



30 days in medicine

Nurse-led management of chronic diseases

This study of 38 public sector primary care clinics in the Western Cape Province, South Africa (SA), suggests that training nurses in the use of a management tool involving an expanded role in managing non-communicable diseases (NCDs) is safe and feasible, but did not result in treatment intensification or improved case detection for index diseases. However, the intervention, with some adjustment, has been adopted for implementation in primary care clinics throughout SA. Primary Care 101 (PC101) is a programme designed to support and expand nurses' role in NCD care, and is made up of educational outreach and a clinical management tool with enhanced prescribing provisions. Nurses in the intervention clinics were trained to use the PC101 management tool during educational outreach sessions delivered by health department trainers and were authorised to prescribe an expanded range of drugs for several NCDs. Control clinics continued use of the Practical Approach to Lung Health and HIV/AIDS in South Africa (PALSA PLUS) management tool and usual training. Patients attending these clinics with one or more of hypertension ($n=3\ 227$), diabetes ($n=1\ 842$) or chronic respiratory disease ($n=1\ 157$) or who screened positive for depression ($n=2\ 466$), totalling 4 393 patients, were enrolled between 28 March 2011 and 10 November 2011. Primary outcomes were treatment intensification in the hypertension, diabetes, and chronic respiratory disease cohorts, defined as the proportion of patients in whom treatment was escalated during follow-up over 14 months, and case detection in the depression cohort. However, treatment intensification rates in the intervention clinics were no better than those in the control clinics.

Fairall LR, Folb N, Timmerman V, et al. Educational outreach with an integrated clinical tool for nurse-led non-communicable chronic disease management in primary care in South Africa: A pragmatic cluster randomised controlled trial. *PLoS Med* 2016. <http://dx.doi.org/10.1371/journal.pmed.1002178> (published 22 November 2016).

Minimally invasive autopsy: Identifying the cause of death in Mozambique

An observational study that coupled minimally invasive autopsy (MIA) and complete diagnostic autopsy (CDA) performed in 112 dead patients in Mozambique suggests that the simple MIA can identify the cause of many adult deaths. In many low-income regions, current methods used to identify cause of death (verbal autopsy, clinical records and complete autopsies) are either inaccurate, not feasible or poorly accepted. In this study, the MIA analyses were done blindly, with no knowledge of the clinical data or the results of the CDA, and the MIA diagnosis was compared with the CDA diagnosis of cause of death. CDA diagnoses comprised infectious diseases ($n=80$, 71.4%), malignant tumours ($n=16$, 14.3%), and other diseases, including non-infectious cardiovascular, gastrointestinal, kidney, and lung diseases ($n=16$, 14.3%). An MIA diagnosis was obtained in 100/112 cases (89.2%). The overall concordance between the MIA diagnosis and CDA diagnosis was 75.9% (85/112). The concordance was higher for infectious diseases and malignant tumours (63/80 (78.8%) and 13/16 (81.3%), respectively) than for other diseases (9/16, 56.2%). The specific micro-organisms causing death were identified in the MIA in 62/74 (83.8%) of the infectious disease deaths with a recognised cause. This tool could have a major role in improving the understanding and surveillance of causes

of death in areas where infectious diseases are a common cause of mortality.

Castillo P, Martinez MJ, Ussene E, et al. Validity of a minimally invasive autopsy for cause of death determination in adults in Mozambique: An observational study. *PLoS Med* 2016. <http://dx.doi.org/10.1371/journal.pmed.1002171> (published 22 November 2016).

