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Optimising global risk reduction: insights from REACH

This supplement is based on the proceedings of a one-day round table meeting held at the National Heart and Lung Institute, London, in June 2007 to discuss findings of the Reduction of Atherothrombosis for Continued Health (REACH) Registry. This international contemporary registry is looking at the association between multiple symptomatic locations of atherothrombosis (i.e. multi-vascular disease) and cardiovascular event rates, considering the characteristics and outcomes of stable patients in a community setting for whom one-year follow-up data were available. The registry is an ongoing study and the wide implications of this study for UK physicians across various different disciplines were discussed.

Meeting participants

Chairman

Dr Jonathan Morrell

General Practitioner, Hastings; Hospital Practitioner, Conquest Hospital, St Leonard's on Sea; UK Lead Investigator, REACH study

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The REACH Registry – baseline and one-year data

Jonathan Morrell

Introduction

Atherothrombosis has multiple manifestations – ischaemic stroke, transient ischaemic attack, myocardial infarction (MI), stable and unstable angina, and peripheral arterial disease (PAD) (i.e. intermittent claudication or critical limb ischaemia).

According to World Health Organization statistics from 2002, atherothrombosis is the number one killer, accounting for 28.7% of deaths worldwide and far outstripping infectious disease and cancer. This is projected to continue until 2020 and beyond.

Atherothrombosis is commonly found in more than one arterial bed in an individual patient. If one vascular bed is affected, it is highly likely that another one will also be affected. This overlap or cross-risk has been demonstrated since the CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events) study, which showed that about a quarter of the medium-risk individuals included had multi-vascular disease (**figure 1**). In about one in 30 individuals, cerebrovascular disease, coronary artery disease and PAD were all present. Since atherothrombosis has a unifying pathology with different manifestations in different arterial trees, this is not surprising.

Normally everyone is born with pristine arteries and the first pathological step in atherothrombois is development of the (clinically silent) fatty streak. Then follows development of the fibro-fatty plaque, which can either remain 'silent' or manifest as clinical symptoms such as chronic stable angina or intermittent claudication. Plaque rupture or fissure with accompanying thrombosis may occur resulting, according to site, in acute coronary syndromes, stroke or transient ischaemic attack, critical limb ischaemia or cardiovascular death. This sequence of events develops with age and exposure to an increasing risk factor burden.

'Most investigators expected contemporary therapies to be having more of an impact'

Jonathan Morrell General Practitioner and Hospital Practitioner in Cardiology; UK Lead Investigator, REACH Registry

The REACH Registry

The REACH (Reduction of Atherothrombosis for Continued Health) project is a contemporary registry exploring risk factors and the burden of atherothrombotic disease in an out-patient setting, across different regions of the world, and across the spectrum of disease from high-risk patients without overt disease to those with established coronary artery disease, peripheral vascular disease or cerebrovascular disease.

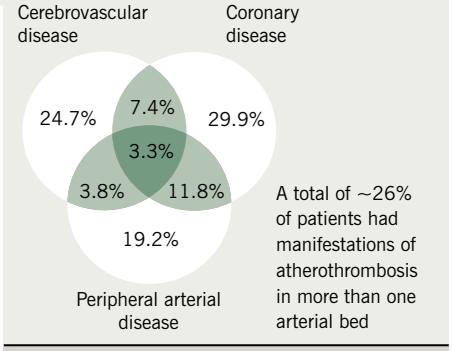
Although registries are regarded as inferior to the gold standard of the randomised controlled trial, the latter are limited by their strict inclusion criteria and methodological discipline. A registry can be seen as providing a real world view of medicine in action. Large registries and population studies, such as Framingham and INTERHEART, have contributed greatly to the understanding of the current burden and risk factors for cardiovascular disease but are criticised for being too parochial or tending to focus on one disease category or risk factor only, most notably coronary artery disease, dyslipidaemia or hypertension. The REACH Registry was therefore set up as a global study focusing on outcomes and risk predictors across the spectrum of cardiovascular risk in patients from a variety of clinical settings.

REACH has recruited out-patients who have had, or who are at high risk of having, symptoms of atherothrombosis. This is a contemporary stable patient population, supposedly optimally treated, from various regions of the world. The aims of REACH are:

- to define the characteristics and management of the patients in each subgroup
- to assess the long-term risk of atherothrombotic events in the global population and each subgroup
- to assess the amount of cross-risk across subgroups
- to compare the outcomes within different subject profiles, and
- to define predictors of risk for subsequent atherothrombotic events in affected individuals.

It has a long follow-up in registry terms, with the aim of follow-up to four years.

Figure 1. Chart showing how atherothrombosis is commonly found in more than one arterial bed in an individual patient

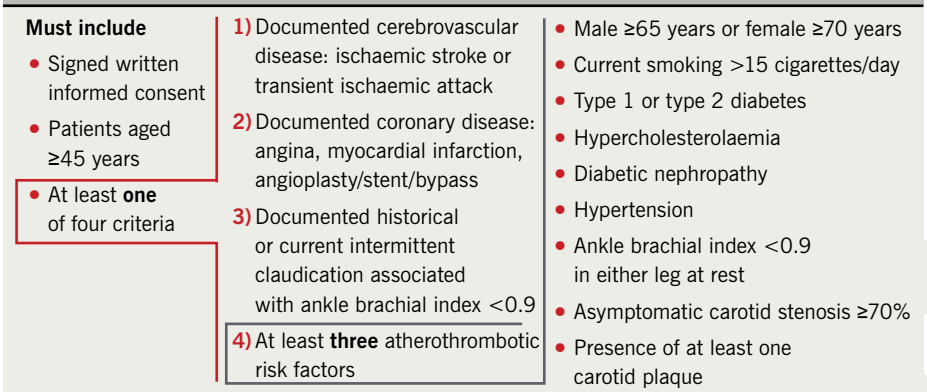


Adapted from Coccheri S. *Eur Heart J* 1998;**19**(suppl): P1268

Baseline data

Baseline data for the study were published in 2006 (*JAMA* 2006;**295**:180–9). Inclusion criteria for the REACH study are shown in **figure 2**. These were patients aged 45 years or over with no upper age limit, who were seen consecutively by the recruiting clinician. They recruited patients with documented cerebrovascular disease, coronary artery disease or peripheral vascular disease; or

Figure 2. Inclusion criteria for the REACH Registry



Adapted from Ohman EM *et al. Am Heart J* 2006;**151:**786e1–10

with a high risk factor profile. The primary prevention part of the registry formed about one fifth of patients in the total cohort. There are two primary end points for the study: the first is cardiovascular death with non-fatal stroke and MI, and the second an expanded end point to include hospitalisation for atherothrombotic events or vascular intervention.

REACH is a global study involving 44 countries and recruiting more than 68,000 patients from a number of sites. There is a large cohort of 28,000 from North America and 23,000 from Europe but no recruitment in Africa and parts of Asia. There were 618 patients recruited from the UK.

The physician profile showed that about two thirds came from primary care and about one third from various secondary care specialties such as cardiology and neurology.

The distribution of individual patients at baseline showed that 18% were in the multiple risk factors primary prevention group and about 82% in the symptomatic group (**figure 3**). Those with single arterial bed involvement dominated, accounting for about two thirds of symptomatic patients, but about one patient in six had documented evidence of declared multi-vascular disease. Of those with single arterial bed involvement, coronary involvement was most common (44.6%), followed by cerebrovascular disease (16.6%) and PAD (4.7%).

Global demographic characteristics reveal that they are quite an elderly group, with a mean age of 68.6 years, and two thirds are men. There is a high representation of cardiovascular risk factors: diabetes was present in 44.1%, hypertension in 81.7%, raised total cholesterol in 72.1%, overweight in 30.0%, obesity in 29.9%, former smokers represented 41.7%, and current smokers represented 15.2%. The risk factors (i.e. the different manifestations of arterial disease) are found consistently across the disease subpopulations.

Although medication use appears reasonable, with 75.2% on lipid-lowering therapy, 69.4% on statins and 78.6% on antiplatelet agents, proven therapies were consistently underused in all patient types. The proportion of patients not receiving proven therapies was lower with coronary artery disease than with cerebrovascular disease and peripheral arterial disease, suggesting that there is room for better implementation of treatment guidelines, which were also consistently not met in all patient types. There are worldwide variations but in Western Europe, for instance, 60.3% and 48.3% of patients are not achieving blood pressure and cholesterol targets, respectively, and 17.0% are still smoking.

