Reducing the risk of injury in young footballers

Using skeletal age rather than chronological age may be better

RESEARCH, p 694

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The risks and benefits of children and adolescents participating in elite sports have long been debated. Reports of growth retardation in elite gymnasts and degenerative joint disease in the elbows of young baseball players have caused anxiety among parents and sporting bodies. In contrast, Ericsson's theory of deliberate practice dictates the need for high volumes of training at a young age to reach expert level in skilled tasks including sport.[1] Health and sports professionals need answers to help with the understandable confusion confronting the parents of our next generation of athletes. In the linked study, Johnson and colleagues assess growth, development, and factors associated with injury in elite schoolboy footballers.[2]

The evidence base shows common themes in different sports. The incidence of injury increases with chronological age and pubertal stage.[3-5] Despite weight for age competitions in several youth sports—including American football, rugby union, and wrestling—the evidence on whether height or weight is associated with the risk of injury is conflicting. Weight for age classification was popular in the past, but its accuracy in matching opponents of equivalent maturity today may be compromised by high rates of childhood obesity.

Many aspects of sports performance, including aerobic capacity, strength, and power, are related to biological maturity. Studies have shown a preponderance of early maturers in adolescent sports that require strength and speed such as tennis, football, and swimming, whereas sports such as gymnastics tend to favour late maturers.[6 7] A normal maturer who plays against an early maturer may therefore be disadvantaged, and late maturers may have an increased risk of injury when playing against stronger and fitter opponents.

Johnson and colleagues investigate the association between maturity status and other factors, including training volume and playing load, and risk of injury in elite schoolboy footballers.[2] Maturity status was defined as the difference between skeletal age and chronological age. The investigators found that maturity status together with playing and training time collectively explained 48% of the variation in injury rates. The study also confirms previously identified research findings in football and other sports that injury rates are higher during match play than during training.[5 8]

Few studies have examined the association between maturity status and the risk of injury. One previous study found no significant difference in the incidence of injury in elite footballers who were early, normal, and late maturers, although the three groups showed different patterns and severities of injury.[9] Another study found no association between maturity status—measured by percentage of predicted mature height—and injury risk in young American footballers.[5] The linked study is the first to show that maturity status combined with other factors may influence the risk of injury.

Childhood and adolescence are times of skeletal vulnerability. The peak incidence of fracture coincides with the time of peak height velocity in both boys and girls.[10] The presence of growth plates and apophyses (tendon-growth plate interfaces) produces a unique pattern of injury in this population. During adolescence, apophyses are susceptible to traction forces, both acute and chronic, which account for the avulsion fractures and traction apophysitis seen in this age group.

"How much is too much?" is a question often asked in relation to children's participation in sport. Evidence based guidelines to answer this question are lacking in most youth sports. The risk of elbow and shoulder injury in adolescent pitchers in Little League baseball increases with increasing pitch counts.[11] This finding has resulted in guidelines that limit competition and training loads in young pitchers, but these guidelines should be regarded as best practice rather than evidence based. The optimum number of pitches per game and per season is unknown. Although reducing training and competition loads seems to be an appropriate response, there is no clear evidence that such policies reduce injury rates.

Most youth sports around the world are classified on the basis of chronological age. However, the maturational status of children of the same age differs significantly during adolescence. Nearly half of the footballers in the linked study were early or late maturers, which questions the validity of forming teams and designing training programmes on the basis of chronological age. Matching for skeletal age on the basis of radiography may not be practical except in elite sports. Proxies of skeletal maturity such as Tanner staging could be considered, although this raises privacy concerns, and self reported Tanner staging is not very reliable.[12]

Johnson and colleagues' study is an important study of a highly specialised population. Although it is valuable, we cannot extrapolate their findings to non-elite athletes or young athletes participating in other sports. Larger studies are needed to identify predictors of injury in community based children's sport. Elite sporting programmes should consider matching players for skeletal age and regulating training and competition loads, and all coaches working in youth sport should be made aware of the potential hazards of overtraining during vulnerable periods of growth.

