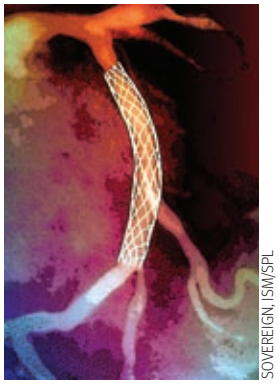
Drug eluting stents in patients with diabetes

Long term aspirin and clopidogrel are key to improving safety



SOVEREIGN, ISM/SPL

RESEARCH, p 668

Pierfrancesco Agostoni
interventional cardiologist, Antwerp Cardiovascular Institute Middelheim, Ziekenhuis Netwerk Antwerpen, 2020 Antwerp, Belgium
agostonipf@gmail.com
Frank Van den Branden
departmental director, Antwerp Cardiovascular Institute Middelheim, Ziekenhuis Netwerk Antwerpen, 2020 Antwerp, Belgium

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2008;337:a1359
doi: 10.1136/bmj.a1359

A quarter of people who need myocardial revascularisation have diabetes. After coronary artery bypass surgery and percutaneous coronary interventions, these patients have worse outcomes than those without diabetes.[1] They have more extensive coronary atherosclerosis, accelerated plaque progression, an increased rate of restenosis after percutaneous coronary intervention, and faster progression of bypass graft disease after bypass surgery.[2] Randomised trials have indicated that—especially in terms of repeated revascularisation procedures—coronary artery bypass surgery is more effective than percutaneous coronary intervention with bare metal stents in patients with diabetes, particularly in multivessel coronary disease.[1] In the linked meta-analysis, Stettler and colleagues compare the effectiveness and safety of sirolimus eluting stents, paclitaxel eluting stents, and bare metal stents in people with and without diabetes.[3]

Because of local pharmacological inhibition of restenosis, drug eluting stents reduce the need for repeated revascularisation compared with bare metal stents. It was hoped that these stents would be as effective as coronary artery bypass surgery, even in patients with diabetes. However, in the past two years there have been concerns that first generation drug eluting stents increase the rate of major adverse events (such as death and myocardial infarction) at long term follow-up.[4] This may be because drug eluting stents have a higher rate of stent thrombosis (also late after stent deployment), which is known to be associated with high short term mortality.[5]

A pooled analysis of four randomised controlled trials (all sponsored by the manufacturer of the drug eluting stents) comparing sirolimus eluting stents (the first commercially available drug eluting stent) and bare metal stents showed that although sirolimus eluting stents did not increase long term mortality in the overall cohort, mortality was significantly higher in the subgroup of patients with diabetes.[6] Patients with diabetes, who should have benefited the most from drug eluting stents, seemed to be at higher risk of late adverse outcomes. In contrast, in a pooled analysis of patients with diabetes enrolled in the five trials sponsored by the manufacturer, paclitaxel eluting stents seemed to be safe—mortality was similar to that seen with bare metal stents.[7]

Stettler and colleagues' meta-analysis sheds more light on this debate.[3] The study has several strengths. Firstly, it includes all the randomised trials available in the literature that compared first generation drug eluting stents with bare metal stents, not just the trials sponsored by the stent industry. Secondly, with the use of validated indirect comparison meta-analytical techniques, trials that directly compared the two types of drug eluting stent could be included. Thirdly, additional data were collected by direct contact with the trial investigators. These strengths make this meta-analysis more complete and valuable than previous ones.

The main message of the meta-analysis for clinicians is that short term (less than six months) double antiplatelet therapy with aspirin and clopidogrel was associated with increased mortality after insertion of a drug eluting stent (compared with a bare metal stent) in patients with diabetes. In contrast, long term double antiplatelet therapy (six months or longer) after insertion of a drug eluting stent was not associated with increased mortality. Interestingly, the only trials where short term double antiplatelet therapy was specified by the protocol compared sirolimus eluting stents with bare metal stents and none looked at paclitaxel eluting stents. These data confirm in part the pooled analysis of four trials of sirolimus eluting stents versus bare metal stents mentioned earlier. Indeed, in all those trials double antiplatelet therapy was given for less than six months.[6] Another indirect confirmation of the higher risk of major adverse events in patients with diabetes treated with drug eluting stents comes from registry studies, in which diabetes was constantly found to be a strong predictor of drug eluting stent thrombosis and adverse events.[8]