One-year data

One-year data from the study have been published and the one-year cardiovascular event rates are summarised in **table 1**. The risk of an event for many patients in the REACH Registry is high. The one-year rate of cardiovascular death, stroke and MI was 4.24%, ranging from 2.15% in the primary prevention multiple risk factor group, to 4.69% in the patients with established disease. Patients with PAD (5.35%) and cerebrovascular disease (6.47%) showed higher event rates than coronary artery disease patients (4.52%). In addition, event rates increased markedly and in a step-wise fashion with the number of symptomatic disease locations and this is shown in **figure 4**.

The figures were a surprise to most investigators, who had expected lower rates because they thought contemporary therapies would be making more impact. The expanded end point shows even higher event rates with more than one in five patients with PAD experiencing an event.

The two-year data presented at the 2007 American College of Cardiology meeting showed a sizeable jump in cardiovascular events, and this is expected to rise further. Thus, cardiovascular death rose to 2.64% at two years; the end point of cardiovascular death, stroke and MI to 6.23%; and the expanded end point to 17.08%. There was a similar stepwise jump for the primary prevention cohort though the rates were lower.

Western European & UK data

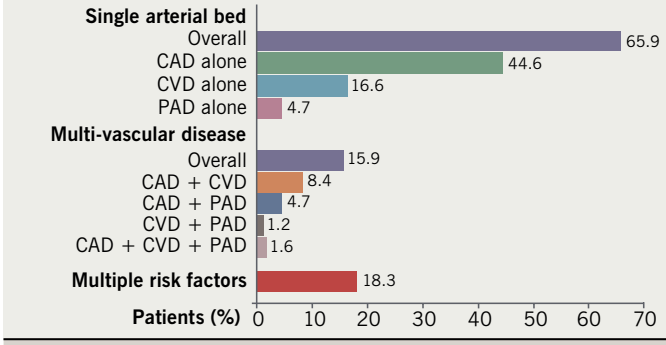
There were 17,886 patients recruited into the REACH Registry from Western Europe and, of the 618 UK patients, general practitioners recruited about 82%. Although physician recruitment was broadly similar between countries, there were subtle differences in patient recruitment. For instance, symptomatic patients were recruited more frequently in the UK. The

Table 1. One-year cardiovascular event rates (%) in the REACH Registry

CV event	Total 64,977	MRF 11,766	Establ. 53,390	CAD 38,602	CVD 18,013	PAD 8,581
1º EP	4.24	2.15	4.69	4.52	6.47	5.35
1º EP exp	12.81	5.31	14.41	15.20	14.53	21.14

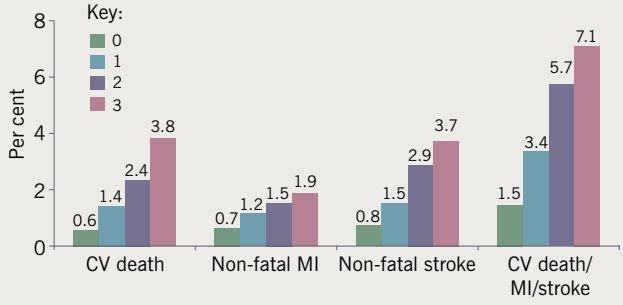
Adapted from Steg G *et al. JAMA* 2007;**297:**1197–1206
Key: CV = cardiovascular; MRF = multiple risk factors; establ = total established disease; CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease; EP = end point; exp = expanded

Figure 3. Distribution of the REACH Registry population at baseline showing prevalence of disease in arterial beds (% of total)



Adapted from Bhatt DL *et al*. *JAMA* 2006;**295**(2):180–9
Key: CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease

Figure 4. One-year cardiovascular event rates (%) in REACH showing the number of symptomatic disease locations



Key: CV = cardiovascular; MI = myocardial infarction. All p values <0.001. Patients with >3 risk factors but no symptoms are counted as 0, even in the presence of asymptomatic carotid plaque or reduced ankle brachial index

primary prevention group accounted for only 9.1% of UK patients versus 17.6% globally. PAD seems to be under-represented (2.5% UK versus 5.4% globally). This could be because of the small numbers of patients involved in the UK or perhaps a subtle neglect of PAD amongst UK primary care physicians.

Looking at the one-year cardiovascular event rates, there were no documented major events among the small group of patients (n=54) with multiple risk factors only (**table 2**). The one-year event rate was 4.51% among the 547 symptomatic patients, with slightly higher figures for PAD (4.82%) compared to cerebrovascular disease (4.46%) and coronary artery disease (4.35%). Looking at the expanded end point, a slightly different picture emerged. The event rates at one year were 1.57% for the multiple risk factors group, 9.56% among all symptomatic patients, 10.07% for coronary artery disease, 8.29% for cerebrovascular disease, and almost double that – 18.54% – for PAD highlighting the high event rate suffered by PAD patients. Cardiovascular event rates and hospitalisations also increased with the number of symptomatic disease locations, underlining the high risk associated with multi-vascular disease.

Medication use in the UK seems to closely mirror the global pattern with relatively high use of evidence-based therapies. There is low use of antiplatelet agents in the primary prevention group but higher use (around 80%) in the secondary prevention population. There is quite good uptake of lipid-lowering therapy, with 76.4% use of statins in the primary prevention group and between 74.6% and 86.5% use in the group with established cardiovascular disease. To further reduce event rates, however, there will need to be a greater implementation of evidence-based therapies.

Future directions

The REACH Registry contains much more data to come including more information on diabetes, obesity, socioeconomic factors, and the differences between management of men and women with cardiovascular disease or at risk for it. One of the most exciting aspects of a recent steering group meeting was developing a risk prediction model for patients with established coronary artery disease. Risk prediction models currently cater for people in primary prevention but this will create a method for risk-stratifying those with established coronary artery disease. Future work includes projects in the fields of stroke and PAD. There will also be regional data from around the world, health economics data, three- and four-year extension data and long-term mortality data

Table 2. One-year cardiovascular event rates (%) in the UK REACH population

	Total (N=601)	MRF only (N=54)	Total symptomatic (N=547)	CAD (N=448)	CVD (N=135)	PAD (N=56)
CV death	1.17	0.00	1.34	1.43	1.27	0.00
Non-fatal MI	1.02	0.00	1.20	0.93	1.52	3.61
Non-fatal stroke	1.68	0.00	1.93	1.95	1.74	1.34
CV death/MI/ stroke	3.87	0.00	4.51	4.35	4.46	4.82
CV death/MI/stroke /hospitalisation for atherothrombotic events*	8.66	1.57	9.56	10.07	8.29	18.54

Key: MRF = multiple risk factor; CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease; CV = cardiovascular; MI = myocardial infarction; *transient ischaemic attack, unstable angina, other ischaemic arterial event including worsening of peripheral arterial disease

Key messages

- Despite use of contemporary therapies, cardiovascular event rates are still high in UK REACH patients, and do not seem different from those in the rest of the world
- The cross-risk of established vascular pathologies is defined and is higher in stroke and PAD patients than in those with CAD
- To further reduce event rates, we need greater implementation of evidence-based therapies

Implications of REACH for the cardiologist

Alistair Hall

Background

The relationship between doctor and patient, guided by the Hippocratic Oath, is based on trust, moral courage and loyalty. The physician's art in counteracting disease is to consider the nature of the disease, the therapeutic evidence base and the risk-benefit ratio.

Lives are saved with good practice. Two projects EMMACE-1 and -2 (Evaluation of Methods and Management of Acute Coronary Events), performed in West Yorkshire in 1995 and 2003, illustrate this. **Figure 1** shows all-cause mortality for the two studies and this fell in the second study compared to the first with more frequent usage of clopidogrel, statins, angiotensin-converting enzyme (ACE) inhibitors and beta blockers. (Although aspirin usage fell slightly, this was mainly because clopidogrel use increased greatly.)

It is important to know whether these beneficial drugs can be afforded. A costing report for implementing National Institute for Health and Clinical Excellence (NICE) guidance in the secondary prevention of myocardial infarction (MI) was recently published. This focuses principally on the 'big four': ACE inhibitors (which reduce mortality, and the risk of MI and heart failure), aspirin (which reduces cardiovascular mortality and morbidity), beta blockers (which reduce total mortality and cardiovascular mortality) and statins (which reduce total mortality and cardiovascular morbidity). Together their cost is about £10 per month.

