PoCT. Thus, practices variously integrated it into existing or new mini-clinics or, more commonly, into the consultation process.

Setting and participants

The relevant criteria for reporting of RCTs and patient baseline characteristics for the trial have been described elsewhere.[11] Briefly, the trial was conducted over an 18-month period, from September 2005 to February 2007. Fifty-eight practices were recruited from three Australian states. Random allocation to the intervention or control group was at the practice level (using randomly

permuted blocks of size 2, 4 and 6), and was stratified by geographical location (urban, rural or remote). Although 32 practices were originally allocated to the intervention group and 26 to the control group, five practices withdrew, leaving 30 practices in the intervention group (8 urban, 9 rural, 13 remote) and 23 practices in the control group (9 urban, 6 rural, 8 remote). Patients in these practices were eligible to participate if they were being managed for established type 1 or type 2 diabetes or for established hyperlipidaemia or required anticoagulant therapy. Patients could have one or more of these conditions. Eligible patients were invited to participate, and a total of 4968 patients were recruited: 3010 in the intervention group and 1958 in the control group. The median number of patients recruited per practice was 84 (range, 11–202).

Testing

Patients in the intervention group had their pathology testing for glycated haemoglobin (HbA_{1c}), urine albumin, albumin–creatinine ratio, blood lipids (total cholesterol, triglycerides and high-density lipoprotein cholesterol) or international normalised ratio (INR) performed using PoCT devices within the practice. Each practice in the intervention group was provided with a CoaguChek S analyser (Roche Diagnostics Australia, Sydney, NSW) to measure INRs; a DCA 2000 analyser (Siemens HealthCare Diagnostics, Melbourne, VIC) to measure HbA_{1c} levels, urine albumin levels and albumin–creatinine ratios; and a Cholestech LDX analyser (Point of Care Diagnostics, Sydney, NSW) to measure blood lipid levels. Practice staff who undertook PoCT were trained and certified. Intervention practices were required to participate in a quality management program involving an accreditation process as well as internal quality control and external quality assurance programs to monitor the analytical performance of the devices.

For patients in the control arm, the same tests were performed using blood samples taken by venepuncture and analysed by a pathology laboratory. The median distance between a practice and its pathology laboratory was 12 kilometres, with distances being greatest for practices in remote areas. All pathology laboratories involved in the trial participated in their own external quality assurance programs and were accredited by the National Association of Testing Authorities.

Measures

To assess medication adherence, a self-administered questionnaire was sent to patients twice during the trial (in April 2006 and January 2007).

Medication adherence was measured using a validated scale, the five-item Medication Adherence Report Scale (MARS-5).[12] The MARS-5 asks participants to indicate the frequency ("always", "often", "sometimes", "rarely" or "never") with which they engage in five components of non-adherent behaviour. Scores for each of the five items are combined to give a total score ranging from 5 to 25, with higher scores indicating higher levels of adherence. Since 1996, the MARS has been used in studies of a variety of illnesses (such as diabetes[13] and hypercholesterolaemia[4]) and in several countries, including Australia.[14]

Scoring of the MARS-5 questionnaire

The MARS-5 scores were strongly negatively skewed (median score, 24; interquartile range, 23–25), with 38.2% of all patients achieving the maximum score of 25 (ie, "never" engaged in any of the five components of non-adherent behaviour). Therefore, we decided to dichotomise the data for the analysis: a MARS-5 score of 25 was considered adherent and any score below 25 was considered non-adherent. This decision was also based on research showing that low adherence is suggested if one or more doses are missed and that if patients admit to missing medication they will overestimate the actual rate of adherence.[15,16] The outcome was defined for each questionnaire in which all five MARS-5 questions were completed. Hence, each patient could have up to two scores corresponding to the two questionnaires disseminated. The nature of missing data was investigated and judged to be unlikely to bias the results.

Statistical analysis

The data were analysed using mixed-model analysis of variance, with adjustment for age at consent and sex, and allowance for clustering at both the practice and patient levels. Statistical inference was based on the normal approximation to the binomial distribution. Statistical significance was assessed at the 0.05 level using a one-sided test for non-inferiority, and results are presented as 90% two-sided confidence intervals[17] rather than the usual 95% confidence intervals. (In a non-inferiority analysis, only the lower limit of the confidence interval is relevant. Use of a two-sided 90% confidence interval means we can be 95% confident that the true difference lies above the lower limit.) The non-inferiority margin was set at 10% of the control-group estimate, indicating that PoCT would be considered non-inferior to pathology laboratory testing if we could be 95% confident that the proportion of adherent responses in the intervention group was no more than 10% lower than the proportion in the control group. The non-inferiority margin was determined a priori by an expert clinical group.