In clinical practice, diabetes should always be considered an important risk factor for major adverse events after implantation of a drug eluting stent, and every effort should be made to keep patients with diabetes and a drug eluting stent on long term double antiplatelet therapy. A recent consensus statement suggested that all patients with a drug eluting stent should receive 12 months of double antiplatelet therapy.[5] This is not always possible, however, because of poor compliance, lack of adequate follow-up, high numbers of drugs prescribed per patient, allergy, comorbidities, and difficulties in reimbursement for clopidogrel. All these problems should be looked at and if possible dealt with before implantation, especially in high risk patients such as those with diabetes. If any of these problems is present, drug eluting stents should be avoided and the patient should be reconsidered for medical treatment only, bare metal stent implantation, or coronary artery bypass surgery,

according to the extent of the coronary artery disease and the severity of the symptoms.

Two areas are particularly important for future research. Firstly, drug eluting stents are more expensive than bare metal stents so their cost effectiveness should be investigated in high risk patients such as those with diabetes.[9] Secondly, in all trials of drug eluting stents diabetes has been classified according to how it is treated (insulin or oral therapy). However, several other parameters (such as glycated haemoglobin, microalbuminuria, and degree of retinopathy) might potentially predict the outcome of the chosen revascularisation procedure and could be used to tailor the choice of treatment more efficiently.

1 Flaherty JD, Davidson CJ. Diabetes and coronary revascularization. *JAMA* 2005;293:1501-8.
2 Nicholls SJ, Tuzcu EM, Kalidindi S, Wolski K, Moon KW, Sipahi I, et al. Effect of diabetes on progression of coronary atherosclerosis and arterial remodeling: a pooled analysis of 5 intravascular ultrasound trials. *J Am Coll Cardiol* 2008;52:255-62.
3 Stettler C, Allemann S, Wandel S, Kastrati A, Morice MC, Schömig A, et al. Drug eluting and bare metal stents in patients with and without diabetes: collaborative network meta-analysis. *BMJ* 2008;337:a1331.
4 Camenzind E, Steg PG, Wijns W. Stent thrombosis late after implantation of first-generation drug-eluting stents: a cause for concern. *Circulation* 2007;115:1440-55.
5 Shuchman M. Debating the risks of drug-eluting stents. *N Engl J Med* 2007;356:325-8.
6 Spaulding C, Daemen J, Boersma E, Cutlip DE, Serruys PW. A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 2007;356:989-97.
7 Kirtane AJ, Ellis SG, Dawkins KD, Colombo A, Grube E, Popma JJ, et al. Paclitaxel-eluting coronary stents in patients with diabetes mellitus: pooled analysis from 5 randomized trials. *J Am Coll Cardiol* 2008;51:708-15.
8 Machecourt J, Danchin N, Lablanche JM, Fauvel JM, Bonnet JL, Marliere S, et al, EVASTENT Investigators. Risk factors for stent thrombosis after implantation of sirolimus-eluting stents in diabetic and nondiabetic patients: the EVASTENT matched-cohort registry. *J Am Coll Cardiol* 2007;50:501-8.
9 National Institute for Health and Clinical Excellence. *Coronary artery disease—drug-eluting stents*. 2008. www.nice.org.uk/guidance/index.jsp?action=byID&o=12013.

Telephone triage in out of hours call centres

Concerns about quality and safety highlight the need for further evaluation

PHANIE AGENCY/REX FEATURES

RESEARCH, p 676

Josip Car director of eHealth unit, Department of Primary Care and Social Medicine, Imperial College Faculty of Medicine, London W6 8RP
josip.car@imperial.ac.uk
Elizabeth Koshy clinical research fellow, Department of Primary Care and Social Medicine, Imperial College Faculty of Medicine, London W6 8RP
Derek Bell professor of acute medicine, Division of Medicine, Imperial College Faculty of Medicine, London SW7 2EH
Aziz Sheikh professor of primary care research and development, Division of Community Health Sciences, University of Edinburgh, Edinburgh EH8 9DX

Competing interests: None declared.
Provenance and peer review: Commissioned; not externally peer reviewed.
Cite this as: *BMJ* 2008;337:a1167
doi: 10.1136/bmj.a1167

Telephone triage, both for in hours and out of hours consultations, has increased dramatically in recent years, and in many respects this is welcome. Telephone consulting can improve access to care for many patients,[1] and out of hours care provided by call centres in particular can improve the efficiency of healthcare provision.[2] Several unanswered questions remain, however, with respect to the quality and safety of such clinical encounters because of the relative paucity of evidence on this mode of consulting.[3]

The linked study by Derkx and colleagues highlights the potential shortcomings of telephone based consultations in the context of out of hours triage of patients in the Netherlands.[4] Strengths of the study include a carefully considered sampling strategy of call centres and the use of standardised clinical encounters using simulated patients.