1 Ericsson KA, Krampe Ralf T, Tesch-Römer C. The role of deliberate practice in the acquisition of expert performance. *Psychol Rev* 1993;100:363-406.
2 Johnson A, Doherty PJ, Freemont A. Investigation of growth, development, and factors associated with injury in elite schoolboy footballers: prospective study. *BMJ* 2009;338:b490.
3 Linder MM, Townsend DJ, Jones JC, Balkcom IL, Anthony CR. Incidence of adolescent injuries in junior high school football and its relationship to sexual maturity. *Clin J Sport Med* 1995;5:167-70.
4 Shaw L, Finch CF. Injuries to junior club cricketers: the effect of helmet regulations. *Br J Sports Med* 2008;42:437-40.
5 Malina RM, Morano PJ, Barron M, Miller SJ, Cumming SP, Kontos AP. Incidence and player risk factors for injury in youth football. *Clin J Sport Med* 2006;16:214-22.
6 Baxter-Jones AD, Helms P, Maffulli N, Baines-Preece JC, Preece M. Growth and development of male gymnasts, swimmers, soccer and tennis players: a longitudinal study. *Ann Hum Biol* 1995;22:381-94.
7 Malina RM, Eisenmann JC, Cumming SP, Ribeiro B, Aroso J. Maturity-associated variation in the growth and functional capacities of youth football (soccer) players 13-15 years. *Eur J Appl Physiol* 2004;91:555-62.
8 Romiti M, Finch CF, Gabbe B. A prospective cohort study of the incidence of injuries among junior Australian football players: evidence for an effect of playing-age level. *Br J Sports Med* 2008;42:441-6.
9 Le Gall F, Carling C, Reilly T. Biological maturity and injury in elite youth football. *Scand J Med Sci Sports* 2007;17:564-72.
10 Bailey DA, Wedge JH, McCulloch RG, Martin AD, Bernhardson SC. Epidemiology of fractures of the distal end of the radius in children as associated with growth. *J Bone Joint Surg Am* 1989;71:1225-31.
11 Lyman S, Fleisig GS, Andrews JR, Osinski ED. Effect of pitch type, pitch count, and pitching mechanics on risk of elbow and shoulder pain in youth baseball pitchers. *Am J Sports Med* 2002;30:463-8.
12 Desmangles J-C, Lappe JM, Lipaczewski G, Haynatzki G. Accuracy of pubertal Tanner staging self-reporting. *J Pediatr Endocrinol* 2006;19:213-21.

Standardised consultations in primary care

Are beneficial for some conditions, but should their extent be limited?

CLAIRE PAXTON & JACQUI FARROW/SPL

RESEARCH, p 696

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How much of primary care should be standardised? The drive for evidence based quality has precipitated guidelines and protocols aimed at setting standards and reducing variation in clinical care. Yet the personal and continuing approach to care, typified by the general practice consultation, sits uneasily with such requirements for uniformity. Some commentators predict that changes in clinical practice towards care based on more formulaic protocols will lead to the disappearance of the family practitioner.[1] Others have highlighted the practical and conceptual barriers that general practitioners face when asked to implement the increasing number of guidelines and decision tools.[2] However, the central concern driving the idea of standardisation is the frequent gaps and variations between evidence and practice. In the linked randomised controlled trial, Ravaud and colleagues assess the effect of standardised consultations about body weight and physical exercise in patients with osteoarthritis of the knee.

Standardisation of procedures is not uncommon or new in primary care. Routine systematic coding of morbidity and activity has transformed consultation records in general practice. Efficient systems for detection, call-recall, and monitoring have been widely introduced for managing chronic disease in primary care, although the evidence for their use and effectiveness is variable.[3]

Proposals for putting evidence into practice can, however, pose a more fundamental challenge to the style of personal care by recommending standardisation of components of the consultation itself. Guidelines may incorporate specific proposals for standardising treatment decisions, such as stepped care for asthma. The study by Ravaud and colleagues concerns a less precise area of the consultation—the content of information given to patients and advice about lifestyle changes, and the ways in which they are provided.[4]

