Anticoagulation in people with atrial fibrillation

Risk prediction tools help, but treatment must be tailored individually

A cornerstone of managing patients with atrial fibrillation is deciding whether or not to prescribe an anticoagulant. Despite strong evidence supporting the efficacy of anticoagulants in preventing thromboembolism related to atrial fibrillation, many people with atrial fibrillation—even those with multiple risk factors for stroke—are not prescribed these drugs. To help clinicians decide on which management path to choose, several tools have been developed to estimate the risk of stroke on the basis of clinical factors. The performance of two such risk tools is described in the linked cohort study by Olesen and colleagues.

One widely used risk scheme is the CHADS₂ index, an acronym representing Congestive heart failure, Hypertension, Age over 75, Diabetes, and previous Stroke, which can easily be applied in general clinical practice. However, like other risk schemes, this index is only moderately accurate at separating patients into different categories of stroke risk. Large numbers of patients considered at high risk for stroke—in whom anticoagulants would be recommended—will not have a stroke. Conversely, some people deemed to have a low risk of stroke, who would therefore avoid anticoagulation, will have a stroke. Hence, more accurate ways of separating people who truly are at low risk from those who would benefit from anticoagulants are actively being sought.

Olesen and colleagues compared the performance of the CHADS₂ index with the more recently developed CHA₂DS-VASc score by applying both schemes to a large nationwide registry of patients admitted to hospital with atrial fibrillation in Denmark. The CHA₂DS-VASc score differs from CHADS₂, in that age is weighted differently. In addition, CHA₂DS-VASc considers female sex and a history of vascular disease to be significant risk factors for stroke. Although the C statistics, which measure a risk scheme’s ability to discriminate between people who will have an outcome and those who will not, were similar when the two risk schemes were tested as continuous point scales, CHA₂DS-VASc had unusually high C statistics when applied using categories of “low,” “intermediate,” and “high” risk groups. This might be related to the selected cut-off points of risk. The annual stroke rate in the CHA₂DS-VASc low risk group (0 points) was 0.78% at one year, compared with 1.67% in the CHADS₂, low risk group. Although pulmonary embolism was included as an outcome and may have inflated the event rates, the core results did not seem to change when pulmonary embolism was removed from the analysis.

Should this study then encourage broader use of CHA₂DS-VASc? An expert task force of the European Society of Cardiology suggested that a CHA₂DS-VASc based approach to estimating stroke risk be used in patients with multiple “clinically relevant non-major” risk factors for stroke. Because age 65 or more and female sex are considered relevant risk factors, essentially the only people who meet the “truly low risk” category are men under 65. In Olesen and colleagues’ study, only 8.7% of the study population met the low risk CHA₂DS-VASc criteria, compared with 22.3% when using the CHADS₂ criteria. This finding is similar to that seen in other assessments of the index, including a large UK study in which only 8.6% of patients with atrial fibrillation in general practice were considered low risk by CHA₂DS-VASc. If the CHA₂DS-VASc criteria were adopted most people with atrial fibrillation would be offered anticoagulation. In Olesen and colleagues’ study, 80% of the patients were considered high risk using CHA₂DS-VASc; fewer than half would meet high risk criteria if CHADS₂ were used.

Should all women with atrial fibrillation be deemed at intermediate risk at least and therefore be considered for anticoagulation? Sex has an inconsistent association with stroke—some observational studies have found higher rates of atrial fibrillation related stroke in women, whereas others have not. A history of vascular disease has not been clearly established as a risk factor either.

Nevertheless, CHA₂DS-VASc does seem to be better than CHADS₂, at identifying those people who are at very low risk. An important consideration for future studies is whether the development of alternative treatments that are easier to use and potentially safer than vitamin K antagonists should induce clinicians to lower the threshold at which they prescribe anticoagulants. For example, the direct thrombin inhibitor dabigatran may result in fewer intracranial haemorrhages than treatment with warfarin in patients with atrial fibrillation. If anticoagulation becomes safer, it might be recommended for use in more patients with atrial fibrillation, particularly those at intermediate or even low risk of stroke. This is an area where consideration must be given to the patient’s preference, the balance between absolute benefit and risk, and the costs of care. Where these thresholds ought to be set is an area that needs further investigation.

