

Specialist Nurse–Led Intervention to Treat and Control Hypertension and Hyperlipidemia in Diabetes (SPLINT)

A randomized controlled trial

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achieved, then such proven methods for delivering care must be adopted.

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OBJECTIVE — To determine the effectiveness of specialist nurse–led clinics for hypertension and hyperlipidemia provided for diabetic patients receiving hospital-based care.

RESEARCH DESIGN AND METHODS — This study was a randomized controlled implementation trial at Hope Hospital, Salford, U.K. The subjects consisted of 1,407 subjects presenting for annual review with raised blood pressure ($\geq 140/80$ mmHg), raised total cholesterol (≥ 5.0 mmol/l), or both. Individuals with diabetes were randomized to usual care or usual care with subsequent invitation to attend specialist nurse–led clinics. Nurses provided clinics for participants, with attendance every 4–6 weeks, until targets were achieved. Lifestyle advice and titration of drug therapies were provided according to the locally agreed upon guidelines. Patients with both conditions were eligible for enrollment in either or both clinics. At subsequent annual review, blood pressure and total cholesterol values were obtained from the Salford electronic diabetes register. Data relating to deaths were obtained from the national strategic tracing service. The primary outcome was the odds ratio of achieving targets in hypertension and hyperlipidemia, attributable to the specialist nurse–led intervention.

RESULTS — Overall, specialist nurse–led clinics were associated with a significant improvement in patients achieving the target after 1 year (odds ratio [OR] 1.37 [95% CI 1.11–1.69], $P = 0.003$). This primary analysis revealed a borderline difference in effect between the two types of clinics (test for interaction between groups: $P = 0.06$). Secondary analysis, consistent with the prior beliefs of the health care professionals involved, suggested that targets were achieved more frequently in patients enrolled in the specialist nurse–led clinic for hyperlipidemia (OR 1.69 [1.25–2.29], $P = 0.0007$) than for hypertension (OR 1.14 [0.86–1.51], $P = 0.37$). Intervention (enrolled to either or both clinics) was associated with a reduction in all-cause mortality (OR 0.55 [0.32–0.92], $P = 0.02$).

CONCLUSIONS — This study provides good evidence to support the use of specialist nurse–led clinics as an effective adjunct to hospital-based care of patients with diabetes. If the standards of care recommended in the National Service Framework for Diabetes are to be

Clinicians' awareness and application of the best evidence available for the treatment of patients is an important facet of quality assurance in health care (1). Important findings from research do not automatically translate into clinical practice. Consequently, the need to understand methods of implementation has been recognized (2,3). Existing evidence of the effectiveness and cost-effectiveness of an intervention, alongside evidence of its suboptimal use, provides the rationale for implementation research to establish whether worthwhile behavioral change can be achieved (4).

Effective blood pressure (BP) control reduces the risk of macro- and microvascular complications in diabetes (5,6) and appears to be cost-effective (7). Similarly, lipid-lowering therapy has recently been shown to be effective, with trial-based evidence of cost-effectiveness to follow and further research due (8,9). Indeed, the standards for care in the National Service Framework for diabetes are based on this evidence (10).

Salford operates a district-wide electronic diabetes register (EDR), recording details of all patients with diabetes, including type of diabetes, care provided (general practitioner or shared care [shared care being where diabetes care is provided both by the general practitioner and the Hope Hospital for the patient's annual diabetes review]), presence of diabetes-related complications, and annual records of BP and glycemic (HbA_{1c}) and lipid control (10). For 1997, the EDR provides data on a total of 5,872 patients, with 3,365 (57%) patients registered for shared care at Hope Hospital. At evaluation, 67% of these subjects recorded either diastolic BP ≥ 80 mmHg or systolic