Guidelines for osteoarthritis care recommend that clinicians provide patients with information about their condition and advice on weight loss and exercise.[5] The problem for clinicians is how to do this in the context of routine practice. Ravaud and colleagues' study investigates the effect of standardised approaches and systematic allocation of clinician's time to tackle each topic separately. They show that standardised consultations can improve weight loss and exercise levels by small but statistically significant amounts. Similar small benefits accrue from systematic advice to stop smoking from the general practitioner.[6] Other studies have reported negative findings; one study concluded that introducing systematic advice about childhood obesity in primary care did not result in sustained reductions in weight.[7]

Standardising factors like lifestyle advice may require much effort for small shifts in outcome. Are the changes in physical activity seen in the current study worthwhile? The failure to deliver core interventions for osteoarthritis partly results from its low priority and the pessimism of doctors and older patients about the likely success of interventions such as those aimed at weight loss. Yet primary care for common problems is delivered to large numbers of people and is in effect a public health intervention. Small changes in primary care practice, tied to small improvements in outcome, may translate into substantial effects in populations. Costs need to be considered, however, and they should be compared with the alternative of investing in society-wide primary preventive strategies aimed at achieving the same effects.

It would be unrealistic for general practitioners to carry out the intervention described by Ravaud and colleagues. An alternative approach would be for other healthcare professionals, who have protected time and appropriate skills and training, to deliver standardised care. This approach is often used for the management of chronic disease. Costs will probably be a problem for any intervention that increases direct clinical contact for each patient, and alternative routes to standardisation that use new technologies, such as automated telephone calls in diabetes care, are being reported.[8]

Ravaud and colleagues' study had several limitations. Studies that tackle only one component of primary care inevitably obscure the system as a whole. Patients and other health professionals were not involved in developing the study interventions, and the study took place in a healthcare system where patients can access specialist primary care directly from a rheumatologist. Whether

the intervention would be as effective when used by the generalist in primary care or by other personnel needs further study. However, the study's standard interventions did improve some outcomes, did fit with patients' wishes that clinicians should provide support for self management in chronic conditions rather than information alone,[9] and align with evidence about the effectiveness of goal setting. The potential of this type of approach should be explored more fully.

Current health services research will highlight the good and bad points of standardisation in other components of the consultation. Currently, the strength of evidence about the advantages of systematically following guidelines in primary care is variable. Positive examples such as those for back pain[10] and depression[11] are offset by negative examples, such as the failure to improve outcomes after introduction of standardised pain assessment.[12] Standardisation per se is not a panacea.

Even where standardisation is beneficial the challenge is to integrate it with the human elements of the consultation, regardless of the setting. Yet elements such as empathy could themselves be included in future measurements of the quality and outcome of primary care. Methods to standardise the delivery and measurement of such interpersonal components of care are developing. This may provoke more alarm in primary care practitioners who are concerned about how much more of their work can be standardised without them losing their identity.

1 McKinlay J, Marceau L. When there is no doctor: reasons for the disappearance of primary care physicians in the US during the early 21st century. *Soc Sci Med* 2008;67:1481-91.
2 Carlsen B, Glenton C, Pope C. Thou shalt versus thou shalt not: a meta-synthesis of GPs' attitudes to clinical practice guidelines. *Br J Gen Pract* 2007;57:971-8.
3 Chaudhry B, Wang J, Wu S, Maglione M, Mojica W, Roth E, et al. Systematic review: impact of health information technology on quality, efficiency, and costs of medical care. *Ann Intern Med* 2006;144:742-52.
4 Ravaud P, Flipo R-M, Boutron I, Roy C, Mahmoudi A, Giraudeau B, et al. ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: pragmatic randomised controlled trial. *BMJ* 2009:338:b421.
5 Conaghan PG, Dickson J, Grant RL. Care and management of osteoarthritis in adults: summary of NICE guidance. *BMJ* 2008;336:502-3.
6 Stead LF, Bergson G, Lancaster T. Physician advice for smoking cessation. *Cochrane Database Syst Rev* 2008;(2):CD000165.
7 McCallum Z, Wake M, Gerner B, Baur LA, Gibbons K, Gold L, et al. Outcome data from the LEAP (live, eat and play) trial: a randomised controlled of a primary care intervention for childhood overweight/mild obesity. *Int J Obes* 2007;31:630-6.
8 Handley MA, Shumway M, Schillinger D. Cost-effectiveness of automated telephone self-management support with nurse care management among patients with diabetes. *Ann Fam Med* 2008;6:512-8.
9 Raynor DK, Blenkinsopp A, Knapp P, Grime J, Nicolson DJ, Pollock K, et al. A systematic review of quantitative and qualitative research in the role and effectiveness of written information available to patients about individual medicines. *Health Technol Assess* 2007;11:1-160.
10 Fritz JM, Cleland JA, Brennan GP. Does adherence to the guideline recommendation for active treatments improve the quality of care for patients with acute low back pain delivered by physical therapists? *Med Care* 2007;45:973-80.
11 Hepner KA, Rowe M, Rost K, Hickey SC, Sherbourne CD, Ford DE, et al. The effect of adherence to practice guidelines on depression outcomes. *Ann Intern Med* 2007;147:320-9.
12 Huas D, Pouchain D, Gay B, Avouac B, Bouvenot G, and the French College Of Teachers. Assessing chronic pain in general practice: are guidelines relevant? A cluster randomised controlled trial. *Eur J Gen Pract* 2006;12:52-7.