The analysis was repeated to test for a questionnaire effect (first or second questionnaire) or a geographical location effect (urban, rural or remote). We also tested for any interaction between treatment group and questionnaire/geographic location for evidence of effect modification by questionnaire/geographic location. Sensitivity analyses were performed to determine whether choosing a different cut-off score for dichotomising the MARS-5 scores or analysing the data using an identity binomial generalised estimating equation with allowance for clustering at the practice level altered the conclusions. Analyses were carried out using SAS software, version 9.1.3 (SAS, Cary, NC, USA).

Ethics approval and registration

The trial was approved by five independent Australian human research ethics committees and registered with the Australian Clinical Trials Registry (ACTRN 12605 000272695).

RESULTS

Participants and response rate

Of the 4968 patients participating in the trial, 4732 were sent the first questionnaire and 4543 the second questionnaire. Questionnaires were not sent to all trial patients for a variety of reasons, including practice/patient withdrawal, death or relocation. A high response rate was achieved for both the first (94.1%) and second (93.4%) questionnaires. Eighty-six per cent of intervention patients and 90% of control patients completed both questionnaires. Statistical analysis of self-reported medication adherence was based on responses from 4381 patients (2585 intervention and 1796 control patients) who completed all five questions in the MARS-5 in one questionnaire (829 patients) or in both questionnaires (3552 patients). Baseline characteristics of these patients are shown in Box 1.

1 Baseline characteristics of patients included in the statistical analysis of self-reported medication adherence*

Characteristic	Intervention ($n = 2585$)	Control ($n = 1796$)	Total ($n = 4381$)
Age group (years)			
18–39	31 (1.2%)	18 (1.0%)	49 (1.1%)
40–49	151 (5.8%)	103 (5.7%)	254 (5.8%)
50–59	492 (19.0%)	302 (16.8%)	794 (18.1%)
60–69	903 (34.9%)	569 (31.7%)	1472 (33.6%)
70–79	759 (29.4%)	625 (34.8%)	1384 (31.6%)
⩾ 80	249 (9.6%)	179 (10.0%)	428 (9.8%)
Median age (years) (IQR)	66.0 (59.0–74.0)	68.0 (60.0–75.0)	67.0 (59.0–75.0)
Male	1408 (54.5%)	930 (51.8%)	2338 (53.4%)
Condition†			
Taking anticoagulant therapy	494 (19.1%)	340 (18.9%)	834 (19.0%)
Established diabetes	1039 (40.2%)	706 (39.3%)	1745 (39.8%)
Established hyperlipidaemia	2055 (79.5%)	1354 (75.4%)	3409 (77.8%)

IQR = interquartile range. * Figures are number (%) of participants, except where otherwise specified. † Some patients had more than one condition. ◆

2 Medication adherence (proportion of patients indicating that they never engage in non-adherent behaviour), by MARS-5 statement, questionnaire and treatment group

	Answered "never" on first questionnaire		Answered "never" on second questionnaire	
MARS-5 statement	Intervention ($n = 2408$)	Control ($n = 1673$)	Intervention ($n = 2254$)	Control ($n = 1598$)
I forget to take them	45.1%	43.2%	42.3%	41.8%
I alter the dose	89.3%	86.6%	87.5%	86.7%
I stop taking them for a while	88.7%	87.6%	89.4%	88.3%
I decide to miss out a dose	87.9%	86.6%	87.5%	87.3%
I take less than instructed	91.7%	90.0%	91.7%	90.5%

MARS-5 = Five-item Medication Adherence Report Scale. ◆

3 Medication adherence (proportion of patients indicating that they never engage in non-adherent behaviour), by condition and treatment group

Condition	Intervention	Control	Difference (90% CL)	Non-inferiority margin	*P*
Taking anticoagulant therapy	44.5%	41.4%	3.1% (–2.1%, 8.3%)	–4.1%	0.01
Established diabetes	38.5%	37.3%	1.2% (–2.5%, 5.0%)	–3.7%	0.01
Established hyperlipidaemia	38.3%	37.3%	1.0% (–1.5%, 3.5%)	–3.7%	< 0.001

Self-reported medication adherence

Descriptive analysis of each item in the MARS-5 questionnaire showed that the intervention group was more adherent than the control group (Box 2). In both groups, over half of all patients reported forgetting to take their medications to some degree, and 10%–12% of patients reported some intentional non-adherence. These findings were consistent across both questionnaires.

The proportion of MARS-5 questionnaire respondents who indicated that they adhered to medication was higher in the intervention group (39.3%) than the control group (37.0%) (difference, 2.3% [90% CL, –0.1%, 4.6%]; SE, 1.4). The lower limit of the 90% confidence interval was greater than the non-inferiority margin (–3.7%), indicating that PoCT was non-inferior to pathology laboratory testing ($P < 0.001$). There was no evidence to suggest that the effect of treatment varied between the first and second questionnaires ($P = 0.76$) or between geographic locations ($P = 0.16$). Similar results were obtained using an identity binomial generalised estimating equation or a different cut-off point for dichotomising the MARS-5 scores.