'REACH data show up to 50% of patients are not taking the agents that show good evidence of benefit'

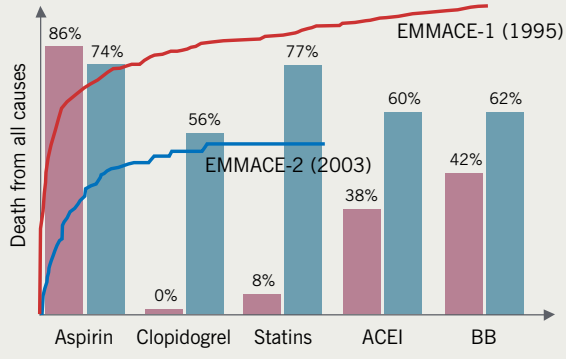
Alistair Hall Consultant Cardiologist and Professor of Clinical Cardiology, Leeds Institute of Genetics and Therapeutics

Improving care hopefully improves the end point of cardiovascular events – although this will never be tested, it is implicit. The CRUSADE (Cardiovascular Disease Quality Improvements Initiative) Registry looked at the variations in care processes by hospital including factors such as acute and discharge medications, and secondary prevention measures. The numbers of patients eligible for treatment and the percentages treated were arranged by hospital adherence quartile. The data suggest that putting patients on evidence-based drugs does make a difference to patient outcome. There was an association between hospital composite guideline adherence rate and in-hospital mortality. In non-ST elevation acute coronary syndrome (NSTE ACS), 20 lives were 'saved' per 1,000 and, in non-ST elevation myocardial infarction (NSTEMI), 30 lives were 'saved' per 1,000, when physicians followed all guidelines' recommendations.

REACH data

Table 1 summarises key findings in the UK baseline data. The REACH Registry highlights that, if there is disease in one vascular bed, many patients will probably have disease in other vascular beds to some degree. The more locations of arterial disease, the more likely the patient is to have a cardiovascular event. Age is a confounder: as people get older, their risk increases as the number of risk factors rises too.

Figure 1. All-cause mortality rates in the EMMACE-1 and -2 studies showing a drop in mortality between the two studies following the more frequent use of the agents shown

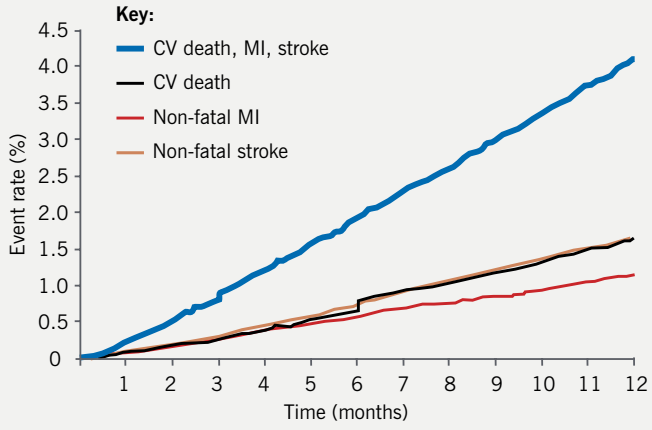


Key: ACEI = angiotensin-converting enzyme inhibitor; BB = beta blocker

Table 1. Key messages from the UK baseline data in REACH

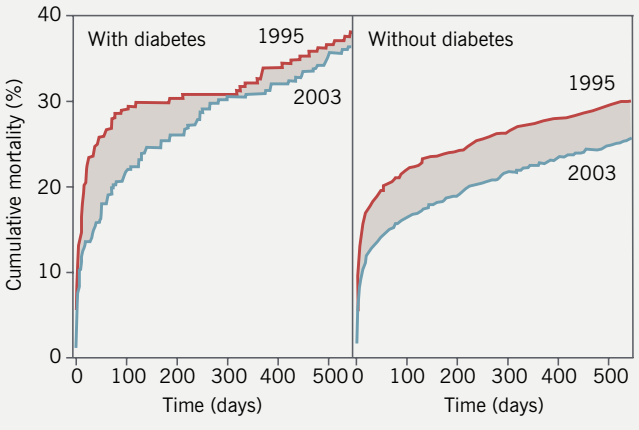
- The cross-risk of symptomatic atherothrombosis in the UK is substantial, with 14% of all at-risk patients having more than one of coronary artery disease, cerebrovascular disease and peripheral arterial disease
- At least half of all UK patients with symptomatic atherothrombosis have one or more risk factors that are inadequately managed
- Management of atherothrombotic risk is better in the UK in patients with symptomatic atherothrombosis than in those at risk of developing symptomatic disease

Figure 2. Event curves for cardiovascular (CV) death, non-fatal myocardial infarction (MI) and stroke from enrolment to one year in the REACH Registry



Adapted from: Steg PG *et al. JAMA* 2007;**297:**1197–1206

Figure 3. Comparing mortality in patients with and without diabetes after acute myocardial infarction in the EMMACE studies (1995 versus 2003)



Adapted from: Cubbon RM *et al. Eur Heart J* 2007;**28:**540–5

One-year data from REACH (**figure 2**) show linear event curves for cardiovascular death, non-fatal MI and stroke from enrolment to one year (unlike event curves for post-MI patients, which have a two-element shape with a steep rise and then a flattening off). This linear increase is consistent with a stable population.

These data also show substantial shortfalls in treatment: 38% of patients take no aspirin, 30% take no statin, 49% take no beta blocker, and 54% take no ACE inhibitor. The question that needs asking now is that if the number of patients taking these agents is now improved, are event rates reduced?

REACH showed therapies were under-used in all areas. The take-up of ACE inhibitors, for example, is one of the bigger areas that could perhaps be improved. Statin use too could be improved, a particularly topical issue since many general practitioners are being offered incentives if they can switch 75% of their patients onto cheaper statins so that the same amount of cholesterol lowering is achieved for less money. It is my personal opinion that patients should be switched the other way to achieve a greater amount of cholesterol lowering. A new, slightly controversial idea is to switch angiotensin II receptor blockers (ARBs).

Some studies have highlighted an increase in mortality with ARBs compared with ACE inhibitors so switching patients from a cheaper ACE inhibitor to a more expensive ARB may need to be reconsidered. The logic of 25% of patients being on ARBs, for example, when perhaps only 5–10% are coughing needs careful thought since the use of an ACE inhibitor can save money and lives at the same time, and there are not many situations where this can be done. The mechanism of the ARB MI paradox has been reviewed in detail in *Circulation* and also in a forthcoming article in *Heart*.

There are good data for the use of ARBs in diabetes, which showed a high incidence (34%) in the symptomatic REACH population and was recorded in 70% of the multiple risk factors group, partly because it was one of the inclusion risk factors. Although these figures are high, we know that 50% of acute coronary syndrome patients will have glucose intolerance or overt diabetes.

Figure 3 compares mortality in patients with and without diabetes after acute MI in 1995 and 2003, using data from the EMMACE projects. Overall, there was little change in the group with diabetes but a substantial change in the group without diabetes. Expressed another way, the hazard ratio of diabetes relative to non-diabetes, has risen from 1.3 ten years ago to 1.74, so that the differential is even bigger even though mortality is lower in both groups. This is because cardiologists are good at managing platelets, cholesterol and blood pressure post-MI, but are less good at managing sugar. This is a real problem and we don't really have anything in the 'big four drugs' to combat this.

So what is better prevention of cardiovascular events worth? Aspirin 75 mg, atenolol 100 mg, simvastatin 40 mg and ramipril 10 mg all together cost roughly £10 per month. These could be given together with other agents in a 'polypill'. This figure can be multiplied 10-fold with the addition of more expensive agents, but even this high figure is money well spent if it saves a heart attack, for example. What is important is whether the drug works. Since REACH data show that up to 50% of patients were not taking the agents that have good evidence of benefit, there is still scope to maximise treatment in the UK

Key messages

- It is likely that multi-vascular beds are affected if disease is present in one vascular bed
- Four major classes of drug can help prevent cardiovascular events
- REACH one-year data show substantial shortfalls in treatment so there is still scope to maximise treatment

Implications of REACH for the diabetologist

Vinod Patel

Background

The REACH Registry has highlighted the need to think outside our speciality when we consider the vascular patient. Coronary artery disease (CAD), kidney disease, diabetes, cerebrovascular disease (CVD) and peripheral arterial disease (PAD) are all clearly linked. We need to consider the totality of risk to develop a strategy for treatment. As renal function decreases (defined as falling glomerular filtration rate), for example, cardiovascular events increase. If a patient has diabetes, his risk of myocardial infarction increases and microalbuminuria (MAU) is associated with double the cardiovascular disease risk. If the patient has proteinuria, whether or not he has diabetes, the amount of CAD and CVD increases progressively with the degree of proteinuria.

Diabetes is a massive problem. There are probably 300 million people with diabetes now globally according to the World Health Organization, and huge numbers are affected in the Middle East and India, with type 2 diabetes accounting for 90% of patients. We rightly worry about the complications of diabetes: there is a two-to four-fold increase in CVD and CAD; it is the commonest cause of non-traumatic foot amputation and the commonest cause of blindness in people of working age; and 33% of all new patients in the UK needing renal replacement therapy have diabetes. A useful marker in men is erectile dysfunction, which may affect up to 50% with long-standing diabetes.