Patient information sheets in emergency care

Can improve mental health outcomes, but other benefits are unknown

RESEARCH, p 700

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In the linked study, Arnold and colleagues assess whether giving an information sheet to patients with acute chest pain reduces anxiety, improves health related quality of life, improves satisfaction with care, or alters subsequent symptoms or actions. Their randomised controlled trial compared verbal advice with advice plus written information sheets in 700 patients presenting to the accident and emergency department with acute chest pain, initially thought to be of cardiac origin, who were discharged after acute coronary syndrome was ruled out.[1]

The study found that people receiving information sheets had significantly lower scores for anxiety and depression and higher scores for mental and general health perception at 30 days. The intervention had no significant effect on satisfaction or subsequent symptoms, which although frequent were of low intensity. Importantly, the intervention did not affect lifestyle changes, information seeking, or planned actions in the event of further pain. The intervention could be simple to use, cheap, and widely applicable.

Chest pain is an important problem for patients. It can cause or exacerbate fear, anxiety, and suffering, and the pain "also carries with it the inherent threat of death."[2] This is particularly true for patients with anxiety or panic attacks.[3] It is important for clinicians too, because chest pain is common both in primary and secondary care, and the consequences of missing an acute coronary event or pulmonary embolism can be catastrophic. Recurrent attendances with further episodes of chest pain cause diagnostic problems and considerable expense.

A subset of chest pain—non-cardiac chest pain—is associated with poor quality of life, considerable health expenditure, and ongoing morbidity.[4] Much of this may be related to underlying mental health problems, particularly panic disorder (present in 25-35% of people with non-cardiac chest pain[5]), anxiety, and depression. We know that interventions aimed at reducing anxiety in people with chest pain improve panic disorder scores, but we don't know about their effects on further episodes of chest pain or attendance rates.[6]

Patient information leaflets have a long history in health care. They were traditionally seen as a way of giving information to a passive recipient but more recently as part of patient empowerment.[7] The use of information leaflets in emergency care settings improves patient satisfaction[8] and is strongly recommended.[9] But the clinical effectiveness of these leaflets is poorly evaluated, and those studies that do report data suggest equivocal results when used as an isolated intervention.[10] Little has been

published about the effect of leaflets for those with chest pain discharged from the emergency department.

Two systematic reviews have assessed the effectiveness of written patient information outside of the emergency care setting. They found that information improves satisfaction and depression scores in those with chronic disease (stroke),[11] and that it also improves knowledge and satisfaction at hospital discharge.[12]

What Arnold and colleagues' paper doesn't tell us is whether these leaflets affect "hard" outcomes, such as rates of reattendance, costs, and further investigations for chest pain. In addition, the reduction in hospital anxiety and depression scale scores was not clinically significant (changes of ≥1.5) and patients' scores were not documented on arrival, so small differences that may have already existed in baseline scores could have confounded the modest differences seen. Furthermore, the intervention was not blinded, and this can affect the interpretation of results. Finally, the comparison group received usual care, which was verbal communication from a specialist nurse. This control "treatment" was unmonitored so we don't know how consistently it was delivered, its content and whether it changed during the trial, or whether the nurses were "contaminated" by reading the discharge material.