Diet, lifestyle, body mass index and mortality

In this longitudinal study, with up to 32 years of follow-up of 74 582 women from the Nurses' Health Study and 39 284 men from the Health Professionals Follow-up Study, the conclusions were that although people with a high BMI can have lower risk of premature mortality if they also have at least one low risk lifestyle factor, the lowest risk of premature mortality is those with a BMI in the range 18.5 - 22.4, with high scores on healthy eating and physical activity, moderate alcohol intake and who do not smoke. During the 32 years of follow-up there were more deaths from cancer ($n=10\ 808$) than from cardiovascular disease ($n=189$) – interesting in itself. A combination of at least three low-risk lifestyle factors, along with the range of BMI mentioned, was associated with the lowest risk of all cause and cardiovascular mortality. The greatest risk was found in those with a BMI in the range 22.5 - 24.9 with none of the four low risk lifestyle factors.

Veronese N, Li Y, Monson JE, et al. Combined associations of body weight and lifestyle factors with all cause and cause specific mortality in men and women: Prospective cohort study. *BMJ* 2016;355:i5855. <http://dx.doi.org/10.1136/bmj.i5855> (published 24 November 2016).

Methylprednisone injected through the eardrum effective in combating Ménière's symptoms

A recent study published in *The Lancet* shows that injections of the steroid methylprednisone through the eardrum are as effective as current standard treatment of gentamicin in reducing the dizziness associated with Ménière's disease, but without the associated risk of hearing loss. This current treatment relies on the ototoxic effect of the antibiotic, and around 20% of patients are left with permanent hearing loss. In this double-blind trial, 60 patients with unilateral Ménière's disease were randomly assigned to two intratympanic injections of methylprednisone or gentamicin, given 2 weeks apart. Patients treated with methylprednisone showed a 90% reduction in the mean number of attacks they experienced, from 16.4 in the 6 months before treatment to 1.6 at 18 - 24 months after treatment. This compared with an 87% reduction in attacks with gentamicin, from a mean of 19.9 to 2.5.

Patel M, Agarwal K, Arshad Q, et al. Intratympanic methylprednisolone versus gentamicin in patients with unilateral Ménière's disease: A randomised, double-blind, comparative effectiveness trial. *Lancet* 2016;388(10061):2753-2762. [http://dx.doi.org/10.1016/S0140-6736\(16\)31461-1](http://dx.doi.org/10.1016/S0140-6736(16)31461-1)

Prediabetes associated with increased risk of cardiovascular and all-cause mortality

A meta-analysis of 53 prospective cohort studies with 1 611 339 individuals suggests that prediabetes is associated with an increased risk of cardiovascular disease. The analysis looked at different definitions of prediabetes and for associations between the risk of composite cardiovascular disease, coronary heart disease, stroke, all-cause mortality and prediabetes. Prediabetes was defined as

impaired fasting glucose level according to the criteria of the American Diabetes Association (IFG-ADA; fasting glucose 5.6 - 6.9 mmol/L), the WHO expert group (IFG-WHO; fasting glucose 6.1 - 6.9 mmol/L), impaired glucose tolerance (2-hour plasma glucose concentration 7.8 - 11.0 mmol/L during an oral glucose tolerance test), or raised glycated haemoglobin (HbA1c) of 39 - 47 mmol/mol (5.7 - 6.4%) according to American Diabetes Association criteria or 42 - 47 mmol/mol (6.0 - 6.4%) according to the National Institute for Health and Care Excellence (NICE) guideline. Increases in HbA1c to 39 - 47 mmol/mol or 42 - 47 mmol/mol were both associated with an increased risk of composite cardiovascular disease (1.21 and 1.25, respectively) and coronary heart disease (1.15 and 1.28, respectively), but not with an increased risk of stroke and all-cause mortality.

Huang Y, Cai X, Mai W, Li M, Hu Y. Association between prediabetes and risk of cardiovascular disease and all cause mortality: Systematic review and meta-analysis. *BMJ* 2016;355:i5953. <http://dx.doi.org/10.1136/bmj.i5953> (published 23 November 2016).