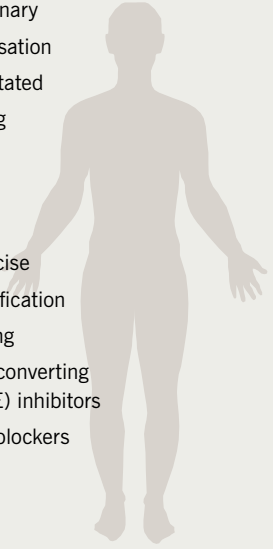
The disease is expensive to treat – diabetes accounts for at least 5%, with some estimates putting this as high as 8–9%, of the total NHS budget. Half of these costs are incurred in caring for the premature complications of diabetes and a huge evidence base now supports many of the treatments patients are offered to offset or prevent these complications. Components of care that need to be considered for the patient with diabetes are numerous (see **figure 1**) placing increasing demands on physicians, nurses, optometrists and others.

'We need to think outside our specialty and think of totality of risk'

Dr Vinod Patel Consultant Physician in Diabetes and Endocrinology, George Eliot Hospital, Nuneaton; Associate Professor in Clinical Skills, University of Warwick Medical School

Prior to the Quality and Outcomes Framework (QOF), a Diabetes UK audit showed UK physicians were not optimally treating diabetes. Only 56.5% of patients had an annual eye examination, 70.1% measurement of $HbA1_c$, 71.1% measurement of blood pressure, and 55.1% had undergone a foot examination. The UK National Service Framework for Diabetes, published in 2003, set out standards and defined service models for high-quality care in the prevention, identification and management of diabetes and its major complications.

Figure 1. Components of care in the patient with diabetes



- Blood pressure control
- Cholesterol profile modification
- Multi-disciplinary
- Smoking cessation
- Patient orientated
- Eye screening
- Statins
- Aspirin
- Weight loss
- Regular exercise
- Dietary modification
- Foot screening
- Angiotensin-converting enzyme (ACE) inhibitors
- AII receptor blockers

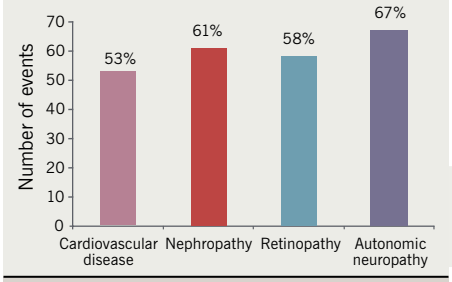
Risk factor control

Recently, the second Joint British Societies' (JBS 2) guidelines were published. It was excellent to have representatives of so many specialties – cardiologists, stroke physicians and diabetologists – sitting around one table to think about a single cardiovascular strategy. The simple but effective approach described in the diabetes section was to formulate a strategy based around the first seven letters of the alphabet – **a**dvice, **b**lood pressure, **c**holesterol, **d**iabetes control, **e**yes, **f**eet and **g**uardian drugs (see **table 1**).

Table 1. The alphabet strategy for the treatment of diabetes

Advice	Education, self-management, smoking cessation, diet, physical activity, weight reduction
Blood pressure	Target <130/80 mmHg Audit standard <140/80 mmHg
Cholesterol	Total cholesterol ≤ 4.0 mmol/L, low density lipoprotein ≤ 2 mmol/L Consider high density lipoprotein (HDL) ≥ 1 mmol/L men, HDL ≥ 1.2 mmol/L women
Diabetes control	Target $HbA1_c$% ≤ 6.5%, audit <7.5%
Eyes	Check yearly and refer if needed
Feet	Check yearly and refer if needed
Guardian drug	Aspirin 75 mg, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers, statins. Consider all three in all patients with diabetes

Figure 2. Event reduction in the Steno-2 study



Adapted from Gaede P *et al. N Engl J Med* 2003;**348**: 383-93

Table 2. Cardiovascular disease event reduction in the Steno-2 study

Event	Conventional	Intensive
Cardiovascular death	7	7
Myocardial infarction: non-fatal	17	5
Coronary artery bypass graft	10	5
Percutaneous coronary intervention	5	0
Stroke: non-fatal	20	3
Amputations	14	7
Revascularisation for peripheral vascular disease	12	6
P<0.002	**85 events in 35 patients 44% overall**	**33 events in 19 patients 24% overall**

Adapted from Gaede P *et al. N Engl J Med* 2003;**348**: 383-93

There is some concern that aggressive multifactorial intervention may do more harm than good to our patients, but one high-quality study, Steno 2, suggests otherwise. The study investigated patients with MAU, a condition affecting about 45% of patients with type 2 diabetes at any given point, with most people with diabetes developing it during their natural history. The study included 160 people with type 2 diabetes, with a mean age of 55 years at trial inclusion, who were followed up for eight years. Of these patients, 80 were allocated conventional treatment and 80 to intensified treatment. Standards of care for blood pressure, cholesterol etc. used were similar to those of the JBS 2 guidelines.

Results showed that blood pressure control improved by 12/6 mmHg in the intensive group, HbA1c by 1%, and cholesterol by 1.2 mmol/L. Some 15% more overall stopped smoking. The incidence of all complications was much reduced in the intensive treatment group (**figure 2**), as were the cardiovascular end points (**table 2**). The conclusion of this study was that target-driven, long-term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes and MAU reduces the risk of cardiovascular and microvascular events by about 50%.

Studies such as this show that the concept of a polypill may be beneficial. This proposes to treat blood pressure, low-density lipoprotein cholesterol (LDL-C), homocysteine and platelet dysfunction by administration of three antihypertensive agents, a statin, folic acid and aspirin to reduce cardiovascular disease by more than 80%. Applying the same methodology to the Steno-2 study, a risk reduction of 71% would be obtained.

The implications from REACH and other studies are quite clear. We do need to work together. Impaired glucose tolerance, which affects something like 25% of the population over the age of 50, increases cardiovascular disease risk by 50%. And the EUROHEART study showed that 42% of patients with CAD have diabetes (in a predominantly white European population).

Specialists need to engage their colleagues in general practice and their patients. Instead of having one letter from a cardiologist and another from a diabetologist, we have to refashion our thinking. This works well for diabetes. Diabetes score cards, passports and care plans using the alphabet strategy (which have been developed with patients) can help patients to start thinking about cardiovascular disease and diabetes as a whole. Also, the strategy enables them to know how good their diabetes control is.

An alphabet mnemonic for all vascular disease

At the George Eliot Hospital, Nuneaton, we have started to work on a unified single approach, with educational leaflets and care plans, for diabetes, coronary heart disease, stroke and peripheral vascular disease using the alphabet mnemonic (**table 3**). A, B and C (advice, blood pressure and cholesterol/ creatinine) stay exactly the same for all four disease areas. D, E, F and G may be adapted to make them more appropriate for the disease in question but the concept of the alphabet strategy still holds

Table 3. A single approach for the treatment of diabetes, coronary heart disease, stroke, and peripheral vascular disease

	Diabetes	CHD	Stroke	PVD
A	Advice	Advice	Advice	Advice
B	Blood pressure	Blood pressure	Blood pressure	Blood pressure
C	Cholesterol Creatinine	Cholesterol Creatinine	Cholesterol Creatinine	Cholesterol Creatinine
D	Diabetes control	Diabetes control Screening	Diabetes control Screening	Diabetes control Screening
E	Eyes	ECG / ETT / Echocardiography	ECG and other investigation	ABPI Angios
F	Feet	Functional status and follow up	Functional disability management	Functional management
G	Guardian drugs	Guardian drugs	Guardian drugs	Guardian drugs

Key: CHD = coronary heart disease; PVD = peripheral vascular disease; ECG = electrocardiogram; ETT = exercise tolerance test; ABPI = ankle brachial pressure index; angios = angiograms

Key messages

- We need to work together, across the different specialties and involving the patient in decision-making and self-care
- A patient with diabetes almost always has disease in at least two vascular beds

Implications of REACH for the vascular specialist

Cliff Shearman

Background

Peripheral arterial disease (PAD) is extremely common. Data from the Edinburgh Artery Study, much used to plan vascular services, show that in a cross-sectional survey of men and women aged between 55 and 74 years from 10 general practices in the city, 4% of so-called 'normal' subjects had symptomatic claudication. A further 25% had reduced ankle pressures indicative of arterial disease. Added to this, around 0.5% of the population have limb-threatening critical limb ischaemia – about 150 or 200 people a year for a hospital catchment population of 500,000.

The Edinburgh researchers followed up patients over five years. The data suggest that three quarters (73%) will lose their symptoms over that time, 8.2% will come to intervention, and there is a <1% risk of amputation per annum. They found a greatly elevated cardiovascular risk in these patients, with a 5–10% per annum risk of cardiovascular death. Other studies have highlighted that patients with PAD receive poor treatment compared to those with angina or heart failure.