Despite these limitations the findings indicate that this simple low cost intervention provides some important health gains. Further trials that deal with these methodological problems should be undertaken, along with ones that replicate the study in other settings, such as in primary care and in people with low literacy or those who do not speak the host language.

The risks and opportunity costs with this intervention are low, and the potential benefits are clear. Although it would be tempting just to provide patient information sheets, further studies are needed first to show that they reduce reattendance and costs. These results should encourage clinicians dealing with patients with low risk chest pain to consider the patients' psychological status and provide more definitive information (written or verbal). Clinicians should consider the need for ongoing assessment and management of mental health problems in people with chest pain.

1 Arnold J, Goodacre S, Bath P, Price J. Information sheets for patients with acute chest pain: randomised controlled trial. *BMJ* 2009;338:b541.
2 Fitzsimons D, Parahoo K, Stringer M. Waiting for coronary artery bypass surgery: a qualitative analysis. *J Adv Nurs* 2000;32:1243-52.
3 Milner KK. Mood and anxiety syndromes in emergency psychiatry. *Psychiatr Clin North Am* 1999;22:755-77.
4 Eslick GD, Coulshed DS, Talley NJ. The burden of illness of non-cardiac chest pain. *Aliment Pharmacol Therapeut* 2008;16:1217-23.
5 Fleet RP, Dupuis G, Marchand A. Panic disorder in emergency department chest pain patients: prevalence, comorbidity, suicidal ideation, and physician recognition. *Am J Med* 1996;101:371-80.
6 Wulsin L, Liu T, Storrow A, Evans S, Dewan N, Hamilton C. A randomized, controlled trial of panic disorder treatment initiation in an emergency department chest pain center. *Ann Emerg Med* 2002;39:139-43.
7 Dixon-Woods M. Writing wrongs? An analysis of published discourses about the use of patient information leaflets. *Soc Sci Med* 2001;52:1417-32.
8 Trout A, Magnusson AR, Hedges JR. Patient satisfaction investigations and the emergency department: what does the literature say? *Acad Emerg Med* 2000;7:695-709.
9 Taylor DM, Cameron P. Emergency department discharge instructions: a wide variation in practice across Australasia. *J Accid Emerg Med* 2000;17:192-5.
10 Tapp S, Lasserson TJ, Rowe B. Education interventions for adults who attend the emergency room for acute asthma. *Cochrane Database Syst Rev* 2007;(3):CD003000.
11 Smith J, Forster A, House A, Knapp P, Wright JJ, Young J. Information provision for stroke patients and their caregivers. *Cochrane Database Syst Rev* 2007;(3):CD001919.
12 Johnson A, Sandford J, Tyndall J. Written and verbal information versus verbal information only for patients being discharged from acute hospital settings to home. *Cochrane Database Syst Rev* 2005;(3):CD003716.

Inequalities in maternal health

Routine collection of more detailed data is key to improving knowledge

RESEARCH, p 704

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Maternal health is important because it sets the scene, not only for survival and subsequent health of the infant, but also for the woman herself. The traditional measurement of maternal health is the maternal mortality ratio. Gross inequalities exist in the maternal mortality ratio between developed and developing countries, and the gap is not closing. The maternal mortality ratio in developed countries is about nine in 100 000 births; in sub-Saharan Africa maternal death is over 100 times more common, and the context is different from that seen in developed countries.[1]

In the linked study, Knight and colleagues use the United Kingdom obstetric surveillance system (UKOSS) to assess another aspect of maternal health—severe maternal morbidity. The study shows that severe maternal morbidity is significantly more common in non-white women than in white women in the UK, particularly those in black African and Caribbean ethnic groups. It also shows that ethnicity is a marker for poor maternal outcomes, not just for an increased likelihood of maternal death.[2]

Studying severe maternal morbidity improves our capacity to understand differences in maternal health beyond mortality, because the event rates are as much as 100 times higher than for maternal death in developed countries like the UK.[3] This allows a more robust analysis and better general application of the policy implications. In addition, the causes of severe maternal morbidity may not be the same as those of maternal death.[4] For these reasons, studying severe maternal morbidity allows us to expand our understanding of inequalities in maternal health.