**Chest compression or conventional CPR after out of hospital cardiac arrest?**

Definitive evidence is lacking, but either is better than no CPR

The proportion of people with cardiac arrest who receive bystander cardiopulmonary resuscitation (CPR) before the arrival of an ambulance remains suboptimal. This is disappointing considering the substantial effort over many decades to promote bystander CPR. Reasons for the public not starting resuscitation include fear of infection, fear of litigation, and the complexity of conventional CPR. Consequently, it might be possible to improve participation in community CPR by removing the rescue breathing component of conventional CPR. However, such a strategy would be acceptable only if outcomes were at least similar for compression only CPR to those seen for conventional CPR.

In the linked observational study, Ogawa and colleagues report that one month survival after out of hospital arrest is significantly better with conventional CPR than compression only CPR (adjusted odds ratio 1.17, 95% confidence interval 1.06 to 1.29). The authors also found that this benefit was most pronounced in younger patients and when resuscitation was delayed. In particular, conventional CPR had significantly better outcomes for cases of non-cardiac origin when the patient was under 20 years old (4.65, 1.46 to 14.81), and in cases of cardiac origin where resuscitation was delayed by nine to 10 minutes (7.36, 2.07 to 26.20). These better outcomes may be a result of the ventilation and oxygenation provided by conventional CPR correcting global hypoxia, which is more prevalent in the two situations above. These findings contradict previously published studies so it is reasonable to put them into the context of current recommendations.

A previous observational study found better survival and neurological outcomes with compression only CPR in specific subgroups of patients who were apnoeic, had a shockable rhythm, or in whom CPR was started within four minutes. Also, any resuscitation was better than no resuscitation. Other observational studies have shown no difference in survival between conventional and compression only CPR. Some of these findings have been interpreted, possibly erroneously, as both strategies being equally effective. Interestingly, these same studies have also shown better outcomes for conventional CPR in particular subgroups of patients defined by either the patient’s age or the duration of arrest before resuscitation started.

Several trials of compression only CPR being performed by emergency medical systems personnel have found better outcomes with this strategy, but it is unclear how generalisable these findings are to a public setting.

The controversy about which type of resuscitation is most effective reflects the difficulty in interpreting evidence in the absence of randomised controlled trials. Observational data are interesting but cannot provide a definitive answer. However, developers of resuscitation guidelines have no choice but to base their recommendations on these methodologically weak data. This position is not uncommon when establishing resuscitation guidelines because undertaking randomised trials in resuscitation is logistically and ethically difficult.

The situation is reflected in the recently published consensus of science statements of the International Liaison Committee on Resuscitation (ILCOR) for conventional versus compression only CPR. Consistent with the evidence they have recommended that all people who have had a cardiac arrest should receive chest compressions at the very least. This recognises that any attempt at resuscitation is better than no attempt and focuses on increasing the community CPR participation rate by removing those aspects known to be a barrier to starting CPR, such as rescue breathing. ILCOR further recommends that people trained in conventional CPR and health professionals should perform conventional CPR.

Strategies to increase bystander resuscitation should be encouraged, but not to the abandonment of conventional CPR. Compression only CPR should be viewed as the first resuscitation step, which should be followed as soon as possible by rescue breathing and other basic life support interventions. Controversy will continue until evidence is available from randomised controlled trials, although such studies are unlikely to occur at the community bystander level. What is clear is that any intervention to increase the number of patients receiving CPR, including the use of chest compression only CPR, would improve outcomes after cardiac arrest.
Primary prevention of cardiovascular disease

The current model in the UK is not necessarily the right one or the only one

Two linked analysis articles and one research study on aspects of prevention of cardiovascular disease raise concerns as to what measures are the most efficient and cost effective. Despite major initiatives and improvements in the prevention of cardiovascular disease, increases in obesity and diabetes have the potential to worsen rather than improve future outcomes.

