Living longer as an anaesthetist: The ‘magic’ lifestyle or the ‘lifestyle polypill’

Rodseth RN, MBChB, DA(SA), DCh(SA), FCA(SA)
Biccard BM, MBChB, FCA(SA), FFARCS(I), MMedSci

Department of Anaesthetics, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa

Correspondence to: Dr Bruce Biccard, e-mail: biccardb@ukzn.ac.za

SAJAA 2009; 15(4): 05-10

ABSTRACT
The central premise of this paper is that interventions that result in prolongation of human life are good for the individual. We examine three broad lifestyle activities (anaesthetic health and health risks, common health misconceptions, accepted lifestyle modifications to improve longevity) identifying interventions that have been reported to result in reductions in all-cause mortality. With regard to anaesthetic health and health risks, issues around life expectancy, anaesthetic mortality risks and suicide risks are examined. The negative effects of both acute and chronic sleep deprivation, as well as work and call stress on the health of the anaesthetist are identified and possible interventions to mitigate them are proposed. Common health misconceptions are addressed, with specific attention being given to the under-reported beneficial effects of coffee, alcohol and chocolate on longevity and health. Finally, accepted lifestyle modifications, including exercise, diet, aspirin and statins are discussed, and the possible utility and feasibility of the ‘poly pill’ is considered. In conclusion, we propose a ‘lifestyle calculator’ to assess the success of lifestyle interventions on all-cause mortality.

Introduction
We have set out to identify the factors that play a role in anaesthetic longevity and health, and to identify interventions that could improve both these aspects. The central premise of this paper is that interventions that result in prolongation of human life are good for the individual. We thus chose to look for interventions that reported reductions in all-cause mortality. All-cause mortality reductions supply us with a robust end point with which to assess the effectiveness of the interventions, and can be used to calculate the cumulative effect of each intervention. We applied this to three broad lifestyle activities, anaesthetic health and health risks, common health misconceptions, and currently accepted lifestyle modifications that improve longevity.

Life expectancy
The World Health Organization (WHO) life tables1 show that 50 year old South Africans, British, North American, Australian and New Zealand citizens have a life expectancy of 68, 81, 81, 84, and 85 years respectively. Clearly, without consideration of profession, anaesthetic practitioners in developing countries have a lower life expectancy than colleagues who have chosen to work in developed countries. In addition, there is the added health burden of living in a developing country with a high prevalence of infectious diseases, in addition to significant cardiovascular risk factors.2

Life expectancy and physicians
As physicians we can expect to have a substantially lower mortality over time, than the normal population.3 This holds true for anaesthetists who have a lower mortality (standardised mortality ratio 0.48, 95% CI 0.46–0.50) than that of the general American population, although suicide, drug, cerebrovascular and deaths from external causes were all significantly increased.4 This increased longevity may be related to the effect that education has on life expectancy, with people receiving twelve or more years of education having a life expectancy than colleagues who have chosen to work in developed countries. In addition, there is the added health burden of living in a developing country with a high prevalence of infectious diseases, in addition to significant cardiovascular risk factors.5

Health hazards to anaesthetists and health implications of anaesthesia
Mortality risks in anaesthesia
Anaesthetists are thought to be at a higher risk of death from suicide than both the general population and other specialist groups.6-11 In one of the largest studies, a comparison of the mortality between anaesthetists (n = 40242) and general internists (n = 40211) found standardised mortality rates for all physicians well below the national average, except for suicide. No difference could be found between anaesthetists and internists when examining all-cause mortality ratios, risks for cancer, heart disease and death from cerebrovascular disease (RR 1.39, 95% CI 1.08–1.79), but higher risk of death from suicide (risk ratio (RR) 1.45, 95% CI 1.07–1.97) and drug-related death (RR 1.53, 95% CI 1.08–1.79) were identified.3 Many explanations for this have been postulated, with suicidal thoughts and tendencies being associated with sleep disturbances, call and general work stress, and anaesthetic personality traits.12,13 In a postal survey of Finnish anaesthetists by Lindfors et al, a quarter of respondents indicated that they had considered suicide. The authors comment that, although higher than the 10% generally quoted for the general population, this is not higher than the incidence reported for other Finnish physicians.14 A study of anaesthetic personality types in Australian anaesthetists found the incidence of extreme personality traits (antisocial, cyclothymic, obsessive-compulsive, etc) to mirror that of the community.15 These similarities in thought patterns and incidence of personality disorders between the community and anaesthetists does not then adequately explain the higher incidence of suicide, suggesting that the key difference is the access to potentially lethal drugs, coupled with an understanding of how to utilise them. A study by Hawton et al found that up to 50% of anaesthetists used anaesthetic agents to commit suicide, while Alexander et al found a higher utilisation of opioids and opioid abuse, particularly in the first five years following graduation.16,17