Much is unclear about the association between ethnicity and poor maternal outcomes. This is compounded by the inconsistent use of terms such as race, ethnicity, and immigrant status. Most epidemiological research fails to define these terms or uses them interchangeably.[5] Ethnicity is a social construct that should be self identified and consists of a range of features including language, race, birthplace, religion, and culture.[6]

One unresolved question is whether ethnicity itself is directly relevant to poor maternal outcomes, or whether

it is a surrogate marker for a constellation of factors like low socioeconomic status, low level of education, and poor nutrition. It is a blunt marker when each ethnic grouping is so diverse. Despite the difficulties associated with the variable use of the terms, however, race, ethnicity, and immigrant status have consistently been associated with an increased likelihood for poor maternal outcomes, and they remain valuable epidemiological variables.[7] Each term offers discrete information, with potentially different targeted actions. For example, consider two pregnant women whose ethnicity has been classified as "black African." One was born, raised, and educated in the UK, and one arrived as a refugee two years ago. The second woman is more likely to have undiagnosed medical disorders like rheumatic heart disease, or to have been exposed to such a disorder, and she brings a higher risk status into pregnancy than her UK born counterpart. Newly immigrant women should have a full medical examination before pregnancy or early in pregnancy to identify such underlying diseases or risk factors.[8]

When tackling inequalities in maternal health in developed countries we need to raise concern for a group of women who, under traditional descriptors, are not considered to be at risk of poor health outcomes. These are the well educated, generally healthy, often more privileged women who choose to delay childbearing beyond the age of 35 years. This delay results in an array of changing reproductive characteristics, including a greater tendency to develop hypertensive and cardiovascular disorders, compounded by an increased frequency of multiple births and increased use of assisted conception. The combined effect of this social change is a group of women who unexpectedly carry a disproportionate burden of poor maternal outcome related to childbirth, even though they are not socially disadvantaged. The additional burden placed on the health of these women needs further investigation because women over 40 are up to eight times more likely to have a pregnancy related death than those in their early 20s.[9] For this group of women, improving access to maternity services is not the solution. However, defining and communicating the risk of delaying childbirth for society may speed policy movements that could support earlier childbearing, such as paid maternity leave and flexible arrangements for return to work.

The UK is the world leader in the systematic examination and review of maternal deaths and has pioneered another world class process in UKOSS for the study of rare conditions in pregnancy. But even in the UK, limitations in the data collected restrict the meaningful interpretation of inequalities in health outcomes. For example, country of birth, main language spoken at home, socioeconomic status, and years in the UK are recommended as supplementary variables to race and ethnicity to help understand the influence of ethnicity on poor maternal health.[10] Databases in the UK and in other developed countries could be improved by the routine collection of these variables for all childbearing women. Accurate, well defined data are necessary to improve our understanding of maternal health inequalities and to develop targeted policy and intervention or support strategies.