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Abbreviations: BP, blood pressure; EDR, electronic diabetes register; NHS, National Health Service.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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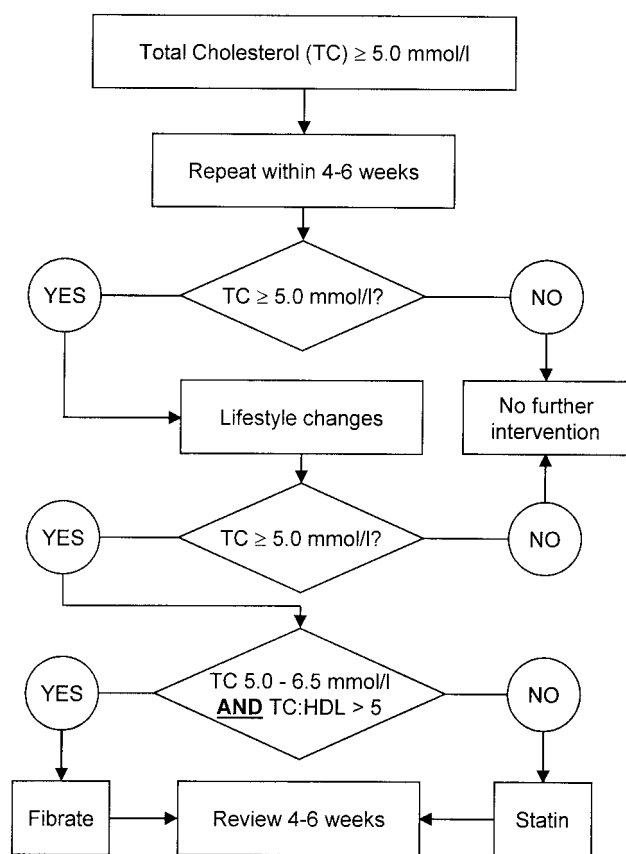


Figure 1—Salford guideline for lipid control.

BP ≥ 140 mmHg, and 54% recorded total cholesterol ≥ 5.0 mmol/l. Diabetes care is designed to minimize the development of complications by optimizing metabolic control using lifestyle and medication. These recommendations are sent to the patient and his or her general practitioner, who adjusts medications according to results, aiming for a BP $< 140/80$ mmHg and a total cholesterol of < 5.0 mmol/l in accordance with the district guidelines.

RESEARCH DESIGN AND METHODS

Protocol

The subjects of the study were all receiving shared care, i.e., their diabetes care was being provided by both their general practitioner and the Hope Hospital for their annual diabetes review. During their annual review, subjects presenting with raised systolic (≥ 140 mmHg) or diastolic (≥ 80 mmHg) BP were randomized to the specialist nurse–led hypertension clinic or usual care. Similarly, subjects with raised total cholesterol (≥ 5.0 mmol/l) were randomized to the specialist nurse–led hyperlipidemia clinic or usual care.

Different specialist nurses provided the two interventions.

These posts were created specifically for the management of hypertension and dyslipidemia and were based on the standards for specialist practice as identified by the U.K. Nursing and Midwifery Council (11). In Salford, as in most of the U.K., diabetes specialist nurses manage their own caseload, initiating and titrating drugs for glycemic control, but have traditionally had little input or experience in managing other cardiovascular risk factors. The nurses recruited to the posts were registered nurses educated to degree level with previous experience of the management of diabetes, hypertension and dyslipidemia, patient education, and working as advisors to other health care professionals. Because no formal training courses exist for nurses in the management of hypertension and dyslipidemia in patients with diabetes, training was provided by the local clinicians and pharmacists.

Intervention

An initial 45-min appointment was offered to each of the patients randomized

to receive specialist nurse intervention from either the hypertension or lipid specialist nurses. This appointment was used to discuss the reason for the visits, targets for their treatment, and the reason for these targets. A detailed medical history was not taken because all patients had been fully assessed within the previous 6 weeks at the diabetes clinic and all data previously recorded on an electronic diabetes information system were accessible to the nurses. The medications were checked and other key conditions likely to influence treatment, such as poorly controlled diabetes, were noted. A history was taken relating to the duration of hypertension or hyperlipidemia, any previous treatments that had been used, and the reason for discontinuation of previous treatments.