Suicide prevention
A suicide prevention strategy formulated in New Zealand in 2006 has summarised the current international recommendations on suicide prevention.18 They identified three areas that have shown strong evidence of effectiveness. These are training for medical practitioners to improve the recognition and treatment of depression; the restriction of suicide methods by controlling the availability of potentially lethal drugs; and finally, enhancing the skills of gatekeepers in the community, organisations and institutions to improve their identification of those at risk. These recommendations have been echoed in a meta-analysis, which drew attention to the success of restricting access to highly lethal suicide means. This resulted in a decline in the annual suicide rate of 1.5–9.5% with the restriction of guns, 19–33% with domestic gas and 25% with barbiturates.19

Guest Editorial

5
Long term sleep deprivation – are your calls killing you? The impact of sustained sleep deprivation and disruption. Medical residents who worked extended shifts were found to have small but significantly increased blood levels of interleukin-6, high-sensitivity C-reactive protein (inflammatory markers that have been associated with increased long term cardiovascular risk) and norepinephrine. Shortened sleep duration is a risk factor for coronary artery calcification, a subclinical predictor of coronary heart disease. In a five year cohort study of 495 healthy middle-aged men and women, the measured incidence of calcification was 12.3% (n = 61) with a longer measured sleep duration being significantly associated with reduced calcification incidence (adjusted OR 0.67 per hour (95% CI 0.49 –0.91 per hour); p = 0.01). This would place these patients with increased coronary artery calcification at a ten fold higher risk of suffering a cardiac event. Short sleep duration has also been identified as an independent risk factor for hypertension after correcting for potential risk periods. Specific measures can be taken to modify risk when driving tired, focused mainly on increasing levels of alertness. The use of 150 mg of caffeine (two cups of coffee) or a 15 minute nap was found to reduce driving incidents. The impact of the intervention was dependant on the amount of sleep the subjects had obtained the previous night, with two hours duration of action if subjects had five hours of sleep the previous night, but only 30 minutes if no sleep had been obtained the previous night. The combination of 150 mg of caffeine and a nap was the most effective intervention in reducing incidents for up to two hours. The use of a functional energy drink containing 80 mg of caffeine, sucrose, glucose, taurine, glucuronolactone and vitamins, also reduced driving potential risk periods. Specific measures can be taken to modify risk when driving tired, focused mainly on increasing levels of alertness. The use of 150 mg of caffeine (two cups of coffee) or a 15 minute nap was found to reduce driving incidents. The impact of the intervention was dependant on the amount of sleep the subjects had obtained the previous night, with two hours duration of action if subjects had five hours of sleep the previous night, but only 30 minutes if no sleep had been obtained the previous night. The combination of 150 mg of caffeine and a nap was the most effective intervention in reducing incidents for up to two hours. The use of a functional energy drink containing 80 mg of caffeine, sucrose, glucose, taurine, glucuronolactone and vitamins, also reduced driving incidents and subjective sleepiness. It is imperative to realise that the use of these interventions marks the underlying problems of progressive sleepiness rather than addressing the root cause, the lack of sleep. Timing one’s drive home to correlate with the upsing in circadian rhythm (10:00) may be beneficial to driving performance.

Risk reduction when driving when tired

While not always practical, the avoidance of driving while fatigued is key. This situation is rectified by avoiding the situation where one is forced to drive after an extended period of wakefulness, such as at the end of an 18 or 24 hour call. Amendments to work hours as discussed above will reduce potential risk periods. Specific measures can be taken to modify risk when driving tired, focused mainly on increasing levels of alertness. The use of 150 mg of caffeine (two cups of coffee) or a 15 minute nap was found to reduce driving incidents. The impact of the intervention was dependant on the amount of sleep the subjects had obtained the previous night, with two hours duration of action if subjects had five hours of sleep the previous night, but only 30 minutes if no sleep had been obtained the previous night. The combination of 150 mg of caffeine and a nap was the most effective intervention in reducing incidents for up to two hours. The use of a functional energy drink containing 80 mg of caffeine, sucrose, glucose, taurine, glucuronolactone and vitamins, also reduced driving incidents and subjective sleepiness. It is imperative to realise that the use of these interventions marks the underlying problems of progressive sleepiness rather than addressing the root cause, the lack of sleep. Timing one’s drive home to correlate with the upsing in circadian rhythm (10:00) may be beneficial to driving performance.

Are your work demands shortening your life?