1 WHO. *Maternal mortality in 2005. Estimates developed by WHO, UNICEF, UNFPA and the World Bank.* 2007. www.who.int/whosis/mme_2005.pdf.
2 Knight M, Kurinczuk JJ, Spark P, Brocklehurst P; on behalf of UKOSS. Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities. *BMJ* 2009;338:b542.
3 Waterstone M, Bewley S, Wolfe C. Incidence and predictors of severe obstetric morbidity: case-control study. *BMJ* 2001;322:1089-94.
4 Mantel GD, Buchmann E, Rees H, Pattinson RC. Severe acute maternal morbidity: a pilot study of a definition for a near-miss. *Br J Obstet Gynaecol* 1998;105:985-90.
5 Ahdieh L, Hahn RA. Use of the terms "race," "ethnicity," and "national origins": a review of articles in the American Journal of Public Health, 1980-1989. *Ethn Health* 1996;1:95-8.
6 Senior P, Bhopal R. Ethnicity as a variable in epidemiological research. *BMJ* 1994;309:327-30.
7 Bhopal R. Race and ethnicity: responsible use from epidemiological and public health perspectives. *J Law Med Ethics* 2006;3:500-7.
8 De Swiet M. Maternal mortality in the developed world: lessons from the UK confidential enquiry. *Obstet Med* 2008;1:7-10.
9 Sullivan E, King J. *Maternal deaths in Australia 2000-2002.* Maternal deaths series 2. Catalogue no PER 32. Sydney: AIHW National Perinatal Statistics Unit. 2006,
10 McKenzie K, Crowcroft N. Describing race, ethnicity, and culture in medical research. *BMJ* 1996;312:1054.

Treatment of intermittent claudication

Should improve both symptoms and cardiovascular risk

RESEARCH, p 704

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Peripheral artery disease of the lower extremities affects more than one in 10 people aged over 55 years.[1 2] Half of those affected present with leg symptoms that limit physical activity and impair quality of life.[1] The most feared complication is loss of limbs, but only 1-3% of those presenting with intermittent claudication progress to amputation over five years.[3] Myocardial infarction and stroke resulting from progressive atherogenesis in other vascular beds are far more common—15% to 30% of people presenting with peripheral artery disease die within five years, mainly from cardiovascular causes.[4]

In the linked meta-analysis, De Backer and colleagues assess the effects of the orally active vasodilator naftidrofuryl on pain-free walking distance in patients with intermittent claudication.[5]

The most important goal of medical treatment in patients with peripheral artery disease of the lower extremities is the prevention of systemic cardiovascular complications.[6] Many treatments that prevent myocardial infarction and stroke also improve leg symptoms (see table on bmj.com), but specific treatments for intermittent claudication have been developed. One such treatment is naftidrofuryl, which has been available for more than 20 years in Europe but is not approved in North America. Naftidrofuryl has been evaluated in multiple randomised controlled trials (RCTs) for the treatment of claudication, but its efficacy is uncertain

because the trials were small and heterogeneous.

De Backer and colleagues' meta-analysis of individual patient data compares the effect of naftidrofuryl 200 mg taken three times daily with that of placebo on pain-free walking distance in patients with intermittent claudication. They indentified 11 potentially eligible RCTs but included only six in their primary analysis; four were excluded because of poor study quality or incomplete availability of individual patient data, and a fifth was included only as part of a sensitivity analysis. The pooled data indicate that naftidrofuryl significantly improved pain-free walking distance compared with placebo (relative risk 1.37, 95% confidence interval 1.27 to 1.49). They also found a similar improvement in maximum walking distance. Results were similar when poor quality studies were included. The authors also reported drug company data indicating that, compared with placebo, naftidrofuryl is associated with a 75% relative increase (25% to 145%) and a 2.85% absolute increase (0.78% to 4.91%) in "gastric" disorders.

The mechanism of action of naftidrofuryl is not well understood. The increase in walking distance is probably explained by peripheral vasodilatation resulting from inhibition of the 5-hydroxytryptamine 2 receptor, which blocks the effects of serotonin, and possibly inhibition of platelet aggregation. Naftidrofuryl has been reported to reduce angina, which might also contribute to the improvement in walking distance.[7]

Several other vasodilators have been evaluated for the management of claudication in patients with peripheral artery disease. The best studied is cilostazol, a phosphodiesterase inhibitor that improves claudication distance by about 50% compared with placebo.[8] However, aspirin was not permitted in most trials of cilostazol, and it is unclear how much of the improvement results from vasodilatation rather than the drug's antiplatelet effects. Cilostazol and naftidrofuryl have not been compared head to head in an RCT. Preliminary data indicate that verapamil, buflomedil, and prostaglandins (alprostadil, epoprostenol, and beraprost) might also improve walking distance in patients with claudication, but these results require confirmation.