Next, an accurate assessment of their presenting condition was made. For individuals with hypertension, three measurements of BP were taken 1 min apart using an Omron 705CP (Omron Health Care, Henfield, U.K.), as per British Hypertension Society guidelines (12). The average of the second two readings was recorded as the actual BP. Twenty-four-hour ambulatory measurements were taken in patients in whom white coat hypertension or postural hypotension was suspected or whose BP remained high on three or more treatments. Individuals randomized with hypercholesterolemia had a full fasting lipid profile repeated. The therapeutic decision was based on total cholesterol and HDL levels, which are unaffected by the nonfasting state of an individual.

Lifestyle factors likely to be contributing to, or affecting response to treatment of, hypertension or hypercholesterolemia were discussed (namely diet focusing on either salt or fat intake and weight reduction as appropriate, alcohol intake, and exercise patterns). The patient's willingness to change these lifestyle factors was discussed, and an individualized action plan was drawn up. Finally, an individualized education program was implemented consisting of information about the risks of hypertension or dyslipidemia, the benefits of treatment and lifestyle changes, drug actions, and potential side effects.

Thereafter, the specialist nurses saw patients in the diabetes center every 4–6 weeks for 30- to 45-min appointments until targets were achieved ($< 140/< 80$

LISINOPRIL

Initial dose 2.5 mg OD

Titration 5 mg, 10 mg, 20 mg OD

Increase every 2-4 weeks

Check U&Es before commencing and one week later

If creatinine rises >10% and/or potassium >5.5 mmol, seek medical advice

Figure 2—Salford guideline for initiating and titrating ACE inhibition. OD, once daily; U&E, urea and electrolyte.

mmHg or <5mmol/l, respectively). At these visits, lifestyle modifications were reinforced and reviewed and medications were titrated according to response to treatment according to the local protocol. At subsequent visits, lifestyle factors were reviewed, the need for behavior changed re-enforced, and the dose of antihypertensive or cholesterol-lowering medication increased by the specialist nurse in a stepped care approach in accordance with protocols agreed on by the local Drugs and Therapeutic Committee and supported by patient group directives (Figs. 1 and 2). The specialist nurse discussed patients who required additional medications with the doctor, who initiated additional therapy when appropriate.

Whereas the main emphasis of the clinics was BP and cholesterol control, patients presenting with poor diabetes control, as judged by raised HbA_{1c} levels, were given advice on glycemic control. The protocol forbade the specialist nurses from providing any management of the other intervention, i.e., individuals in the cholesterol arm received no advice relating to hypertension.

Both baseline and follow-up BP and cholesterol concentrations were collected during the patients' following annual review, independently of the study. Ethics committee approval was gained for the trial.

Upon completing the study, all patients were linked to the National Strategic Tracing Service to determine whether they had died during the study (13).

Standard care

The control group of patients received standard care for the management of their

hypertension and hypercholesterolemia. The BP and cholesterol concentrations were measured before the patient saw the diabetologist, and these results were available during their 20-min annual diabetes review. During this review, the diabetologist would address the patient's control of glucose, cholesterol, and BP, as well as examine the patient's feet for signs of neuropathy or vascular disease, perform dilated funduscopy, and decide on an action plan for the following year. This plan would be discussed with the patient, who, along with the general practitioner, received a letter outlining this strategy. If medication was required, the patient would be asked to collect a prescription from his or her general practitioner, who would assess the effectiveness of the intervention and increase the medication if required. All general practitioners and practice nurses had received copies of the district policy for managing hypertension and hypercholesterolemia (the same used by the nurse specialists). Furthermore, they were invited to 4 monthly education sessions where these guidelines were discussed.

Although these patients would not be reviewed in the diabetes department until 12 months later, they were reviewed in primary care as thought necessary by the primary care clinicians.

Assignment

For each eligible patient, an administrator e-mailed the patient's hospital number and general practitioner practice code to a remote randomization service. The hospital numbers for patients randomized to intervention were e-mailed to the respective lipid and hypertension nurses. Be-

cause patients were randomized to receive the hypertension or hypercholesterolemia interventions separately, patients with both hypertension and hyperlipidemia could be randomized to receive one intervention and be a control for the other intervention. To avoid possible contamination of the results by control patients inadvertently receiving advice from the nurse specialist, the study was designed to ensure that each intervention was provided by a separate nurse specialist who could not provide any advice relating to the other intervention. Consequently, the hypertension and hyperlipidemia clinics were run independently by a different nurse throughout the study.