Work and call stress

The demands of a high stress or high demand work environment lead to physical and emotional stress. When this becomes excessive and the individual can no longer cope with the resultant stress, health may suffer as a result. A key aspect in determining how much stress can be successfully tolerated is seated in a concept known as decision latitude. Decision latitude is the ability of a worker to make decisions as to how and when work is done, allowing them the ability to develop coping strategies, supplying a sense of control over the situation. When decision latitude is limited and individuals experience high work demands, they may experience adverse health consequences.

An evaluation of Dutch specialists found support for this concept when they found that job satisfaction protected against high job stress and resulted in lower burnout scores.
than other Dutch health care professionals. When job stress was high and job satisfaction low, the risk for emotional exhaustion increased considerably. Key aspects as to how stress was experienced related to perceived working conditions and the effects of time pressure. These issues have been studied as they relate to anaesthesia specifically.12

While the levels of perceived stress were not higher than the average population, the most significant findings were that perceived lack of control over work results in work stress and loss of job satisfaction. Factors causing increased stress were related to time management (overtime, pressure from non-clinical tasks), work planning (getting the work schedule in advance, frequent changes during the day) and medical risk control (difficult intubation, high risk patients).13,14 These stress inducers seem to have been mitigated by high levels of job satisfaction, job challenge, work commitment and empowerment.15,16

The impact of sustained work stress on coronary heart disease has been evaluated in a meta-analysis by Kivimaki et al, in which they found an increased risk of coronary heart disease for high versus low job strain (RR 1.16, 95% CI 0.94–1.43). In a work combination of high efforts and low rewards this risk increased to 1.58 (95% CI 1.24–2.15).17

How then do we improve job satisfaction and allow anaesthetists to obtain more control over their work environment? Key aspects seem to be related to improved work organisation. This relates to aspects such as the planning and organisation of work, work scheduling and time control.18 Interestingly, one of the most effective stress reduction tools was the presence of a skilled assistant in theatre.19 After-hours work plays a significant role in stress induction and reductions in this field, while difficult to achieve, may have significant benefits.20

Common health misconceptions

There’s no such thing as too much coffee…

Coffee is one of the world’s most popular drinks with between 1.6 billion cups of coffee drunk per day. Coffee beans in their natural state have no flavour, with the roasting process developing the flavours of the coffee. Caffeol, referred to as the heart of the coffee bean, is a collective term referring to the many volatile compounds that make up coffee flavour and aroma. By manipulating the amount of roasting the bean, various flavour can be extracted. Roasting to 230°C delivers an intense heavier body flavour and is often used in Italian or French espresso. Water is then used to extract the caffeine resulting in a coffee infusion.57

230˚C delivers an intense heavier body flavour and is often used in Italian or French espresso. Water is then used to extract the caffeine resulting in a coffee infusion.57

One of the predominant chemicals contained in the coffee bean is caffeine, a xanthine alkaloid with a white bitter psychoactive and a mild diuretic effect. The average 150 ml cup of coffee contains an average of 115 mg of caffeine when produced by the drip method, 80 mg via the percolator and 65 mg when instant coffee is used. The average coffee user drinks 3–4 cups of instant coffee (300 mg of caffeine) a day. Tea provides less caffeine per cup, with average doses ranging from 30 to 60 mg per cup, while soft drinks contain 35–45 mg per unit.21

Caffeine impacts on human performance by improving cognitive performance and restoring impaired functioning. The use of caffeine has been shown to improve memory, logistical reasoning, free recall, numerical working memory and sentence verification accuracy.22 The improvement in the performance of complex tasks does not seem to be as strong as the improvement in attention and psychomotor performance and range from improvements in sleepy driver performance to faster sighting and trigger firing times in sleep-deprived marksmen.23,24

Although evidence for its improvement of sports performance is limited, caffeine has been shown to improve time to exhaustion in 30–60 min exercise.61 In 2004 the World Anti-doping Agency removed caffeine from the list of prohibited substances. Since then there has been increased utilisation of caffeine under elite competitors in endurance events.62,63 An analysis of plasma caffeine levels in athletes competing in the 2005 Ironman Triathlon World Championships, found that most competitors finished the race with levels high enough to improve endurance performance (20 micromol/L).64

Finally, caffeine has been found to enhance clopidogrel induced platelet inhibition 2–4 hours after intake, a finding that may impact on cardiac stent efficacy.65

Despite these potentially beneficial effects, concern has been raised around the long-term effects of sustained coffee intake. These have generally centred on potential risks such as an increased incidence of bladder cancer and coronary artery disease. Coffee drinkers have been found to be at a moderately higher risk of bladder cancer, but the risk is moderate and not dependant on the dose or the duration of the coffee intake, thus excluding a strong association.66 A meta-analysis concluded that coffee and tea consumption were probably not associated with bladder cancer.67