De Backer and colleagues' results seem to provide convincing evidence for the efficacy of naftidrofuryl in the treatment of patients with claudication. However, several caveats should be considered. Firstly, most of the trials included in the meta-analysis were performed in the 1980s and early 1990s, before the widespread use of antiplatelet agents and statins, which can both prevent cardiovascular events and improve walking distance.[4 9 10] It is unclear whether naftidrofuryl provides incremental benefit in patients with peripheral artery disease receiving antiplatelet treatment, a statin, blood pressure lowering treatment, and an angiotensin converting enzyme inhibitor.[6] Secondly, naftidrofuryl was evaluated for a mean of only 6.3 months in the trials included in the meta-analysis, and it is unclear whether the benefits are sustained in the long term. Thirdly, the number of patients enrolled to date in randomised trials of naftidrofuryl is modest, and safety data are limited. There were neurological and cardiovascular safety concerns with the intravenous preparation of naftidrofuryl,[11] and additional data on the oral preparation would provide reassurance that it is safe.

What are the implications of De Backer and colleagues' findings for clinical practice and future research? In the treatment of patients with claudication, the relief of symptoms should proceed along with efforts to reduce the risk of systemic cardiovascular complications. Thus, first line medical treatment of peripheral artery disease should consist of interventions that effectively relieve symptoms and reduce cardiovascular risk (table).

Patients should be encouraged to "stop smoking and keep walking," and drugs should include aspirin (or clopidogrel), a statin, a blood pressure lowering agent, and an angiotensin converting enzyme inhibitor.[6] Unfortunately these drugs are underused in patients with peripheral artery disease.[12] Vasodilators such as naftidrofuryl or cilostazol might be considered in patients who have claudication symptoms that are refractory to conventional treatment. However, their role will probably remain uncertain until it is shown in RCTs that they provide incremental benefit in patients receiving currently established treatments that reduce systemic complications and leg symptoms.

1 Fowkes FG, Housley E, Cawood EH, Macintyre CC, Ruckley CV, Prescott RJ. Edinburgh Artery Study: prevalence of asymptomatic and symptomatic peripheral arterial disease in the general population. *Int J Epidemiol* 1991;20:384-92.
2 Gregg EW, Sorlie P, Paulose-Ram R, Gu Q, Eberhardt MS, Wolz M, et al. Prevalence of lower-extremity disease in the US adult population ≥40 years of age with and without diabetes: 1999-2000 national health and nutrition examination survey. *Diabetes Care* 2004;27:1591-7.
3 Dormandy J, Mahir M, Ascady G, Balsano F, De Leeuw P, Blombery P, et al. Fate of the patient with chronic leg ischaemia. A review article. *J Cardiovasc Surg (Torino)* 1989;30:50-7.
4 Hankey GJ, Norman PE, Eikelboom JW. Medical treatment of peripheral arterial disease. *JAMA* 2006;295:547-53.
5 De Backer T, Vander Stichele R, Lehert P, Van Bortel L. Naftidrofuryl for intermittent claudication: meta-analysis based on individual patient data. *BMJ* 2009;338:b603.
6 Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic). *Circulation* 2006;113:e463-654.
7 Hirsch JL, Bensoussan JJ, Mosnier M, Lehert P. Evaluation of the efficacy and tolerance of naftidrofuryl in patients presenting with exertional angina. Multicenter double-blind versus placebo study [in French]. *Ann Cardiol Angeiol (Paris)* 1999;48:137-45.
8 Robless P, Mikhailidis DP, Stansby GP. Cilostazol for peripheral arterial disease. *Cochrane Database Syst Rev* 2008;(1):CD003748.
9 Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994;344:1383-9.
10 Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000;342:145-53.
11 Smith FB, Bradbury AW, Fowkes FG. Intravenous naftidrofuryl for critical limb ischaemia. *Cochrane Database Syst Rev* 2000;(2):CD002070.
12 Cacoub PP, Abola MT, Baumgartner I, Bhatt DL, Creager MA, Liau CS, et al. Cardiovascular risk factor control and outcomes in peripheral artery disease patients in the reduction of atherothrombosis for continued health (REACH) registry. *Atherosclerosis* 2008 Oct 31 [Epub ahead of print].