Severe hypertension and familial hypercholesterolaemia are single risk factors for cardiovascular disease, but blood pressure and cholesterol are measured on a continuous scale and risk of cardiovascular disease is multifactorial. Guidelines from the United States and United Kingdom cover the identification of people who are at high risk from multifactorial causes, but these guidelines are due for revision shortly.

Most events occur in people with modest values of cholesterol (or low density lipoprotein-cholesterol) that overlap with those seen in people without cardiovascular disease, and Hingorani and Hemingway debate whether to target high risk people or screen whole populations. They favour wider eligibility for treatment with inexpensive generic statins and a wider population effort to reduce cardiovascular disease. However, a previous editorial in the BMJ concluded that although universal screening was cost effective compared with no screening, small gains did not justify the extra cost compared with targeted screening.

Secondary prevention of cardiovascular disease should be straightforward, but not all people with the disease are treated and many are not treated optimally. Even people at very high risk are often not identified for primary prevention, let alone treatment. Only 15% of 120 000 people with familial hypercholesterolaemia in the UK are identified and, when one family member has had an event, family cascade screening is being implemented only patchily. People at high risk may be identified at casual consultations, but the National Institute for Health and Clinical Excellence advised a formal process. Primary care should undertake “virtual” patient assessments from practice computer records, impute missing values, and call people who might be at higher risk for full profiling and management.

Khunti and colleagues discuss the NHS health checks programme, which extended screening to everyone aged 40-75 years for cardiovascular disease and metabolic factors. This major programme has been modelled but not fully implemented, and pilot schemes have shown variable results. Screening may do no physical harm but some people find it emotionally distressing. Apart from drug treatment, can we provide appropriate and effective lifestyle changes for so many people when adherence is known to be poor, especially in people who are difficult to reach? Geographical variation of implementation and appropriate outcome audit are important factors in determining practicality and cost effectiveness and in tackling inequalities.

With the present financial pressures will there be enough local uniform and appropriate funding? The current quality and outcomes framework in primary care does not fully incentivise screening for cardiovascular disease risk. Its targets are too conservative compared with the extensive evidence base, which shows benefit from additional lowering of low density lipoprotein-cholesterol in the population at risk (down to low density lipoprotein-cholesterol values below 1.8 mmol/L in those at risk). Serumaga and colleagues found that these payments to primary care had no effect on controlling hypertension. Health Service for England 1998-2008 data also show limited improvement in the management of blood pressure in patients with hypertension. However, for lipids, treatment has increased over this period for men with coronary heart disease (22% to 76%), stroke (6% to 47%), and diabetes (7% to 61%) (data from www.ic.nhs.uk/statistics-and-data-collections). EuroAspire-III data (comparing 1995, 2000, and 2007) show that the UK is in the top three of 22 European countries for achieving blood pressure and cholesterol targets for secondary prevention. For primary prevention, the UK was second best of 12 European countries for non-smoking rates, and for achieving blood pressure targets it was fourth for people without diabetes and second for those with diabetes. The UK was best (by at least 20% more than other countries) at reaching targets for cholesterol. However, much more could be done to achieve effective prevention in all high risk patients.
Targeted identification is more cost effective but identifies fewer people than NHS population screening health checks. All those identified will need dietary and lifestyle advice, and large numbers of “well” people will be identified for drug treatment. Perhaps half of asymptomatic men would be eligible for statins in their last 25 years of life, which raises concerns about “medicalising” such large numbers of people. Equality of access and treatment requires particular efforts to include those from deprived backgrounds, who are often at higher risk, and to improve concordance of those who are normally poor medical attendees. NHS cardiovascular disease health checks will need to involve these groups and not be over-represented by the “worried well” or “semi-worried, semi-well.” Financial pressures may limit screening implementation and lead to patchy uptake.