Examining each condition separately, PoCT was shown to be non-inferior to pathology laboratory testing for patients with diabetes ($P = 0.01$) or hyperlipidaemia ($P < 0.001$) and for patients requiring anticoagulant therapy ($P = 0.01$) (Box 3).

DISCUSSION

Our study provides evidence that PoCT is non-inferior to pathology laboratory testing in relation to medication adherence, both overall and for each condition studied. Although the observed difference in medication adherence between the intervention and control groups (2.3%) was not large, even small improvements can be beneficial, given that low adherence to medication compromises the effectiveness of treatment, at considerable cost to patients and the health care system. Our results suggest that using PoCT may lead, at worst, to a 0.1% reduction in medication adherence and, at best, to a 4.6% improvement.

Descriptive analysis of each MARS-5 statement showed that over half of all patients forgot to take their medicines to some degree and over 10% of patients reported some intentional non-adherence. A high level of non-adherence has been observed consistently in other studies and is not unique to our study. A systematic review by Kripalani and colleagues reported that an estimated 30%–50% of patients fail to take medications as prescribed.[18]

In our study, patients requiring anticoagulant therapy reported a higher level of medication adherence than patients with diabetes or hyperlipidaemia. The difference in adherence rates may be related to the consequences of missing medication. The health consequences of non-adherence are likely to be more severe, and even life-threatening, for patients receiving anticoagulant therapy compared with patients with diabetes or hyperlipidaemia.

As our results form part of the larger trial, it is important to discuss them in relation to trial outcomes reported elsewhere[19,20] to gain a clearer picture of the impact of PoCT on the management of chronic conditions. PoCT was shown to be non-inferior to pathology laboratory testing in relation to both the proportion of patients and the proportion of tests within therapeutic range for most tests considered.[19] The trial also demonstrated that PoCT could have significant benefits in terms of patient satisfaction. Patients in the intervention group reported that their relationship with their GP had strengthened, that having immediate test results was beneficial, and that they were more motivated to look after themselves,[20] which is evidenced in their adherence to medication.

To date, there has been no quantitative research investigating whether PoCT influences patient medication adherence compared with pathology laboratory testing. However, a qualitative study by Brown and colleagues assessing the perceptions of patients and health professionals regarding the impact of PoCT on diabetes management revealed that both groups believed that PoCT assisted in adherence with disease management and that it supported shared decision making.[21] Research by Shephard investigating whether PoCT was effective in improving clinical outcomes for Aboriginal patients with diabetes showed that 93% of patients felt that regular PoCT encouraged them to look after their health better.[22] These studies endorse our trial findings and concur with other research showing that a strong relationship between patient and medical practitioner results in better medication adherence.[23]

Currently, management of patients with chronic disease is fragmented. In most circumstances, the GP does not have all the information required to make informed management decisions in a single consultation. In an investigation of GP attitudes towards facilitating self-management of chronic disease, Blakeman and colleagues found that although GPs believed in the importance of involving patients in their own care, they perceived the organisation of the system to be a barrier to successfully implementing such care.[24] A model of care that includes PoCT provides GPs with complete data and the opportunity to discuss test results and disease management at a time when it is uppermost in their minds.

It may be argued that outcomes similar to those reported in our study could be achieved by rearranging workflow so that patients had laboratory tests before the GP consultation. However, given the high proportion of patients who forget appointments (about a third of patients in one study[25]), we suspect that this may not be the case. Missed health care appointments, including pathology laboratory visits, can compromise patient care. PoCT embraces a new way of delivering health care, as it not only provides GPs with virtually instantaneous test results required for treatment decisions but also removes an important barrier to adherence by offering patients the convenience of a single visit. PoCT also has the potential to increase compliance with disease management by minimising loss to follow-up. Acceptable, cost-effective interventions that foster and support the patient–GP partnership are a worthwhile investment for averting preventable morbidity and mortality.

A limitation of our study was the fact that patient self-report is susceptible to overestimation of adherence. However, no single measure is seen as the gold standard, and a combination of methods is thought to be the most effective way of estimating adherence.[26] A multifaceted approach was outside the scope of the trial. A second limitation was that the numbers of patients in the intervention and control groups differed substantially (3010 v 1958). This was most likely due to differential motivation to participate between groups, with eligible patients in the intervention practices more likely to give consent because of the perceived value of having access to a new method of testing. Nevertheless, the sample size for the control group was still large, making this one of the largest studies to date comparing PoCT with pathology laboratory testing. Strengths of our study were that it was a multicentre RCT and that response rates to the questionnaires were very high.