Out of hours consultations are risky because the patients and professionals usually do not know each other and the situation is often a clinical emergency. Predictably, the study found that the quality of these consultations was consistently poor for all cases and for all centres. The quality of the history taking, decision making, and providing advice phases of the consultation varied greatly. More surprisingly, general practitioners were little better than less trained "triagists." Triage management outcomes were appropriate in only 58% of calls, and urgency was underestimated in 41% of cases.

For patients with serious conditions, such as meningitis or malaria, incorrect risk stratification and the subsequent delay in treatment could have grave consequences. Several high profile cases of serious adverse outcomes associated with telephone provision of out of hours care have been reported in the United Kingdom.[5] However, the findings from the limited number of robust studies are mixed. They identify safety concerns in relation to the process of care but indicate that telephone consulting is safe overall in terms of clinical outcomes.[6] Although we need to clarify the link between the quality of telephone consultation (questions asked, evaluation of the answers, and the care advice given), process measures, and actual clinical outcomes in patients, the most credible explanation for this discrepancy is that because serious adverse outcomes are relatively rare, most of the studies have lacked the power to detect harm to patients.[7]

Internationally, call centres employ "triagists" with variable amounts of clinical knowledge, skills, and experience. They can be trained lay people, nurses, or doctors, working with or without protocols. The organisation of these call centres is also diverse; for example, some have a tiered approach, with an initial screen by personnel who are paid less and then, if necessary, second level triage by a doctor to reduce the need for face to face clinical encounters further.[8] The best approach to use is unclear, and it may depend on the quality of management protocols used by triagists. We do not know the degree to which protocols vary between call centres and countries—because they are invariably confidential—or to what extent variation from the guidelines is tolerated or even recorded. How then can we know that these protocols are up to date, evidence based, and followed? Why are they not public like other clinical guidelines? Moreover, why are they not available online to empower patients who may wish to use them?

So what is the future for out of hours telephone consulting? We need to define the contexts in which telephone consulting is most appropriate and develop

safeguards to minimise the risk of inadvertent harm to patients. We can then closely monitor performance using methodologically robust approaches.[9 10] It would be useful if evaluations of call centres in other countries were also published, including details of the methods used to triage patients (for example, the protocols used) and the approaches used to evaluate the care provided.

International cross cultural descriptive and evaluative approaches, such as recording consultations and comparing management with best care standards and guidelines would also be welcome to help develop interventions that can be locally implemented and evaluated. Underpinning all this is a need for policy makers, funders, and academics to recognise the importance of treating new models of care—such as out of hours call centres—as interventions in their own right and to evaluate them before rather than after they are introduced. Until we have such upfront commitment to evaluation we will not know whether developments such as the one reported by Derkx and colleagues are beneficial or harmful.

1 Car J, Sheikh A. Telephone consultations. *BMJ* 2003;326:966-9.
2 Salisbury C, Trivella M, Bruster S. Demand for and supply of out of hours care from general practitioners in England and Scotland: observational study based on routinely collected data. *BMJ* 2000;320:618-21.
3 McKinstry B, Sheikh A. Unresolved questions in telephone consulting. *J R Soc Med* 2006;99:2-3.
4 Derkx HP, Rethans J-J, Muijtjens AM, Maiburg BH, Winkens R, van Rooij HG, et al. Quality of clinical aspects of call handling at Dutch out of hours centres: cross sectional national study. *BMJ* 2008;337:a1264.
5 BBC News. *Helpline advice "linked to diabetic's death."* 2001 Oct 17. http://news.bbc.co.uk/1/hi/england/1605250.stm.
6 Bunn F, Byrne G, Kendall S. Telephone consultation and triage: effects on health care use and patient satisfaction. *Cochrane Database Syst Rev* 2004;(4):CD004180.
7 Katz HP, Kaltsounis D, Halloran L, Mondor M. Patient safety and telephone medicine: some lessons from closed claim case review. *J Gen Intern Med* 2008;23:517-22.
8 Kempe A, Dempsey C, Hegarty T, Frei N, Chandramouli V, Poole SR. Reducing after-hours referrals by an after-hours call center with second-level physician triage. *Pediatrics* 2000;106:226-30.
9 Hurwitz B, Sheikh A, eds. *Health care errors and patient safety.* London: Wiley Blackwell (in press).
10 Car J, Freeman GK, Partridge MR, Sheikh A. Improving quality and safety of telephone based delivery of care: teaching telephone consultation skills. *Qual Saf Health Care* 2004;13:2-3.