One of the largest prospective cohort studies comprising 128 493 patients followed from 1986 through to 2000, was unable to demonstrate that cumulative coffee consumption increased the risk of coronary heart disease.68 A meta-analysis of over 400 000 subjects showed that while cohort studies suggest increased risk associated with 3–4 cups per day or more (OR 1.53, 95% CI 1.04–1.71, P < 0.0001 and OR 1.85, 95% CI 1.49–2.24, P < 0.0001), the long-term follow up studies could not confirm this, even in the highest category (RR 1.16, 95% CI 0.95–1.41, P = 0.14).69 Indeed, the most recent meta-analysis showed significantly lower coronary heart disease in both men and women who were moderate coffee drinkers, defined as 1–3 cups per day or 3–4 cups per day.70 This has further been supported by a continuation of the Lopez-Garcia study in which they found a trend to a reduction in all-cause mortality in men across most categories of coffee consumption (2–3 cups per day (OR 0.97, 95% CI 0.89–1.05); 4–5 cups per day (OR 0.93, 95% CI 0.81–1.07); 6 cups per day (OR 0.8, 95% CI 0.62–1.04)).71

There may even be a protective vascular effect in the regular use of coffee or tea related to their roles as antioxidants and in the case of coffee, as an insulin sensitizer.72

Alcohol and mortality

There is strong evidence to suggest that alcohol has a J shaped curve effect on mortality. The dose of alcohol suggested to reduce all cause mortality is 1–2 drinks per day for women and 2–4 drinks per day for men,26,27 with some authors recommending doses of 6 g/day1 (half a drink).73 This reduction in mortality has been confirmed in many studies, including a meta-analysis that examined over one million participants.74,75 Early explanations centred on the finding that people who regularly consume moderate amounts of alcohol have an associated higher intake of fruit, vegetables, and fish, with a lower intake of saturated fat. Further study has shown alcohol to be an independent factor in the reduction of cardiovascular risk, with the mechanism of action possibly related to an increase in high-density lipoprotein cholesterol levels.76–80 This protective effect is thought to extend beyond purely cardiovascular risk, to reducing cancer risk and modifying the prevalence of metabolic syndrome.81,82 The benefits from low dose alcohol intake may, however, be negated by heavy binge drinking.83 Research surrounding the protective effects of polyphenols, added to that from large epidemiological studies, suggests that wine may...
confer additional benefit above other alcoholic beverages. According to Gronbeck et al, light drinkers who avoided wine were found to have a reduced relative risk for death from all cause mortality of 0.90 (95% CI 0.82–0.99) compared to non drinkers. In those light drinkers who consumed wine, the relative risk was found to be further reduced to 0.66 (95% CI 0.55 to 0.77). The reader is referred to an excellent review of the subject by Opie et al, in which the suggestion is made that French red wine may represent the optimal choice due to its superior induction of human endothelial nitric oxide synthase. Should one have to choose a specific variety, the evidence suggests that pinot noir is the beverage of choice as it is high in resveratrol and procyanidins, which are both strong anti-oxidants and are associated with a decrease in cardiovascular morbidity and mortality.

**Chocolates**

Saturated fats are known to be a cardiovascular risk factor. However, there is increasing evidence that there is a difference in stearic acid which is plant derived (chocolate) as opposed to animal derived. In addition, stearic acid may be desaturated to oleic acid which is cardioprotective. The potential benefit of the anti-oxidant flavonoids in chocolate may therefore be beneficial. A meta-analysis of flavonoid intake showed that the RR for coronary heart disease mortality between the lowest and highest tertile was 0.81 (95% CI 0.71–0.92). In addition, cocoa has a blood pressure reducing effect, improves coronary vasomotion and reduces platelet reactivity. When examining the intake of cocoa-containing foods and their effect on all-cause mortality, the Zutphen Elderly Study found those in the highest tertile (4.18 g/day) had a relative risk of 0.50 (95% CI 0.39–0.72) compared to those in the lowest tertile (0 g/day).

**Accepted lifestyle modifications or interventions to improve longevity**

Lifestyle factors are independent predictors of all-cause mortality, cardiovascular mortality and cancer related death. A history of smoking, exercise of less than 30 min/day, body mass index > 25 kg.m⁻², low diet quality and abstinence or heavy alcohol drinking have been identified as independent predictors for cancer, cardiovascular and all-cause mortality in North American women. Fifty-five percent of deaths were attributable to the first four risk factors.