Masking (blinding)

Randomization was performed centrally in a fully concealed process and stratified according to general practice. Separate randomizations operated for each condition. Data at baseline and follow-up at 1 year were abstracted from Salford's EDR by staff blinded to allocation. The database was passed to the remote data center, where randomization status was incorporated and analyses were performed.

Power calculation

The power calculation was based on the number of patients who were not at target for each condition and the binomial (r/n) that describes the proportion of patients who subsequently attained target levels, using data on patients undergoing repeated annual hospital reviews during 1996–1997. In 1997, ~15% (150) of 1,000 hypertensive subjects and 7% (49) of 700 subjects with hyperlipidemia at first review progressed to within the target because of usual care. Both interventions were assumed to achieve a further 15% reduction, but this would be diluted to 7.5% because only 50% of patients would adhere to the request to attend the specialist nurse-led clinics. The hypertension intervention was powered ($1-\beta$) at 80% with a two-sided α of 0.05 to find a change of 7% with 1,020 patients (510 in each arm). Similarly, the hyperlipidemia intervention was powered ($1-\beta$) at 80% with a two-sided α of 0.05 to find a change of 7% with 660 patients (330 in each arm).

The primary outcome examines the effect of the specialist nurse-led clinic across both hypertension and hyperlipid-

Table 1—Patient characteristics

	Hypertension		Hyperlipidemia	
	Clinic	Usual care	Clinic	Usual care
Enrolled (n)	506	508	345	338
Attended follow-up	406 (80.2)	429 (84.5)	317 (91.9)	310 (91.7)
Visits	2 (1–4)	NA	2 (1–3)	NA
Age (years)	63.5 (55.4–72.1)	63.7 (56.4–71.9)	56.5 (45.1–66.9)	58.6 (49.3–69.6)
Male	259 (51.0)	270 (49.0)	186 (50.7)	181 (49.3)
BMI (kg/m ²)	30.7 (26.3–34.2)	30.5 (26.4–3.8)	31.2 (26.4–35.2)	30.4 (30–33.6)
Type 2 diabetes*	407 (83.7)	410 (83.7)	255 (75.7)	253 (76.2)
Prior cerebrovascular disease	4 (0.8)	1 (0.2)	16 (4.7)	28 (8.1)
Prior myocardial infarction	40 (11.8)	83 (16.4)	40 (11.8)	57 (16.5)
Systolic BP	159 (147–167)	159 (148–166)	NA	NA
Diastolic BP	78 (70–85)	77 (70–84)	NA	NA
Total cholesterol	NA	NA	5.8 (5.2–6.2)	5.8 (5.2–6.2)
LDL cholesterol	NA	NA	3.3 (2.8–3.7)	3.3 (2.9–3.7)
HDL cholesterol	NA	NA	1.3 (1.1–1.5)	1.4 (1.1–1.6)
Triglycerides	NA	NA	2.6 (1.5–3.2)	2.4 (1.4–3.0)

Data are n (%) or means (interquartile range). *Remainder: type 1 diabetes. NA, not applicable.

emia interventions. The study had 80% power (1- β) to identify a 5% change in the combined primary outcome at an overall two-sided α of 0.05.

Outcomes

The primary outcome is the increased proportion of patients achieving the specified targets for either intervention, specified as an odds ratio from the generalized linear model. Patients could be included in both clinical areas if they met the inclusion criteria. Nonattenders and subjects who died before attending the second annual review were deemed not to have achieved targets and were included in the analyses. Secondary analyses examined the change achieved in the individual hypertension and cholesterol interventions, the analyses of the continuous measures, and all-cause mortality.

Statistical analysis

Principle analyses were conducted using generalized linear models that estimated the effect of intervention on patient outcome. Binary analyses were conducted with a logit link and binomial error (14). Analyses of continuous data were conducted using an identify link function and normal error. Analysis of continuous data routinely used the patient baseline value (for BP or total cholesterol) as a covariate. All analyses were conducted using SAS (version 8.01; SAS Institute, Cary, NC).