E-cigarettes raise risk of persistent cough and wheeze in teenagers

A questionnaire administered to more than 2 000 teenagers aged between 16 and 18 years as part of the Southern California Children's Health Study showed that those who used e-cigarettes had twice the risk of respiratory symptoms such as persistent cough, bronchitis and wheeze as those who did not. The risk of bronchitis rose with frequency of use, from a two-thirds higher risk in teenagers who used e-cigarettes for 1 - 2 days in the previous months to two and a half times the risk in those using them on ≥ 3 days, when compared with never users. Just under a tenth (9.6%, $n=201$) of the adolescents who responded to the survey were current users of e-cigarettes, having used them at least once in the previous 30 days, 14.4% were past users, reporting that they had used e-cigarettes previously but not in the past month, and 76% said that they had never used e-cigarettes. E-cigarettes contain chemicals toxic to the lungs, including oxidant metals, glycerol vapour, diketone flavouring compounds and nicotine.

McConnell R, Barrington-Trimis JL, Wang K, et al. Electronic-cigarette use and respiratory symptoms in adolescents. *Am J Respir Crit Care Med* 2016. <http://www.atsjournals.org/doi/abs/10.1164/rccm.201604-0804OC> (published online 2 November 2016).

Alcohol consumption and different stroke types

Light and moderate alcohol consumption appears to be inversely associated with ischaemic stroke, while heavy drinking is associated with increased risk of all types of stroke, particularly haemorrhagic stroke, according to a meta-analysis conducted by Swedish researchers. Additional data from 73 587 Swedish adults in two prospective studies were included. Study-specific

results were combined in a random-effects model. The meta-analysis included 27 prospective studies with data on ischaemic stroke (25 studies), intracerebral haemorrhage (11 studies), and/or subarachnoid haemorrhage (11 studies). Light and moderate alcohol consumption was associated with a lower risk of ischaemic stroke, whereas high and heavy drinking was associated with an increased risk. Light and moderate alcohol drinking was not associated with any haemorrhagic stroke subtype. High alcohol consumption ($> 2 - 4$ drinks/day) was associated with a non-significant increased risk of both haemorrhagic stroke subtypes, and the relative risk for heavy drinking (> 4 drinks/day) was 1.67 for intracerebral haemorrhage and 1.82 for subarachnoid haemorrhage.

Larsson S, Wallin A, Wolk A, Markus HS. Differing association of alcohol consumption with different stroke types: A systematic review and meta-analysis. *BMC Med* 2016;14:178. <http://dx.doi.org/10.1186/s12916-016-0721-4>

Stage at breast cancer diagnosis and survival in sub-Saharan Africa

A recent meta-analysis of breast cancer stage at diagnosis in sub-Saharan Africa suggests that strategies for early diagnosis of breast cancer should be regarded as a major priority by cancer control programmes in the region. The authors included 83 studies, which consisted of 26 788 women from 17 sub-Saharan African countries. They found wide between-study heterogeneity in the percentage of later-stage disease at diagnosis. The percentage of patients with late-stage disease at diagnosis did not vary by region in black women, but was lower in non-black women from southern Africa than in black women in any region (absolute difference from black women in western Africa -18.1%), and higher for populations from mixed (urban and rural) settings rather than urban settings (13.2%, 5.7 - 20.7, in analyses restricted to black women). The percentage of patients with late-stage disease at diagnosis in black Africans decreased over time (-10.5% , $-19.3 - -1.6$; for 2000 or later v. 1980 or before), but it was still higher around 2010 than it was in white and black women in the USA 40 years previously. The incidence of breast cancer in sub-Saharan Africa is relatively low, but as survival from the disease in the region is poor, mortality rates are as high as in high-income countries. Stage at diagnosis is a major contributing factor to poor survival from breast cancer.

Jedy-Agba E, McCormack V, Adebamowo C, dos-Santos-Silva I. Stage at diagnosis of breast cancer in sub-Saharan Africa: A systematic review and meta-analysis. *Lancet Global Health* 2016;4(12):e923-e935. [http://dx.doi.org/10.1016/S2214-109X\(16\)30259-5](http://dx.doi.org/10.1016/S2214-109X(16)30259-5)

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