**Mediterranean diet**

A recent meta-analysis of the effect of a Mediterranean diet on longevity showed that a two point increase in Mediterranean diet characteristics significantly decreased all-cause mortality (RR 0.91, 95% CI 0.89–0.94) as well as cardiovascular and cancer mortality and Parkinson’s and Alzheimer’s disease. A point was added for each of the following Mediterranean constituents: vegetables, fruits, legumes, cereals, fish and a moderate red wine intake with meals, and a point was deducted for diets containing red meat, processed meat and dairy products.

**Exercise**

Exercise of more than 30 minutes per day is an independent predictor of survival, cardiovascular survival and decreased cancer death. Studying monozygote twins has shown that the survival benefit is due to the physical activity and not necessarily genetically linked. When activities are divided into light (200–599 kcal/week or < 3 MET hours/week), moderate (600–1499 kcal/week or 3–6 MET hours/week), or heavy (> 1500 kcal/week or > 6 MET hours/week), a survival benefit is shown for both men and women when moderate activity is compared with light, and further benefit, when heavy is compared with moderate.

**Accepted medications and the concept of the ‘polypill’ or ‘magic bullet’**

The concept of the polypill is one of primary prevention or prophylaxis, as opposed to screening. Wald and Law in 2003 proposed that a single daily pill which included a beta-blocker, aspirin, a statin, an ACE-inhibitor and folic acid would decrease the incidence of cardiovascular disease if it was given to everyone over the age of 55 years. However, little progress has been made with the polypill and it remains in its infancy due to physician, patient and pharmacologic factors as well as public health policy makers and commercial interests.

While all the interventions used in the polypill are shown to decrease cardiovascular mortality, when analysing all-cause mortality as in this paper, and focussing purely on primary prevention, then there is little data to support all these interventions, unless the individual has an existing cardiac risk factor such as hypertension.

Recent progress in primary prevention using statins would suggest that following the protocol of The Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) would be appropriate. JUPITER recruited patients ≥ 50 years and females ≥ 65 years with no cardiovascular disease history with an LDL-cholesterol < 3.4 mmol.L⁻¹ and a C-reactive protein > 2 mg.L⁻¹. Rosuvastatin 20 mg daily was administered to the treatment group. The trial was stopped early (median 1.9 years) as the treatment group had significantly less myocardial infarction, stroke, revascularisation or unstable angina and all-cause mortality.

In patients with stable cardiovascular disease, low dose aspirin (5–325 mg.d⁻¹) has been found in a meta-analysis to reduce both adverse cardiovascular events (RR 0.88, 95% CI 0.81–0.96) and all-cause mortality (RR 0.75, 95% CI 0.71–0.81). Regarding primary prevention, a meta-analysis of the six primary prevention studies, failed to show a significant decrease in all-cause mortality (OR 0.94, 95% CI 0.87–1.00, P = 0.071) or coronary heart disease mortality although it did significantly decrease the incidence of coronary heart disease. This is in contrast to findings from the Nurses Health Study that have shown a reduction in all cause mortality in women who report using aspirin on a regular basis (RR 0.7; 95% CI 0.71–0.81). Currently, the role of aspirin as a primary prevention agent remains contentious and potential benefits must be weighed up against bleeding risks.

**The polymeal, the “natural” counter to the polypill**

An interesting counter to the polypill is the proposed polymeal. By creating a diet consisting of seven foods (wine, fish, dark chocolate, fruit and vegetables, garlic and almonds) all known to reduce cardiovascular disease, an estimated 75% reduction in cardiovascular disease could be achieved. This would result in an increase in life expectancy of 6.6 years for men taking the polymeal.

**The ‘magic’ lifestyle or the lifestyle polypill, calculating your modified life expectancy**

The mathematics to describe the effect of these interventions is relatively simple. The product of the relative risks associated with each intervention will result in a relative risk for all the combined interventions. We could devise a ‘magic’ lifestyle or ‘lifestyle polypill’ calculator by multiplying the relative risks of various lifestyle interventions that are simultaneously employed by an individual. By making use of the WHO life tables we can calculate the probability of dying within the next five years for an individual in a specific country. This is done by multiplying the predicted mortality by the calculated cumulative relative risk reduction for specific lifestyle interventions (listed in Table 1). In this way, we can calculate the effect of these interventions on survival.
Table I: The relative risk of death associated with specific lifestyle interventions