Collection of data on ethnic origin in England

Is improving, but information needs to be acted on for health inequalities to narrow

Veena S Raleigh fellow in information policy, Healthcare Commission, London EC1Y 8TG
Veena.Raleigh@healthcarecommission.org.uk

Competing interests: None declared.
Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2008;337:a1107
doi: 10.1136/bmj.a1107

A recent *BMJ* article marking the 60th anniversary of the NHS noted that "the patchy collection of ethnic data by the NHS needs to be improved."[1] Why are such data important, what is the current position, how is it likely to change in the near future, and how does data collection in the UK compare with other countries?

Around 7.7 million people in England (15% of the population) belong to ethnic minority populations, defined as all ethnic groups other than white British (and therefore including white Irish and white other). In some areas—such as the London boroughs of Newham, Tower Hamlets, and Ealing—ethnic minorities comprise more than 50% of the local population. In 46 of the 354 English local authorities, more than 20% of the population is not white British. The population of the United Kingdom is also ethnically diverse and changing, as exemplified by the recent inward migration from Eastern Europe.

Government targets for reducing inequalities in life expectancy focus on "spearhead" areas with the highest mortality and greatest deprivation, but the latest figures show that inequalities are widening.[2] In England, about 37% of people from ethnic minority groups live in these areas, and they make up about 20% of the spearhead population. Furthermore, significant epidemiological differences exist between ethnic minority groups, and—contrary to the spirit of personalisation central to the Darzi review[3]—people in minority ethnic groups sometimes report poorer experience of using services.[4] Some health disadvantages in ethnic groups are related to socioeconomic determinants, but these effects often cannot be distinguished from other effects because of inadequate data.

Information is the bedrock of a good health service. Improving health and reducing inequalities require information to support needs assessment, which should then be reflected in the planning and commissioning of services. The Local Government and Public Involvement in Health Act 2007 places a duty on local authorities and primary care trusts to undertake joint strategic needs assessments to inform commissioning priorities.

Effective commissioning requires information about population numbers, health status, risk factors, disease prevalence, and access to health care by key determinants of need such as ethnic origin. Such information is essential also for monitoring the effect on access and equity of policy initiatives such as patient choice, the 18 weeks target, and introduction of NHS funded independent healthcare services, such as independent sector treatment centres.

The Race Relations Amendment Act 2000 places duties on public bodies to promote race equality and undertake race equality impact assessments on all policies. The Darzi review highlights the role of information in patient choice and quality improvement.[3]

Without suitable data, we will not know whether ethnic differences in access, quality, outcomes, and choice are being ameliorated or exacerbated.

Historically, however, information about the ethnic origin of patients in health datasets has been poor, as noted in the Cabinet Office's equalities review.[5] The equality review of the national screening programmes, for instance, noted that ethnic inequalities in access and uptake cannot be measured because of a lack of information.[6] With a few exceptions, such as hospital episode statistics and the mental health minimum data set, ethnic origin is not routinely recorded in most NHS datasets or in primary care, although more than 90% of all patients' contacts are with general practitioners. Ethnic origin is not known for sentinel outcomes such as the 636 000 births and 470 000 deaths annually in England, because only the mother's country of birth is recorded at birth registration and the deceased's country of birth at death registration.

However, important developments are in the pipeline. In response to the equality review's recommendations,[5] the Office of National Statistics conducted a cross government review of the availability of data for monitoring equality, and the Department of Health's Equality Monitoring Group, chaired by the permanent secretary, Hugh Taylor, is dealing with filling in the gaps. Mandatory recording of ethnic origin in commissioning datasets for outpatients, people attending accident and emergency departments, and births was announced in June, for implementation from April 2009. The "standard" contracts for commissioners introduced by the department include uniform information requirements across both NHS and (NHS funded) independent health care. Proposals announced by the department in May 2008 to improve access to general practitioner services include consultation with the BMA on the recording of ethnic origin and first language by general practitioners. The report recommends that practices should "collect data as indicated in the national minimum ethnicity dataset" and the department should "promote ethnicity data monitoring in primary care and measure progress towards achieving equality."[7] Although parliament rejected legislation enabling the collection of ethnic origin at registration of births and deaths some years ago as being too complex to implement, the Office of National Statistics has used data linkage to compile infant mortality for England and Wales according to ethnic group.[8] Similar approaches could be used to analyse other deaths by ethnic origin.