Interestingly, the severity of symptoms appears to very closely match cardiovascular risk. The San Diego Artery Study divided subjects with large-vessel PAD into normal, asymptomatic, symptomatic and severely symptomatic groups, who were then followed up for 10 years. There was a 15-fold increase in rates of mortality due to cardiovascular disease and coronary heart disease (CHD) in severely symptomatic patients compared to normal patients (**figure 1**).

It is easy to detect PAD. The history may reveal cardiovascular disease or intermittent claudication. On examination, the peripheral pulses are sought and Doppler ankle: brachial pressure index is measured, with ankle pressure being a powerful independent predictor of cardiovascular death and events.

'REACH promotes PAD as a way of identifying people at high risk'

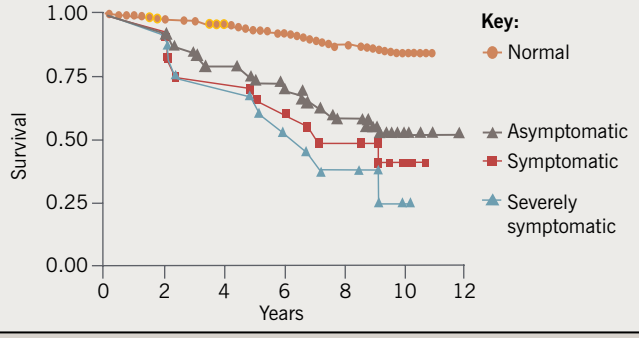
Professor Cliff Shearman Professor of Vascular Surgery, University of Southampton; Consultant Vascular Surgeon, Southampton University Hospitals NHS Trust

Evidence for benefit of treatment

There is good evidence for treating patients with PAD. Smoking cessation gives 30% benefit in terms of cardiovascular event reduction. Lipid-lowering treatment evidence comes from a subgroup of the Heart Protection Study, where patients with PAD treated with simvastatin showed a 10–15% reduction in events. Evidence of benefit with antiplatelet agents (25%) comes from the Antiplatelet Trialists' Collaboration which showed that patients with PAD seemed to have the greatest benefit from antiplatelet agents in their subgroup analysis. The CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events) study further showed that PAD patients seemed to derive greater benefit from clopidogrel than other groups. Diabetes appears to amplify the effects of other cardiovascular risk factors but, equally, tight diabetic control and treating these risk factors, such as hypertension, seems to gain more benefit. Finally, there is some evidence for dietary supplements such as fish oils and treatment with the specific agent cilostazol. Exercise is also beneficial, both for local symptoms and for the reduction of cardiovascular morbidity (improvement in walking distance and reduction in inflammatory markers).

Although the evidence is clear, it is frequently ignored. PARTNERS (Peripheral Arterial Disease Awareness, Risk and Treatment: New Resources) – a large study enrolling 6,979 patients aged 70 years plus; or aged 50 to 69 years with a history of diabetes or smoking – looked at risk factor management for

Figure 1. Peripheral arterial disease survival rates in the San Diego Artery Study



Adapted from Criqui MH *et al*. *N Engl J Med* 1992;**326**:381-6

Table 1. Factors complicating the treatment of peripheral arterial disease (PAD)

- There is no National Service Framework for PAD
- There are no clinical targets when a patient comes into hospital
- PAD is not in the new General Medical Services contract and so GPs have no incentive to look for patients whose primary problem is PAD and to treat these patients to any form of target
- Most PAD patients are elderly and generally not very vocal
- There is very little public awareness of PAD compared to heart attack or stroke
- There are large numbers of people involved in delivery of care – GPs, vascular surgeons, diabetes physicians, angiologists, care of the elderly doctors and cardiologists, all working in different environments

patients with PAD, coronary heart disease or both. Fewer patients with PAD alone received advice or treatment, in particular with cholesterol-lowering and antiplatelet agents. Treatment of PAD is also complicated by a number of other factors (see **table 1**).

REACH data

REACH baseline data are shown in **table 2**. Although the REACH Registry contains a very large number of patients (n=67,888), there was a relatively small group (n=8,273) of PAD patients. Similar to other groups, there was a high prevalence of risk factors in these patients such as hypertension (81.8%), high cholesterol (66.7%) and obesity (30.2%). The findings peculiar to PAD include the high prevalence (44.2%) of diabetes among these patients. This, interestingly, concurs with data from our own practice where nearly 40% of PAD patients have diabetes and the recently published BASIL study where 43% of patients with severe limb ischaemia had diabetes. The other remarkable finding is the high incidence (24.5%) of current smokers among PAD patients, which is greater than the incidence in the other groups. Half of PAD patients are also ex-smokers, making smoking an important issue among these patients.

Another interesting aspect of the baseline data concerned the patients who had clinical evidence of disease in other vascular beds – the multi-vascular patients. A large proportion (61.5%) of PAD patients had disease in other vascular beds in symptomatic form, which is a much higher proportion compared to patients with disease in other vascular beds.

The numbers of PAD patients receiving medication in the REACH Registry were much better than for the PARTNERS study, and their treatment seems to be better aligned with those patients having symptomatic disease in other vascular beds. The REACH data suggest, however, that PAD is still under-recognised, under-diagnosed and under-treated.

One-year data

One-year outcome data are shown in **table 3** and these show that, remarkably, the PAD group has the highest all-cause mortality, compared to patients with coronary artery disease or cerebrovascular disease. The PAD group also show higher rates of cardiovascular death and the Registry also indicates that these patients have a very high risk of some sort of cardiovascular event. It can be argued that compiling composite end points, such as hospitalisation and death, has difficulties and drawbacks but an extraordinary number of PAD patients will be hospitalised, have a cardiovascular event or die from cardiovascular causes within one year.

REACH patients with multi-vascular disease (21.7% with expanded end point at one year) fared much worse than patients with disease of a single vascular bed (12.6%). Since 61.5% of PAD patients have multi-vascular disease, this fits with their bad outcome. Indeed, 10% of patients underwent some form of revascularisation or amputation, which was a much higher figure than might have been expected from earlier studies, such as the Edinburgh Artery Study.

Table 3. One-year REACH outcome data (%)

	CAD	CVD	PAD	Risk	Total
All-cause mortality	2.89	3.14	3.76	1.51	2.58
CV death	1.93	2.05	2.51	0.75	1.65
CV death/ CV events/ hosp	15.2	14.5	21.1	5.3	12.8

Adapted from Steg PG *et al. JAMA* 2007;**297:**1197–1206
Key: CV = cardiovascular; CAD = coronary artery disease; CVD = cerebrovascular disease; hosp = hospitalisation; PAD = peripheral arterial disease

In summary, the conclusions from the one-year outcome data are:

- there is a high rate of cardiovascular deaths in patients with PAD
- there is a high rate of cardiovascular events and hospitalisation
- a large number of PAD patients have multi-vascular disease
- PAD patients have a higher rate of revascularisation and amputation than anticipated.

The challenge now is to control risk factors. The REACH Registry data have highlighted the enormous risk that PAD patients have. Patient awareness of PAD must be raised and they need to become experts in their condition. Specialist nurses must be recruited and the primary-secondary care interface needs to be changed so that many different people are no longer treating patients for different reasons and to different ends. Finally, clear, nationally agreed guidelines for the treatment of PAD patients must be developed

Table 2. Global REACH baseline data

	Total 67,888	Symptomatic 55,499	CAD 40,258	CVD 18,843	PAD 8,273	Risk factors 12,389
Age (years)	68.5	68.4	68.3	69.4	69.2	69.0
Men (%)	63.7	66.9	69.8	59.5	70.7	49.5
Diabetes (%)	44.3	37.5	38.3	37.4	44.2	74.9
BP (%)	81.8	80.0	80.3	83.3	81.0	90.3
Cholesterol (%)	72.4	70.2	77.0	58.2	66.7	82.2
Obesity (%)	30.2	27.4	29.9	23.7	23.8	42.4
Smoker (ex) (%)	41.6	44.6	47.1	38.6	50.9	28.4
Smoker (current) (%)	15.3	14.4	13.0	14.3	24.5	19.2

Adapted from Bhatt DL *et al. JAMA* 2006;**295:**180–9
Key: CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease; BP = blood pressure

Key messages

- Peripheral arterial disease (PAD) is extremely common and the majority of patients have symptomatic disease in other vascular beds
- It is under-diagnosed and under-treated
- Public awareness of PAD needs to be raised and national guidelines developed
- Different disciplines should work together to optimally manage this condition

Implications of REACH for stroke physicians

Damian Jenkinson

Background

Stroke is a major disease both in terms of human suffering and cost to the healthcare system. In the UK, there are more than 110,000 new strokes each year and more than 20,000 transient ischaemic attacks (TIAs). Data suggest that people who have had a TIA have a very high and immediate risk of going on to have a vascular event, particularly stroke but also myocardial infarction (MI) and vascular death. There are currently around one third of a million people in the UK living with significant post-stroke disability. It is the single largest cause of adult disability, the third commonest cause of death, and one in four people affected are of working age and need to be rehabilitated to get back to work and family life.