| Risk factor          | Intervention                                                                 | RR (95% CI)          |
|----------------------|-------------------------------------------------------------------------------|----------------------|
| Profession           | Anæsthesist                                                                  | SMR 0.48 (0.46–0.50) |
| Alcohol              | Half a drink per day (6g/day†)                                               | 0.81 (0.80–0.83)     |
| Light wine drinker   |                                                                               | 0.66 (0.55–0.77)     |
| Coffee               | 2–3 cups per day                                                             | OR 0.97 (0.89–1.05)  |
|                      | 4–5 cups per day                                                             | OR 0.93 (0.81–1.07)  |
|                      | ≥ 6 cups per day                                                             | OR 0.8 (0.62–1.04)   |
| Chocolate            | 4.8g day†                                                                    | 0.50 (0.39–0.72)     |
| Exercise             | Moderate                                                                     | 0.81                  |
|                      | Highly active                                                                 | 0.78 (0.72–0.84)     |
|                      |                                                                               | 0.69 (0.53–0.90)     |
| Mediterranean diet   | 2 point increase†                                                            | 0.91 (0.89–0.94)     |
| JUPITER              | Rosuvastatin 20mg daily                                                      | 0.80 (0.67–0.95)     |
| Aspirin              | Aspirin – low dose                                                           | 0.75 (0.71–0.81†)    |
| Life time shift work |                                                                               | 1.47 (1.12–1.93)     |

SMR standardised mortality ratio
OR odds ratio
†Add a point for vegetables, fruits, legumes, cereals, fish and a moderate red wine intake with meals, deduct a point red meat, processed meat and dairy products
† female only

Limitations
The effectiveness of the proposed interventions discussed in this paper are subject to the methodological flaws inherent in each of these population-based studies. It may be that there are multiple confounding factors which are not evident when using data from separate population based studies examining different lifestyle interventions on survival. It may be that economic status and subsequent quality of life is the biggest factor in determining longevity. In addition these interventions may not be reproducible in populations other than those in which they were identified.

Conclusion
It would seem that anæsthesia rewards its practitioners by conferring on them a longevity benefit. Through simple and in many cases surprisingly pleasurable interventions, this benefit may be further extended. Perhaps living the good life and living the long life are not two mutually exclusive endpoints.