The goal is to identify, treat, and treat to target high risk individuals. Adoption of one method should not preclude the use of others, and the NHS health checks programme must not prevent other pathways. Practitioners should target patients with cardiovascular disease and those in known risk groups, identifying some opportunistically. Cascade screening is needed for families affected by premature cardiovascular disease (such as familial hypercholesterolaemia). An arbitrary treatment threshold of 20% risk over 10 years will limit numbers, although treatment is clinically effective and cost effective at a 10% risk over 10 year threshold if low priced statins are used. An individual who is a little below the 20% risk over 10 year threshold who wants treatment after full counselling should not be denied, and perhaps lifetime rather than 10 year risk thresholds should be used. The NHS health checks programme is not the only answer and not the only way to go.

Adverse outcomes from IVF
Should be systematically reported so that lessons can be learnt and appropriate action taken

The fundamental measure of women’s health and maternity services—maternal mortality—has been creeping up for two decades in the United Kingdom, and more recently in the United States, Denmark, Austria, Canada, and Norway.1 The first published case report of a maternal death related to in vitro fertilisation (IVF) predicted that maternal morbidity and mortality would rise with increasing use of assisted reproductive technologies as a result of pregnancies at an older age, multiple pregnancies, and pre-eclampsia.3

The most comprehensive work on this topic to date, which used multiple sources of information, including 24 years of the Dutch maternal mortality database,4 examined the late effects of ovarian hyperstimulation syndrome and other deaths related to IVF to derive estimates of mortality. With 23 pregnancy related deaths and conservative assumptions, the study showed convincingly that overall mortality in IVF pregnancies was higher than the maternal mortality rate in the general population in the Netherlands. Compared with the national maternal mortality rate (12.8/100 000),5 it was estimated that 6/100 000 were directly related to IVF and 42.5/100 000 were related to IVF pregnancy. No other sizeable studies have directly tackled this question.

The NHS Choices website emphasises that maternal death is rare, and it found the lack of deaths from ovarian hyperstimulation syndrome after 1997 in the Dutch study reassuring, notwithstanding the continued occurrence of such deaths in the UK. The last Confidential Enquiry into Maternal Death recorded four deaths directly related to IVF via ovarian hyperstimulation syndrome and three deaths related to multiple pregnancy after IVF.7 Thus, more deaths were related to ovarian hyperstimulation syndrome than to abortion (two) despite many fewer procedures (for example, 48 829 IVF cycles v 198 500 abortions were performed in the UK in 2007).7 IVF associated maternal deaths may be underestimates, because record linkage is not allowed by the Human Fertilisation and Embryology Act, and some women do not disclose assisted reproduction or egg donation to maternity services. The assessors noted “important lessons for the provision of infertility treatment . . . which is not currently subjected to such critical review,” and that “many of the women
Prevention and control of chronic diseases

A UN General Assembly meeting is a unique opportunity to put them on the world’s agenda

Chronic diseases—cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes—are the leading global causes of death. Mental illnesses, injuries, osteoarthritis, and chronic kidney diseases also contribute substantially to disability but are often excluded from consideration. Of 58.8 million deaths globally, 60% were attributed to chronic diseases in 2004.1 Even in sub-Saharan Africa, where infectious diseases remain the major disease burden, with AIDS as the single leading cause of death, chronic diseases account for 25% of all deaths. Deaths from chronic diseases are projected to increase dramatically between now and 2030.2