The National Audit Office (2005) estimates that total stroke costs to the nation are £7 billion a year, higher than those for coronary disease. These costs include direct care costs, nursing costs, lost productivity, community costs after discharge and informal care costs for people undergoing rehabilitation. The scale of these costs had not previously been realised.

Stroke is poorly managed in the UK and our costly stroke service does not compare well internationally in terms of clinical outcomes. The UK spends 4.7% of health expenditure on stroke, compared to the European Union (EU) average of 2.4%. A Stroke Strategy being developed by the Department of Health hopes to improve the cost-effectiveness of stroke management. Despite our high spend, mortality is 63.9 per 100,000 in the UK compared with 31.7 per 100,000 in Switzerland. Thrombolysis is given to only 0.2% of patients in the UK compared with 9% in North America and Australia, which has the best international practice. On average, 62% of UK patients are treated in a stroke unit. We know from a strong evidence base that such patients are more likely to be alive, independent and able to go home after a relatively short stay; in Sweden the comparative figure is 78.3%.

'We do not prevent stroke well and we do not manage it effectively or rapidly'

Dr Damian Jenkinson Consultant Physician in Stroke, Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust

Stroke is at least as common as coronary artery disease and affects a similar age profile. Stroke is also an urgent condition. Those who have had a minor stroke have a 19% stroke risk rate within 90 days and those who have had a TIA have a 17% stroke risk. Most of that risk occurs in the first hours and days and very early intervention is needed to intitiate antiplatelet therapy, control blood pressure, lower cholesterol and perform carotid endarterectomy, where appropriate. A TIA indicates that a patient has generalised vascular disease and those risks continue for the rest of the patient's life: at 10 years, the risk of any stroke is 18.8%, for MI/vascular death it is 27.8%, and for stroke/MI/vascular death it is 42.8%.

Table 1. Modifiable risk factors after stroke

All stroke

- Lifestyle changes (smoking, diet, exercise)
- Lower blood pressure

Ischaemic stroke

- Antiplatelet treatment
- Anticoagulant treatment if there is atrial fibrillation or an embolic source
- Cholesterol lowering
- Detection and treatment of carotid stenosis

Modifiable risk factors after stroke are shown in **table 1**. Royal College of Physicians (RCP) National Clinical Guidelines for Stroke 2004 – currently being revised to take in more recent data – state:

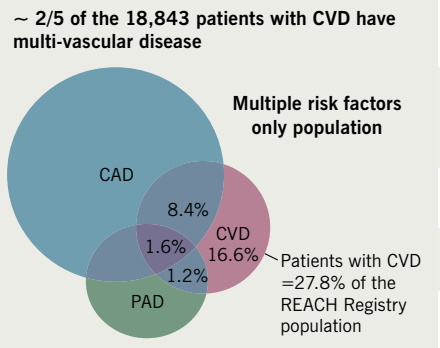
- all patients should be receiving lifestyle advice on smoking, exercise, diet and alcohol
- blood pressure should be reduced to a target of 140/85 mmHg (130/80 mmHg if the patient has diabetes)
- patients with a total cholesterol >3.5 mmol/L should be treated with statins
- patients in sinus rhythm should be taking antiplatelet agents unless they are contraindicated
- patients in atrial fibrillation should be on warfarin unless contraindicated.

The new guidance recommends that endarterectomy should be performed within a fortnight for anterior circulation TIA or minor stroke.

REACH data on cerebrovascular disease

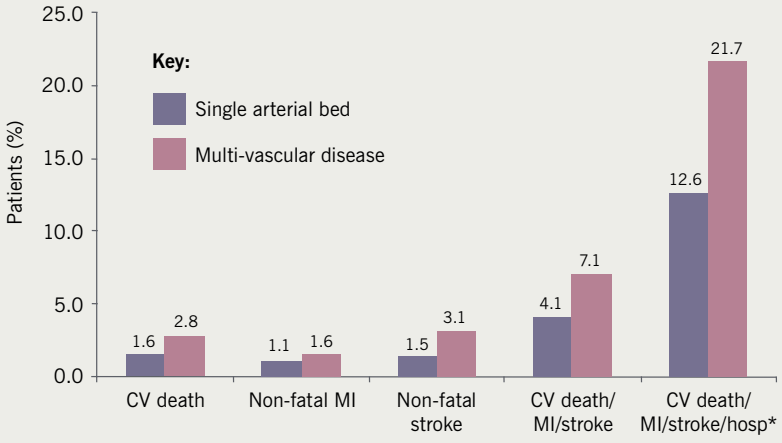
The REACH Registry has shown that 40% of patients with cerebrovascular disease have multi-vascular disease (**figure 1**). One-year cardiovascular events are more common in patients with multi-vascular disease than in those with disease of a single arterial bed for any of the outcome measures (**figure 2**). Proven therapies are consistently underused in stroke patients – 44% of patients are not receiving statins, for example, 39% of patients are not receiving any lipid-lowering treatment and 18% of patients are not receiving antiplatelet therapies.

Figure 1. Venn diagram to show the percentages of patients with cerebrovascular disease who also have multi-vascular disease



Adapted from: Bhatt DL *et al*. *JAMA* 2006;**295**:180-9
Key: CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease

Figure 2. Incidence of cerebrovascular events in the REACH Registry in patients with multi-vascular disease



Adapted from: Steg PG *et al*. *JAMA* 2007; **297**:1197–1206
Key: CV = cardiovascular; MI = myocardial infarction; hosp* = hospitalisation such as transient ischaemic attack, unstable angina, worsening of peripheral arterial disease, adjusted for age and gender

REACH does reflect data from other studies, such as OXVASC (2002–2004). There is a suggestion that the reduction in incidence of stroke in this latter population compared to the same population in the Oxford Community Stroke Project, which was carried out 20 years earlier, may be related to the changes in medication and prescription habits. There were increases in the use of blood pressure-lowering drugs, antiplatelet agents, anticoagulants and lipid-lowering therapies for both primary and secondary prevention over this period. The numbers of patients not being treated were consistent with REACH data.

Antiplatelet drugs

Guidelines for administration of antiplatelet drugs from the RCP, the National Institute for Health and Clinical Excellence (NICE) and the Joint British Societies vary but the most recent JBS 2 guidelines recommend that:

- patients with coronary artery disease or peripheral arterial disease should receive aspirin 75 mg once daily, or clopidogrel 75 mg once daily if aspirin-intolerant
- patients with cerebrovascular disease should receive aspirin 75 mg once daily and MR dipyridamole 200 mg bd (with no suggestion of stopping at two years), and clopidogrel if aspirin-intolerant or with recurrences on treatment.

Positive evidence for the use of dipyridamole came from the European Stroke Prevention Study 2. This gave better results with aspirin and dipyridamole combination therapy compared to either dipyridamole or aspirin alone. Those findings have been reinforced by ESPRIT (European and Australian Stroke Prevention in Reversible Ischaemia Trial).

The data for clopidogrel come from CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events), which showed an 8.7% overall relative risk reduction in the cumulative event rate (MI, ischaemic stroke or vascular death) for clopidogrel compared to aspirin. The *post hoc* analysis suggested that the peripheral arterial disease group may have benefited most, with stroke patients realising less benefit. A *post hoc* retrospective analysis of CAPRIE suggested that greater benefit might have occurred in those with a prior history of any ischaemic event or prior history of a major acute event (MI or stroke).

The future

The new Stroke Strategy, published for consultation by the Department of Health in July 2007, offers a clear opportunity to 'join up' services at a local level, particularly between cardiology, stroke and vascular surgery since they share similar care pathways for the treatment of their patients. Reflecting this, the National Director for Heart Disease, Professor Roger Boyle, is now also the National Director for Stroke

Key messages

- Clinical teams need heightened awareness that a significant proportion of cerebrovascular patients have multi-vascular disease, with associated increased risks
- Peripheral arterial disease, in people with transient ischaemic attack and stroke, needs to be systematically and routinely detected
- Continued efforts must be made to improve secondary prevention and clinical outcomes, perhaps centred on patient-held records
- Services need to be joined up at a local level
- There are substantial benefits for patients in ensuring local pathways for stroke, heart disease and vascular surgery are as consonant as possible

Implications of REACH for primary care

Terry McCormack

Lessons for primary care

REACH has many implications for primary care since vascular disease is all encompassing. There are many aspects of the Registry, which make its database particularly relevant for general practice. These include the fact that it is a' real-life study' and there were few drop-outs – worldwide the study retention was 95.2% – which gives the findings much credence (**figure 1**). The study's database is huge containing 68,375 patients at baseline and 64,977 at one-year follow-up. Women accounted for 36% of the total. General practitioners were the largest specialty, enrolling 27,392 patients.