References
1. WHO. Life Tables for WHO Member States. [cited 18 February 2008]; Available from: http://www.who.int/whosis/database/life-tables/life–tables.cfm.
2. Opie LH, Mayosi BM. Cardiovascular disease in sub-Saharan Africa. Circulation. 2005 Dec 6;112(24):3563–40.
3. Alexander BH, Checkoway H, Nagahama SI, Domino KB. Cause-specific mortality rates of anaesthesiologists. Anesthesiology. 2000 Oct;93(4):922–30.
4. Gurakar JM, Land KC, Blazer D, Fyllingbaum GC, Branch LG. Educational status and active life expectancy among older blacks and whites. N Engl J Med. 1995 Jul 8;332(1):110–6.
5. Crimmins EM, Saito Y. Trends in healthy life expectancy in the United States, 1970–1990. Gender, racial, and educational differences. Soc Sci Med. 2001 Jun;52(11):1629–41.
6. Neil HA, Fairer JG, Coleman MP, Thurston A, Vessey MP. Mortality among male anaesthetists in the United Kingdom, 1970–93. Br J Med (Clin Res Ed). 1987 Aug;829(594):360–2.
7. Hartwick K, Clemens A, Sakakowitch C, Simkin S, Deeks J. Suicide in doctors: a study of risk according to gender, seniority and specialty in medical practitioners in England and Wales, 1979–93. J Epidemiol Community Health. 2001 May;55(5):306–311.
8. Swanson SP, Roberts LJ, Chapman MD. Are anaesthetists prone to suicide? A review of rates and risk factors. Anaest Intensive Care. 2003 Aug;31(4):434–45.
9. Bruce DL, Eide KA, Linde IW, Eikenhoff JE. Causes of death among anaesthesiologists: a 20-year survey. Anaest Intensive Care. 1998 May-Jun;26(3):544–59.
10. Bruce DL, Eide KA, Smith NJ, Setzer F, Dykes MH. A prospective survey of anesthesiologist mortality. 1967–1971. Anesthesiology. 1974 Jul;41(1):71–4.
11. Carpenter LM, Werdowel AJ. Fear NT. Mortality of doctors in different specialties: findings from a cohort of 20000 NHS hospital consultants. Occup Environ Med. 1997 Jun;54(6):398–95.
12. Lindfors PM, Nurmia KE, Meretaho OA, Laaksonen RA, Viljanen AM, Leino Tj, et al. Post-call stress among Finnish anaesthetists. Anaesthesia. 2006 Sep;61(9):853–66.
13. Kruger MT, Lindlau TM, Kruger N, Harrison MJ. Personality traits of anaesthetists and physicians: an evaluation using the Cloninger Temperament and Character Inventory (TO–125). Anaesthesia. 1995 Oct;50(10):526–35.
14. Harton K, Clemens A, Simkin S, Malmberg A. Doctors who kill themselves: a study of the methods used for suicide. QJM. 2000 Jun;93(6):351_7.
15. Beauregard A, Ferguson D, Coggins C, Collinge C, Dougherty C, Ellis F, et al. Effective strategies for suicide prevention in New Zealand: a review of the evidence. N Z Med J. 2007 Dec 21;120(1251):51–49.
16. Mann JJ, Apter A, Bertolote J, Beauregard A, Carrier D, Haas A, et al. Suicide prevention strategies: a systematic review. JAMA. 2005 Oct 26;294(16):2004–74.
17. Steinbrook R. The debate over residents’ work hours. N Engl J Med. 2002 Oct 17;347(16):1296–302.
18. Pickering T. The European working time directive for doctors in training. BMJ. 2001 Dec 1;323(7324):1260.
19. Bhansali SM, Cullen RF. Resident work hours. Curr Opin Anaesthesiol. 2003 Dec;16(6):605–9.
20. Murray D, Dodds E. The effect of sleep disruption on performance of anaesthetists--a pilot study. Anaesthesia. 2003 Jun;58(6):520–5.
21. Baumberg LK, Cade ME, Aron NT, Gronin JW, Rosen R, Spencer FE, et al. Extended work shifts and the risk of motor vehicle crashes among interns. N Engl J Med. 2009 Jan 13;360(2):125–34.
22. Amre ST, Wilde GL, Muir WW, MacLeAn AW. How do prolonged wakefulness and alcohol compare in the decrements they produce on a simulated driving task? Accid Anal Prev. 2001 May;33(5):37–44.
23. Zheng H, Patel M, Hyuniewicz K, Katz SD. Association of extended work shifts, vascular function, and inflammatory markers in internal medicine residents: a randomized crossover trial. JAMA. 2006 Sep 26;296(9):1049–50.
24. Riddell PM, Cushman M, Stumper MJ, Tracy RP, Hennekens CH. Plasma concentration of C-reactive protein and risk of developing peripheral vascular disease. Circulation. 1998 Feb 10;97(7):425–8.
25. Zethelius B, Beighley L, Sandstrom J, Ingelsson E, Biau S, Larsson A, et al. Use of multiple biomarkers to improve the prediction of death from cardiovascular causes. N Engl J Med. 2008 May 15;359(21):2107–16.
26. King CR, Knutson KL, Rathouz PJ, Sidney S, Liu K, Lauderdale DS. Short sleep duration and incident coronary artery calcification. JAMA. 2008 Dec 24;300(24):2859–66.
27. Budoff MJ, Gul KM. Expert review on coronary calcium. Vasc Health Risk Manag. 2008 Apr;4(2):335–40.
28. Gangwisch JE, Heymsfield SB, Boden-Alba B, Bujo RS, Kreier P, Pickering TG, et al. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. Hypertension. 2005 May;45(5):835–9.
29. Ayas NT, White DP, Manson JE, Stampfer MJ, Speizer FE, Malhotra A, et al. A prospective study of sleep duration and coronary heart disease in women.
Pelucchi C, Tavani A, La Vecchia C. Coffee and alcohol consumption and bladder cancer. Scand J Urol Nephrol Suppl. 2008 Sep(218):37–44.

Van Thuyne W, Delbeke FT. Distribution of caffeine levels in urine in different occupational groups. Chronobiol Int. 2004;21(6):1055–61.

Nyssen AS, Hansez I, Baele P, Lamy M, De Keyser V. Occupational stress and burnout in anaesthesia. Br J Anaesth. 2003 Mar;90(3):333–7.

Smith A. Effects of caffeine on human behavior. Food Chem Toxicol. 2002 Nov;40(11–12):1581–5.

Tharion WJ, Shukitt-Hale B, Lieberman HR. Caffeine effects on marksmanship training. Physiol Behav. 1995 Feb;57(2):289–94.

Reyner LA, Horne JA. Suppression of sleepiness in drivers: combination of caffeine and co-administered amphetamines. J Environ Med. 2001;17(3):209–23.

Tuomilehto H, Peltonen M, Partinen M, Seppa J, Saaristo T, Korpi-Hyovalti E, Tiihonen J, et al. A prospective study of self-reported sleep duration and incident diabetes in women. Diabet Care. 2003 Feb;26(2):390–4.