RESULTS— Patient characteristics at baseline are described in Table 1, and the flow of participants through the trial is described in Fig. 3. Patients included because of raised cholesterol were ~5 years younger, on average, than those who were included because of hypertension. There were similar numbers of males and females in each group. About one in five patients included had type 1 diabetes. Average follow-up was 1.5 years (interquartile range 1.3–1.8). Patients attended the BP clinic for a median of two visits (interquartile range 1–4) and the lipid clinic for two visits (interquartile range 1–3)

Primary outcome measure

More patients achieved target levels among those randomized to attend the specialist nurse-led clinic in comparison to those who received normal care (odds ratio 1.37 [95% CI 1.11–1.69], $P =$

0.003). Overall, 315 (37.2%) patients randomized to the specialist nurse-led clinic achieved target, whereas 261 (30.7%) in the normal follow-up group achieved target.

There were some differences in the results achieved between the specialist nurse-led hypertension and lipid clinics. The principal analysis included a term describing the type of clinical intervention, although the unadjusted results were not materially different. There was some evidence of an interaction between the effect of the specialist nurse-led clinics and the clinical target (lipids or BP control) ($P = 0.06$).

Secondary analyses

The study design included three pre-defined secondary analyses relating to the effects of the intervention in the cholesterol and hypertension groups individu-

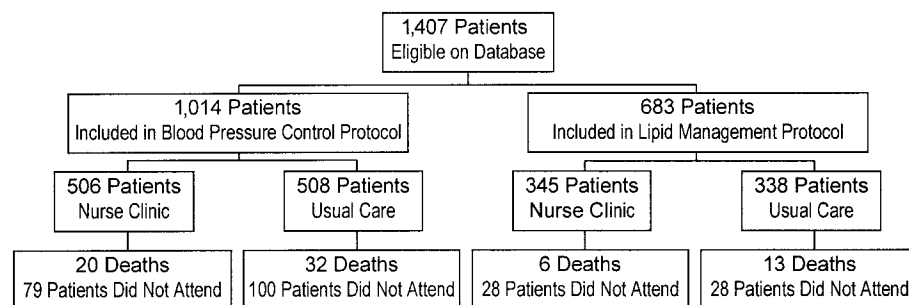


Figure 3—Patient flow.

ally, as well as all-cause mortality in the treatment and control groups.

Cholesterol control. When rerunning the primary analysis but including only the patients with hyperlipidemia, the benefit of the specialist nurse-led clinic was clear (odds ratio 1.69 [95% CI 1.25–2.29], $P = 0.0007$). Overall, 180 patients (53.3%) achieved the cholesterol target in the specialist nurse-led clinic group compared with 139 (40.3%) in the normal follow-up group. The change in total cholesterol attributable to the intervention was -0.28 mmol/l (95% CI -0.44 to -0.13 , $P = 0.0004$). The initial cholesterol was 5.8 mmol/l for both the intervention and control groups, respectively, falling to 4.9 and 5.2 mmol/l by the completion of the study.

BP control. Rerunning the primary analysis but including only hypertensive patients, the benefit of the hypertension specialist nurse-led clinic was less clear (odds ratio 1.14 [95% CI 0.86–1.51], $P = 0.37$). Overall, 135 patients (26.6%) who were randomized to attend the hypertension specialist nurse-led clinic achieved target, whereas 122 (24.1%) patients who received normal follow-up achieved target. The mean reduction in diastolic BP attributable to the intervention was -0.79 mmHg (95% CI -2.18 to 0.60 , $P = 0.27$), and the mean reduction in systolic BP was -1.95 (-4.49 to 0.60 , $P = 0.13$).

The initial BPs were 159/78 and 159/77 mmHg for the intervention and control groups, respectively, falling to 147/74 and 149/74 mmHg by the completion of the study.