There are many lessons for primary care in the study. These include the almost doubling of mortality in the 'disease group' compared to the 'at risk' group (2.81% *vs.* 1.51%, respectively). REACH also shows that multi-vascular disease increases risk from 2.2% (in the risk factors alone group) to 9.2% (where there is disease in three vascular beds). More effort is needed to address these very highest-risk populations.

Looking at specific vascular diseases, peripheral arterial disease (PAD) alone is associated with the lowest cardiovascular mortality, possibly because the numbers were small, but when this is associated with other disease locations, it becomes the biggest risk factor for death and events (**figure 2**). PAD is clearly under-treated and under-recognised, which will have the greatest impact in primary care.

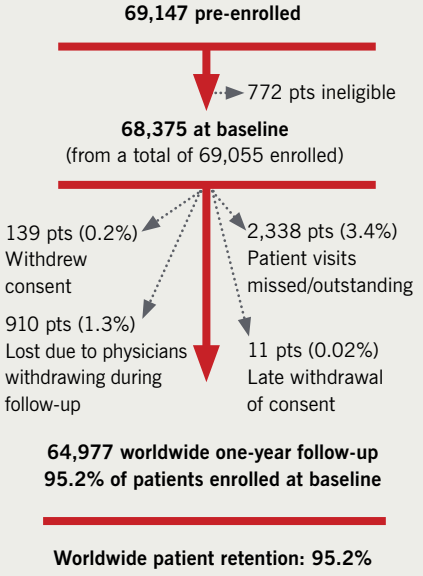
The cerebrovascular disease (CVD) group carried the highest risk of an event, if hospitalisations were excluded, but this is not recognised by the Quality and Outcomes Framework (QOF), where CVD is under-represented, except for hypertension points.

Despite high use of medication, REACH patients were not reaching target, perhaps due to agents not being prescribed at the right dose or not being titrated up. Proven therapies were consistently under-used in all patient types (**figure 3**). Additionally, even though patients may have all three conditions (i.e. CVD, coronary artery disease [CAD] and PAD), GPs may not use all the indicated drugs

'We are talking about a vascular disease that is all-encompassing'

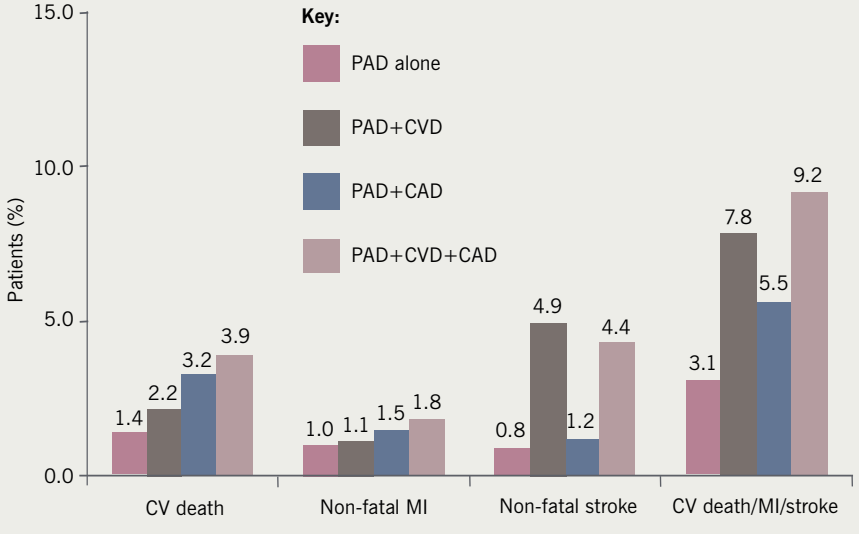
Dr Terry McCormack General Practitioner, Whitby, North Yorkshire; Hospital Practitioner, Whitby Hospital, and Chairman, Primary Care Cardiovascular Society

Figure 1. Diagram showing the high retention of patients worldwide in REACH



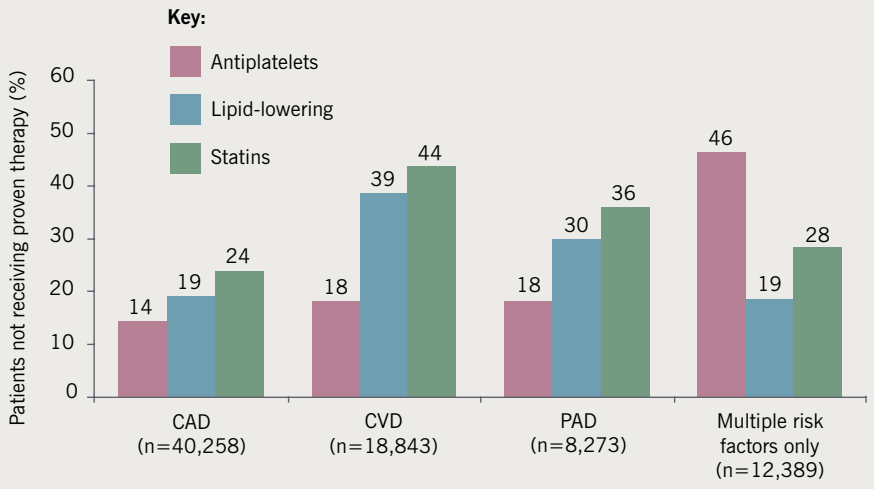
Adapted from Steg PG *et al. JAMA* 2007; **297:**1197–1206
Key: pts = patients

Figure 2. One-year cardiovascular event rates in PAD patients compared to those with multi-vascular disease



Adapted from Steg PG *et al. JAMA* 2007; **297:**1197–1206
Key: PAD = peripheral arterial disease; CVD = cerebrovascular disease; CAD = coronary artery disease; CV = cardiovascular; MI = myocardial infarction

Figure 3. Chart showing how proven therapies are consistently underused in all patient types in the REACH Registry*



Adapted from: Bhatt DL *et al*. JAMA 2006;**295:**180-9
Key: CAD = coronary artery disease; CVD = cerebrovascular disease; PAD = peripheral arterial disease;
* data shown may differ from published abstracts owing to subsequent database lock

Key messages

- Multi-vascular disease increases cardiovascular risk from 2.2% (risk factors alone) to 9.2% (disease in three vascular beds)
- Peripheral arterial disease in association with other disease locations becomes the biggest risk factor for death and events. It is also under treated
- There are concerns that the Quality and Outcomes Framework focuses too much on cardiovascular disease to the detriment of other disease areas
- Proven therapies are consistently under-used in all patient groups

because patients are classified as having CVD, CAD or PAD alone.

Other things to note in the study were that there was a high use of non-steroidal anti-inflammatory drugs (NSAIDs), especially in primary care. This would be a confounder but is to be expected since there is a greater patient mix in general practice. In addition, 50% of the working population were still out of work one year after suffering an event. This is a key economic driver and important in primary care.

UK implications

Moving on to lessons specific to the UK, although a relatively small number of patients were recruited in the UK, these were predominantly (82.5%) from primary care. Compared to the whole study, there was a low proportion (9%) of at-risk patients and relatively small numbers (14%) of patients with multi-vascular disease.

Uncontrolled hypertension was more likely in the at-risk group and was as common as controlled hypertension, although the proportion of uncontrolled hypertension (30%) is low in comparison to the rest of Western Europe. UK data also showed how hypertension is much better controlled than in the past. QOF attainment in blood pressure and cholesterol lowering is now the envy of many international health economies, although there are concerns that QOF focuses too much on cardiovascular disease to the detriment of other disease areas.

Looking at the PAD group, this contained the highest proportion of ex-smokers and also the highest proportion of patients with diabetes compared to other groups. Overall, the data show that there is still much untreated atherothrombosis in the UK which could be reduced with better risk factor management.

Limitations

Although the REACH study is ongoing for several years, a limitation of the current results are that they are only one-year data, a short study period. Follow-up data on drugs being taken by patients are not included so REACH findings tell us more about risk than intervention, which is a missed opportunity. REACH is very much a North American and European study: Africa and much of Asia are excluded, with relatively few people (618 patients) from the UK.