But, at what stage of contact between patients and the healthcare system should ethnic origin be recorded? Currently the position on this is unclear and it can happen at multiple stages. However, recording ethnic origin in primary care and the electronic care record system of *Connecting for Health* may obviate the need for repeated collection of this information at different stages in the patient's journey.

Governmental commitment to reducing ethnic differentials in health is not unique to the UK, and neither is the call for better data on ethnic origin. For example, much work has been done on racial and ethnic disparities in health and access to care in the United States, and calls have been made for standardised data stratified by race, ethnic origin, socioeconomic status, and language.[9 10] In New Zealand ethnic differences in mortality over two decades have been examined through creative use of data linkage.[11] However, here too, the need for better data to support monitoring by ethnic origin is acknowledged. To overcome limitations in data, retrospective record linkage has also been used in Scotland for examining ethnic differences in morbidity and mortality.[12] In contrast, major differences in ideology and interpretation of data protection laws exist between EU member states. For example, official resistance to, and restrictions on, collecting data on ethnic origin is seen in France and Germany, and the UK is one of the few European countries that records ethnic origin in national censuses and officially recognises the need for ethnic data for monitoring purposes.

Although the collection of data in England is improving, the data are worthless unless they are used to target need and reduce inequalities. In this respect the NHS can show greater imagination. Datasets such as hospital episode statistics can already be used for monitoring access to inpatient care, outcomes, and general practitioner referrals by ethnic origin, but we have little evidence of this being done comprehensively at a local level. When current initiatives to improve information yield results, the challenge will be for managers, clinicians, commissioners, and providers to use the information to good effect.

1 Delamothe T. Universality, equity, and quality of care. *BMJ* 2008;336:1278-81.
2 Department of Health. *Tackling health inequalities: 2007 status report on the programme for action*. 2008. www.dh.gov.uk/en/Publicationsandstatistics/Publications/DH_083471.
3 Darzi A. *High quality care for all: NHS next stage review final report.* 2008. Department of Health. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_085825.
4 Department of Health. *The GP patient survey 2007: national report*. 2007. www.dh.gov.uk/en/Publicationsandstatistics/PublishedSurvey/GPpatientsurvey2007/DH_075127.
5 Cabinet Office. *The equalities review.* 2007. http://archive.cabinetoffice.gov.uk/equalitiesreview/.
6 National Screening Committee. *Equality review: national screening programmes. A scoping report for the National Screening Committee.* 2007. www.nsc.nhs.uk/pdfs/equalityreview-nationalscreening.pdf.
7 Lakani M. *No patient left behind: how can we ensure world class primary care for black and ethnic minority people.* Department of Health, 2007. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_084971.
8 Office of National Statistics. *Large differences in infant mortality by ethnic group.* 2008. www.statistics.gov.uk/ReleaseCalendar/findreleases.asp?releasetitle=infant+mortality&releaseorganisation=42&releasetheme=3&daterange=2&sday=24&smonth=6&syear=2008&showHits=10&sortOrder=0.
9 Institute of Medicine. *Unequal treatment: confronting racial and ethnic disparities in health care.* Washington DC: National Academies Press, 2003.
10 Agency for Healthcare Research and Quality. *National healthcare disparities report.* 2007. www.ahrq.gov/qual/nhdr07/nhdr07.pdf.
11 Ministry of Health, New Zealand. *Tracking disparity: trends in ethnic and socioeconomic inequalities in mortality*, 1981-2004. 2007. www.moh.govt.nz/moh.nsf/pagesmh/6689/$File/tracking-disparity-inequalities-in-mortality-1981-2004.pdf.
12 Bhopal R, Fischbacher CM, Steiner M, Chalmers J, Povey C, Jamieson J, et al. *Ethnicity and health in Scotland: can we fill the information gap?*www.chs.med.ed.ac.uk/phs/research/Retrocoding%20final%20report.pdf.