Mortality. Of the 1,407 patients included in the trial, 778 were randomized to a specialist nurse-led clinic (for BP control, lipid control, or both) and 629 were allocated to receive normal follow-up. There were 25 deaths (3.2%) among individuals randomized to the specialist nurse-led clinics compared with 36 deaths (5.7%) among individuals randomized to normal follow-up (odds ratio 0.55 [95% CI 0.32–0.92], $P = 0.02$).

CONCLUSIONS— In this randomized trial of the management of patients with diabetes, we established that specialist nurse-led clinics can effectively improve the achievement of hypertension and cholesterol targets when added to care routinely provided by the diabetes clinic.

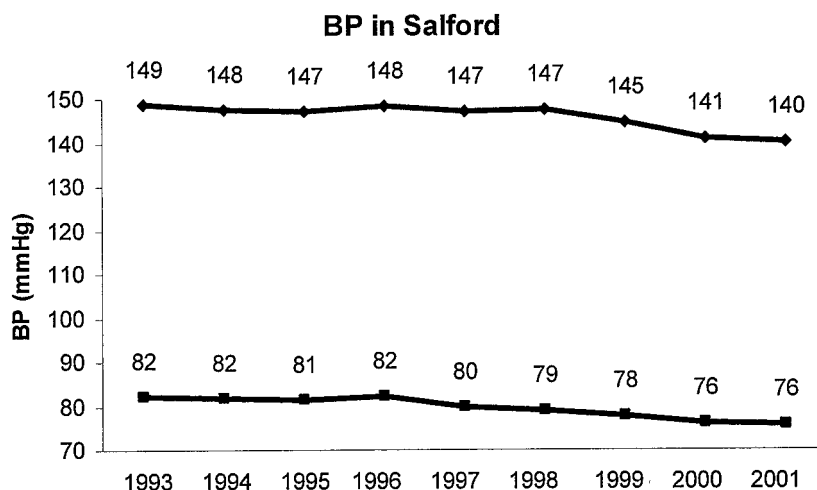


Figure 4—Trend in BP in patients at the annual review in Salford, U.K.

During the trial, there was an ongoing reduction in BP in our patient population consistent with, and possibly due to, the implementation of local guidelines in response to the results of the U.K. Prospective Diabetes Study (Fig. 4). A further reduction in BP and total cholesterol was achieved using specialist nurse-led clinics. The intervention is pragmatic, adapting to the needs and responses of individual patients, and could be easily implemented in other hospitals. Both interventions were delivered at a cost to the National Health Service (NHS) of the equivalent of one full-time diabetes nurse specialist, additional clinic time, and pharmacological treatment.

A surprising and significant reduction in mortality for the intervention group was found in a secondary analysis. The numbers of events were small, but this finding emphasizes the importance and value of efforts to manage patients to targets. Another recent trial demonstrated that specialist nurses can improve patient outcome. Specialist nurse intervention after acute hospital admission for heart failure reduced subsequent morbidity and hospital readmissions (15).

Patients were drawn from Salford, an inner city with high levels of social deprivation. Sixteen percent of patients randomized to specialist nurse-led intervention for hyperlipidemia, and 41% for hypertension, did not attend the clinics to which they were invited, which may have diluted the effects of an intervention.

The district-wide diabetes information system is used to promote consistent standards of care for patients with diabe-

tes in Salford. An additional benefit is that it permitted this trial to run without the need for a complex case report form. Baseline and end point data (with the exception of mortality) were retrieved from the existing electronic diabetes record, with the data being routinely collected during the provision of care.

The National Service Framework for Diabetes sets clear standards for the provision of diabetes care. Currently, these standards are not achieved by many diabetes services (16). The major obstacles to providing effective diabetes care are presented by the large numbers of patients and challenging targets for BP, lipid, and glucose control. Good diabetes care, although time-consuming for patients and health care professionals, is known to lead to cost-effective reductions in the development and progression of diabetes-related complications (7). This study demonstrates that significant improvements can be achieved in clinical practice by modifying the way care is provided. If people with diabetes are to receive the care proposed in the National Service Framework for Diabetes, then clinicians need new, more effective methods of providing this care. Furthermore, these methods must be practically applicable to all primary and secondary care and possible to implement within the finite resources available to the NHS. This study provides such evidence.

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