In conclusion, the trial provides evidence that PoCT results in the same or better medication adherence compared with traditional pathology laboratory testing. Providing a PoCT model of care to support chronic disease management in general practice can help GPs to involve patients in self-management. This is crucial to achieving effective treatment and quality health-related outcomes.

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COMPETING INTERESTS

None identified.

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REFERENCES

1 World Health Organization. Diet, nutrition and the prevention of chronic diseases. Geneva: WHO, 2003.
2 Cramer J. A systematic review of adherence with medications for diabetes. *Diabetes Care* 2004; 27: 1218-1224.
3 Huser M, Evans T, Berger V. Medication adherence trends with statins. *Adv Ther* 2005; 22: 163-171.
4 Senior V, Marteau T, Weinman J; Genetic Risk Assessment for FH Trial (GRAFT) Study Group. Self-reported adherence to cholesterol-lowering medication in patients with familial hypercholesterolaemia: the role of illness perceptions. *Cardiovasc Drugs Ther* 2004; 18: 475-481.
5 Jackevicius C, Mamdani M, Tu J. Adherence with statin therapy in elderly patients with and without acute coronary syndromes. *JAMA* 2002; 288: 462-467.
6 Sabaté E. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization, 2003.
7 Horne R, Weinman J, Barber N, et al. Concordance, adherence and compliance in medicine taking. London: National Co-ordinating Centre for NHS Service Delivery and Organisation Research and Development, 2005. http://www.sdo.nihr.ac.uk/files/project/76-final-report.pdf (accessed Sep 2009).
8 Tabrizi J, Wilson A, Coyne E, O'Rourke P. Clients' perspective on service quality for type 2 diabetes in Australia. *Aust N Z J Public Health* 2007; 31: 511-515.

9 Kaplan S, Greenfield S, Ware JE Jr. Assessing the effects of physician–patient interactions on the outcomes of chronic disease. *Med Care* 1989; 27 (3 Suppl): S110-S127.
10 Delaney B, Hyde C, McManus R, et al. Systematic review of near patient test evaluations in primary care. *BMJ* 1999; 319: 824-827.
11 Laurence C, Gialamas A, Yelland L, et al. A pragmatic cluster randomised controlled trial to evaluate the safety, clinical effectiveness, cost effectiveness and satisfaction with point of care testing in a general practice setting — rationale, design and baseline characteristics. *Trials* 2008; 9: 50.
12 Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999; 47: 555-567.
13 Farmer A, Kinmonth AL, Sutton S. Measuring beliefs about taking hypoglycaemic medication among people with Type 2 diabetes. *Diabet Med* 2006; 23: 265-270.
14 George J, Kong D, Thoman R, Stewart K. Factors associated with medication nonadherence in patients with COPD. *Chest* 2005; 128: 3198-3204.
15 Haynes R, McDonald H, Garg A. Helping patients follow prescribed treatment: clinical applications. *JAMA* 2002; 288: 2880-2883.
16 Stephenson B, Rowe B, Haynes R, et al. The rational clinical examination: is this patient taking the treatment as prescribed? *JAMA* 1993; 269: 2779-2781.
17 Piaggio G, Elbourne D, Altman D, et al; CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. *JAMA* 2006; 295: 1152-1160.
18 Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. *Arch Intern Med* 2007; 167: 540-550.
19 Bubner TK, Laurence CO, Gialamas A, et al. Effectiveness of point-of-care testing for therapeutic control of chronic conditions: results from the PoCT in General Practice Trial. *Med J Aust* 2009; 190: 624-626.
20 Laurence C, Gialamas A, Bubner T, et al. Patient satisfaction with point of care testing in general practice. *Br J Gen Pract* 2009. In press.
21 Brown J, Harris S, Webster-Bogaert S, Porter S. Point-of-care testing in diabetes management: what role does it play? *Diabetes Spectr* 2004; 17: 244-248.
22 Shephard M. Cultural and clinical effectiveness of the "QAAMS" point-of-care testing model for diabetes management in Australian Aboriginal medical services. *Clin Biochem Rev* 2006; 27: 161-170.
23 Kerse N, Buetow S, Mainous A, et al. Physician–patient relationship and medication compliance: a primary care investigation. *Ann Fam Med* 2004; 2: 455-461.
24 Blakeman T, Macdonald W, Bower P, et al. A qualitative study of GPs' attitudes to self-management of chronic disease. *Br J Gen Pract* 2006; 56: 407-414.
25 Zailinawati A, Ng C, Nik-Sherina H. Why do patients with chronic illness fail to keep their appointments? A telephone interview. *Asia Pac J Public Health* 2006; 18: 10-15.
26 Farmer K. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clin Ther* 1999; 21: 1074-1090.

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