Chronic diseases are a heterogeneous group but many share underlying causes. Direct causes and risk factors for chronic disease, such as high blood pressure, diabetes, and raised blood lipids, are linked to lifestyle factors—for example, smoking, unhealthy eating, and physical inactivity. Although it is not unusual to blame individuals for their behaviours, societal factors often determine these behaviours.3 Such factors include the promotion of tobacco; the high levels of saturated and trans-fats, sugars, and salt hidden in processed foods; and urbanisation. Lack of progress on the control of chronic diseases is one of the major obstacles to achieving the health related millennium development goals.4
Myths about chronic disease have contributed to their neglect. A first myth is that they are “diseases of affluence,” which places them outside of a global concern with poverty. In fact, risk factors are socially patterned—rates of smoking are higher in poorer people, and age-standardised mortality rates for chronic diseases are almost twice as high in low income countries as in high income ones. A second myth is that “you have to die from something,” and that chronic diseases are not a cause of premature death. In fact, about 60% of chronic disease deaths in low and middle income countries occur in people aged under 60 years. A third myth is that no cost effective interventions exist. In fact, highly cost effective interventions are available to prevent and control common chronic diseases. Tobacco control, together with population wide restriction of salt, would stop 13.8 million premature deaths over 10 years in low and middle income countries and would cost about $0.5 (€0.3; €0.4) per person per year. Treating people at high risk of cardiovascular disease with aspirin, a statin, and two blood pressure lowering drugs is highly cost effective and would save about as many premature deaths as the population strategies. However, focusing on the distal determinants by means of fiscal and legal mechanisms is more attractive than individual interventions because this can provide a final “fix,” whereas individual interventions require continued surveillance, diagnosis, and treatment.

There are many other reasons why chronic diseases have not yet acquired their place at the top of the world’s health and political agendas. These include lack of unified international leadership and of powerful actors and community activists, including people affected by the diseases; lack of a clear and unified strategy, in particular about how to tackle the problem and at what cost; an emphasis on technical debates and on treatment, instead of creating and using favourable political contexts; a lack of documentation and of recognition of the role of chronic diseases in the alleviation of poverty, which is also reflected by their absence from the millennium development goals.

The decision by the United Nations General Assembly to convene a “high level meeting on the prevention and control of non-communicable diseases worldwide” in September 2011 provides a unique opportunity to elevate chronic diseases to the global political agenda—just as the 2001 UN General Assembly special session on HIV/AIDS was a tipping point in the global response to AIDS. However, generating such a paradigm shift for the global response to chronic diseases will require a dramatic change in how they are framed and linked with global development and the alleviation of poverty; a well coordinated alliance across the various disease constituencies (as initiated by the NCD Alliance) and funders (Global Alliance for Chronic Diseases); and a unified strategy including technical consensus on cost effective solutions.

UN sessions tend to pass very general resolutions and agree on grandiose goals, with little accountability. Crucially, therefore, the chronic disease communities must develop as soon as possible the concrete “ask” for this UN session—a platform for action for political negotiation by UN member states. Elements of such a call to action include full and immediate implementation of the Framework Convention on Tobacco Control by all member states; endorsement of the World Health Organization’s strategy on non-communicable diseases; regulation of the salt, fat, and sugar content of processed foods; elimination of national and European Union subsidies for harmful crops; and access to essential treatments for the most common chronic diseases, which will require the strengthening of health systems. A strong declaration would set specific goals for reducing the incidence and burden of chronic diseases, and possibly for funding these efforts, as well as committing to public policy audits of health impacts in various sectors such as education, employment, transport, urban and rural development. Lobbying for the specific inclusion of every single disease or for technical elements—as important as they may be—would be counterproductive, because this would risk dividing the field, creating confusion among diplomats, and diverting attention from the core agenda, which by definition is political in the General Assembly.

Finally, besides a unified platform, the road map to a successful high level session requires three forces to work in synergy. Firstly, political champions among the UN member states, including a few permanent representatives in New York who are willing to dedicate a large proportion of their time to the preparation of the session. Secondly, a proactive secretariat in New York within the UN system to support political process and ensure technical accuracy (this may require the appointment by the UN secretariat general of a personal representative for 12 months, with support from WHO). And, lastly, a unified activist civil society, comprising not only disease specialists and public health experts, but also businesses and the people directly concerned, such as patients with diabetes and survivors of breast cancer, because such people have been powerful agents in the AIDS movement.

Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coiDisclosure.pdf (available on request from the corresponding author) and declare: PP had no support from any organisation and SE had support from the Wellcome Trust for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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