Fuchs CS, Stampfer MJ, Colditz GA, Giovannucci EL, Manson JE, Kushi L, et al. Coffee consumption and risk of coronary heart disease: A prospective cohort study. Ann Intern Med. 2004 Feb 10;140(3):189–95.

Buijsse B, Feskens EJ, Kok FJ, Kromhout D. Cocoa intake, blood pressure, and cardiovascular mortality: the Zutphen Elderly Study. Arch Intern Med. 2006 Feb 20;166(4):411–7.

Maiorana A, Navalesi P, Tiberti C, Tziomalos K, et al. Association of drinking pattern and alcohol beverage type with the prevalence of metabolic syndrome, diabetes, coronary heart disease, stroke, and peripheral arterial disease in a Mediterranean country. Cardiovasc Dis. 2007 Dec;17(3):209–23.

Jain A, Kaur A, Mathuria N, Donati MA, Iavicelli L, de Gaetano G. Alcohol dosing and total mortality in men and women; an updated meta-analysis of 34 prospective studies. Arch Intern Med. 2006 Dec 4;166(22):2437–45.

Nyang R, Sinaki M, Gohlke HH, Levy R, Stein JH, Parisi AE, et al. A prospective cohort study of scotch men with 21 years of follow up. BMJ. 1999 Jun 26;318(7193):1275–9.

Bergen BS, Bocca B. Caffeine and risk of coronary heart disease: a meta-analysis. Am J Med. 2008 Jan;121(1):43–52.

Franco OH, Borello-Ferguson L, Shaper AG. Coffee consumption and coronary heart disease: an updated analysis. BMJ. 2006 Aug 11;333(7566):365–7.

Bourne RB, Borello-Ferguson L, Shaper AG. Coffee consumption and coronary heart disease: a meta-analysis. BMJ. 2007 Aug 25;335(7617):543–9.

Baekeland F, Stein JH, Gohlke HH, Levy R, Parisi AE, et al. The Polymeal: a more natural, safer, and probably tastier (than the Polypill) cardiovascular disease prevention strategy. Curr Opin Cardiol. 2006;21(3):148–56.

Wu JW, Ho SC, Zeng Y, Chen WH, Cheng WQ, Wang CL, et al. Coffee consumption and risk of coronary heart disease: A meta-analysis of prospective studies. Int J Cardiol. 2008 Aug 1;127(3):395–400.

Van Dam RM, Ros E, van der Schouw YT, Manson JE, Rimm EB, Willett WC, et al. Coffee consumption and risk of coronary heart disease: a prospective cohort study. Circulation. 2006 May 21;113(20):2455–63.

Lotito SR, Mancuso CR, Farris FJ, Mattioli V. Urinalysis, information, and medical consequences of sleep deprivation. Prog Cardiovasc Nurs. 2007;22(4):291–2.

Levi EM, Arikan ME, Vaduganathan M, Alviar CL, Tellez A, Mathuria N, et al. The relationship of coffee consumption and risk of cancer with mortality. Ann Intern Med. 2006 Jun 13;144(12):891–901.

Rher RL, Benevenga JS, Bockenhoff A, Knapp G. Physical Activity and All-cause Mortality: An Updated Meta-analysis with Different Intensity Categories. Int J Sports Med. 2007 Mar;28(2):106–15.

van Dam RM, Li T, Spiegelman D, Franco OH, Hu FB. Combined impact of cigarette smoking, beverage consumption, diet and bladder cancer: a systematic literature review. Int J Cancer. 2007 Apr 15;120(8):1839–44.

Lollgen H, Bockenhoff A, Knapp G. Physical Activity and All-cause Mortality: An Updated Meta-analysis with Different Intensity Categories. Int J Sports Med. 2007 Mar;28(2):106–15.

Carlsson S, Andersson T, Lichtenstein P, Michaelsson K, Ahlbom A. Genetic effects on physical activity: results from the Swedish Twin Registry. Med Sci Sports Exerc. 2006 Aug;38(8):1403–12.

Sedentary lifestyle, waist circumference, body mass index, and cancer risk in the Zutphen Elderly Study. Ann Intern Med. 2008;149(11):833–41.

Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 75%. BMJ. 2004 Dec 11;329(7477):1415–19.

Lambin P, Desveaux D, Meadow J, Mahé X. The red wine hypothesis: from concepts to protective signalling molecules. Eur J Heart. 2007 Jul;28(14):1084–93.

Tomaszlam A, Gronbaek M, Nystedt C, Overvad K. The connection between food and alcohol intake habits among 48,763 Danish men and women. A cross-sectional study in the project “Food, cancer and health”. Ugeskr Læger. 1999 Dec 15;161(52):6111–6114.