There were some curious definitions for the at-risk group: an ankle:brachial pressure index below 0.9 indicates that the patient already has disease, not that he is at risk for it, so this may not be a valid way of identifying a primary prevention group. A conventional risk assessment might have been preferable, although this would have been difficult to do in the 20-minutes REACH assessment period.

The future

What more could we discover from the REACH data? One big question is whether women benefit from statins – this has always been under-investigated in the past. Other questions include: were the effects of immigration measured? Will there be a substudy of body mass index (BMI) against waist circumference? How many GPs routinely measure ankle:brachial indices?

Round table discussion

During the meeting there was wide-ranging discussion amongst the panel about the implications of the REACH study for UK practice. This ranged from how all the disciplines involved should work together to better manage the vascular patient to how the findings of the study should be reported and afforded by primary care trusts. We summarise the main points of the discussions.

Working together

The panel felt the biggest problem flagged up by REACH in management terms was that patients are receiving different treatments from different people with different ideas and the vascular tree as a whole is not being considered by the current system. Patients are compartmentalised within a specialty to their detriment. 'We are talking about a joined-up disease so we need to tackle it in a joined-up way,' said the meeting chair, Jonathan Morrell.

The idea of a unified alphabet strategy across diabetes, coronary heart disease (CHD), stroke and peripheral arterial disease (PAD), was welcomed by the panel, since this would offer a consensus across the disciplines on a simple approach to be applied to anyone with cardiovascular disease. The development of one-page, evidence-based guidelines for all healthcare professionals would be invaluable in the treatment of the vascular patient.

Perhaps all doctors and nurses need to be vascular specialists, the panel felt. Working practices combining the expertise of various disciplines will need to be implemented to better manage the vascular patient's risks.

Treatment and targets

An important message from REACH is that more people need to be treated in order to maximise the benefits of evidence-based interventions. REACH data have highlighted the higher risks of the PAD patient despite similar levels of medication to other groups. The panel recommended that more intensive treatment should be given to this group.

'We are talking about a joined-up disease so we need to tackle it in a joined-up way'

In the area of statin therapy, REACH showed a good compliance of around 80% in the UK but, in reality, many people discontinue their medication despite health professionals' efforts to prevent this. This essential support must continue, the panel thought, to ensure patients comply with therapy as best they can.

The panel also pointed out that despite a recent survey claiming that half of the GPs surveyed were working to the tougher Joint British Societies (JBS) 2 targets, these findings may not be an accurate portrayal of practice. GPs may aim for lower targets as a means of achieving audit targets but may accept failure to achieve them.

Raising the profile of PAD

Traditionally, PAD has had a low status with regard to government backing for its management, compared to other manifestations of cardiovascular disease. The panel drew attention to the fact that there is very low public awareness of PAD despite some 7,000 amputations a year being performed in patients with diabetes and PAD. People also do not recognise the associations between smoking, arterial disease and amputation. This low public awareness, the panel felt, does not encourage change. A parallel situation is that despite overwhelming evidence for the benefit of screening for abdominal aortic aneurysm – it is probably one of the most cost-effective screening programmes ever evaluated – there remains little public awareness of the problem or pressure to introduce screening.

There may also be a lack of awareness among the clinicians who treat PAD patients, the panel thought, even though it is beginning to emerge that these patients may have the highest cardiovascular risk of all. Their treatment, they felt, should be intensified and combination treatment given more readily. One recommendation is for stroke physicians or cardiologists to search routinely for PAD or multi-vascular disease. This would help to heighten awareness amongst patients and health professionals as well as recognising the increased risk of future events.

PAD should be included in the Quality and Outcomes Framework (QOF), the panel felt. PAD should be viewed similarly to diabetes as a major driver of high cardiovascular risk and should be looked for more assiduously in primary care.

TIA and stroke

The existing guidance within the Royal College of Physicians (RCP) stroke guidelines is that patients with a transient ischaemic attack (TIA) should be seen within a fortnight. New guidance will recommend that they should be seen within one to two days since the risks for these patients are both significant and immediate.

One scoring system for TIAs, based on simple measures of age, blood pressure, presenting symptoms and duration of symptoms, has been validated. The scoring system is able to determine the likelihood of an individual who has had a TIA going on to have a stroke. Some individuals will have a 25–30% chance of having a stroke in the next few days whereas others have a 5% chance. Those with a low chance of stroke could perhaps be seen in a neurovascular clinic within 24–48 hours but the others should probably be admitted for investigation and control of risk factors.

There is now a genuine opportunity for central guidance in the UK Stroke Service, the panel said. One of the prime recommendations

will be that clinicians and local people work together to create clinical networks to provide comprehensive care in stroke, covering the entire stroke pathway. If identification of disease in other vascular beds, such as PAD, were factored in then that could be the beginning of a national drive for targeting multi-vascular disease.

Cardiovascular risk factor management

The REACH Registry used a relatively short questionnaire and interview between research doctor and nurse to collect data and the panel pointed out that it was not possible to cover everything in this time. Lifestyle, for example, was highlighted as one omission despite its importance. The panel felt that it was important to remember that physical activity, obesity and smoking, should all be addressed in the management of the vascular patient.

The EUROACTION study, a nurse-led project on coronary rehabilitation in hospitals and primary prevention in primary care, was cited as a study that has shown that proactive engagement and targeting can lead to significant changes. Nurses have achieved benefits in adherence to medication and target achievement – they could be important in rolling out the messages from the REACH study and improving care of the vascular patient.

Work in the wider community is also important to engage hard-to-reach individuals. Vascular disease is widespread, the panel pointed out, and so patients need to be involved and engaged by novel strategies to reach those who aren't currently being treated. The Grampian study was one of the first to show that nurses working with patients to achieve targets in coronary disease could actually improve mortality.

Global REACH data showing a 48% prevalence of obesity in the North American cohort versus a 4% prevalence in Japan (which has the lowest CHD rate in the world but a high incidence of stroke) were a warning for UK practitioners, the panel thought. This is because the UK is 10 years behind the US with respect to obesity and we now have the fastest-growing population in terms of obesity.

Age

The affect of age on the REACH results was considered by the panel, since if age was the dominant factor, more events would be expected to cluster towards the end of the first year of REACH. Yet the rise in events was linear, they noted. This may be because ageing is not a continuum. The concept of burden of arterial disease may be relevant here. Depending on genotype, some patients develop thrombosis and infarction early on whereas others co-exist with a large burden of atherosclerosis for decades. Attrition of the cohort may explain why the second-year figures have not risen to the anticipated level.

Diabetes

The panel felt the incidence of diabetes was surprisingly low in the REACH UK population (15%) compared to the worldwide incidence of 37% in the study. They felt a recent study, BASIL, in patients with severe limb ischaemia which indicated an incidence of diabetes of 43%, tied in better with the global REACH findings.

The high incidence of diabetes in different countries was also noted by the panel – there has been an explosion in diabetes in Eastern Europe and the Middle East, for example, and these very high rates have massive implications for healthcare there.

Implications of REACH for the primary care trust

Although the REACH data provide support for intensification of treatment, the panel highlighted how, in the real world, it comes down to affordability. Findings from REACH are competing against many other items to get onto the Primary Care Trust agenda and these convincing data need a good business case to be made in order to effect changes in practice. Even mortality data need to be reviewed and presented correctly if results are to be achieved.

The inclusion of hospitalisation within REACH end points has important implications for health economic data, the panel thought. In randomised trials, hospitalisation is always considered to be a 'soft' part of any end point since there is a huge variation between countries, making these data weak and inaccurate. But in registry terms, hospitalisation is justified because it is very expensive and will have an impact on those who plan services.

The panel also felt that the medical profession may perhaps have become too aware of cost. Rather than thinking about what the standard of care should be and then calculating whether it can be afforded, the profession tends to assume that it cannot be afforded and settles for a compromise. The starting point ought to be what makes up good practice.

The challenge now, the panel felt, is to ensure the delivery of a consistent message from all healthcare professionals involved in care for the vascular patient. Sustained and systematic change seems unlikely unless there are national directives. Enthusiasts will put protocols into place locally, but ultimately some central form of words and guidance is necessary to ensure that there is adherence to evidence-based guidelines and that atherothromboisis is addressed as a global arterial disease

Summary take home messages

- Atherothrombosis is a widespread disease in all senses
- The more vascular beds affected, the greater the risk of a cardiovascular event
- Despite good evidence-based therapy, cardiovascular event rates remain high and there are shortfalls in treatment
- The areas of stroke and peripheral arterial disease are particularly neglected; one-year outcome data show these manifestations have worse outcomes than coronary artery disease
- The entire vascular tree should be considered in treatment of the vascular patient with consistent messages from all professionals involved in their care
- Good health economics data must now be presented so that the REACH findings can be used to reduce the burden of atherothrombotic disease

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