ORIGINAL ARTICLE

Better than any pill—and no side effects! Healthy lifestyles, statins, and aspirin

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Abstract

Behaviors which are associated with the preservation of health include nonsmoking, regular exercise, a low body weight, a healthy diet, and a low alcohol intake. Together, as a healthy lifestyle, these have been shown to be associated with marked protection against a wide range of diseases: diabetes, vascular disease, cancer, and dementia. On the other hand, the protection associated with statins and aspirin, the two most commonly used preventive drugs, is limited to vascular disease and, probably for aspirin, cancer.

These are not alternative prophylactics and any two, or all three—a healthy lifestyle, a statin, and aspirin—can reasonably be taken together.

Only a small proportion of the members of the community follow a healthy lifestyle. Yet a small increase in the uptake of the healthy behaviors throughout the community can be shown to have relatively large effects on the incidence of disease.

There is therefore an urgent need for health promotion activities across the whole community to be greatly increased and for new challenging and encouraging strategies to be devised and tested.

KEYWORDS
aspirin, dementia, diabetes, lifestyle, statins

1 | INTRODUCTION

> The unexamined life is not worth living. Socrates

Clinical practice focuses on the individual rather than the community and yet, as Geoffrey Rose pointed out 40 years ago,[1] the bulk of disease and disablement comes not from the subgroup of high-risk subjects but from the general community, simply because the community is numerous and the risk factors for most diseases are multiple and are distributed throughout the whole population.

WHO defines the ultimate aim of medical practice to be "a state of complete physical, mental and social wellbeing and not merely the absence of disease"[2] and so a major goal of health authorities and healthcare workers should include the raising of the level of well-being throughout the community, and not just the reduction of the suffering and misery of patients with disease.

TABLE 1 Estimates of reductions in incident disease associated with a healthy lifestyle in a large long-term observational cohort study; and reductions attributable to daily statin taking and daily aspirin taking in selected primary randomized controlled trials

Prophylactic strategy	Reductions in disease incidence			
	Diabetes	Vascular disease	Cancer	Dementia
Healthy living	72% reduction[a] (P < .0005)	62% reduction[a] (P < .0005)	32% reduction[a,b] (P < .0001)	65% reduction[a] (P < .0005)
Statins	Increase[c]	44% reduction[d] (P < .00001	No change	No change
Aspirin	No change	11% reduction[e] (P < .001)	29% reduction[f] (P < .003)	No change

[a] Reductions in the Caerphilly Cohort Study. Adjustments have been made for age and social class and for dementia adjustments were also made for premorbid cognitive function (Ref. 4).

[b] Reduction in 14 500 cancers in 350 000 subjects in BIOBANK UK (Ref. 5).

[c] See text and Refs 13–15.

[d] The reduction in "17,802 apparently healthy men and women" (Ref. 12).

[e] The reduction in primary prevention in a meta-analysis of 17 randomized trials (Ref. 18).

[f] The reduction in incident cancer in 32 996 subjects in six primary trials (Ref. 19).

In what follows we compare the reductions in the incidence of a number of important chronic diseases associated with the following of a healthy lifestyle and the reductions associated with the taking of two commonly used prophylactic drugs: statins and aspirin. We also consider the side effects of the three preventive measures.

2 | A HEALTHY LIFESTYLE

The Caerphilly Collaborative Cohort Study was a 35-year prospective study, set up in 1979 and based on a representative population sample of 2,500 men aged 45–59 years.[3] Caerphilly in Wales, UK, was chosen for the study because the social class distribution of the population in the town was closely similar to that of the whole of England & Wales. Electoral rolls and Primary Care practice lists were used as a sampling frame, and 89% of the eligible subjects within the defined area gave signed agreement to long-term involvement in the research.

Special afternoon and evening clinics were held, and following attendance each man was asked to return the next morning, before breakfast, for a fasting blood sample to be taken. Every 5 years the men were seen again: requestioned, reexamined, and further fasting blood samples taken. Around 95% of the survivors were questioned and examined at each 5-year examination.

Data were collected every 5 years on five behaviors which have repeatedly been shown to be associated with reductions in disease: nonsmoking; regular physical activity (at least ½ an hour 5 days each week); a low body weight (BMI 18.5-25); a healthy diet ("five a day" fruit and vegetables), and an intake of alcohol within the current guidelines. Two subgroups of men were identified: 111 men (5% of the cohort) who consistently reported that they were following either four or five of the healthy behaviors and on these criteria were judged to be living a "healthy" lifestyle, and 881 men (39% of the cohort) who said they followed either none, or only one of the behaviors and were judged to be living an "unhealthy" lifestyle.

Evidence on incident disease was collected repeatedly from primary care and hospital records and was evaluated against accepted clinical criteria as described elsewhere.[4] Within the total cohort, 214 men developed diabetes within the 35 years of follow-up, 753 experienced a myocardial infarct or a stroke, and 299 men were diagnosed with cancer. Dementia was diagnosed in a clinical examination by a geriatrician and a neurologist in 121 men following detailed and repeated testing of cognitive function.[4]

The trends in disease incidence and the number of healthy behaviors followed were significantly associated with incident diabetes, vascular disease, and dementia (see Table 1). For incident cancer, the reduction (32%) was only suggestive (P = .06). However, access to BIOBANK UK gave opportunity for the conduct of a closely similar analysis and the association between a healthy lifestyle in 350,000 subjects with 14,500 new cancers. This confirmed a reduction associated with a healthy lifestyle of 32% in incident cancer, during a 5-year follow-up (HR 0.68, 95% confidence intervals 0.63, 0.74; P < .0001).[5]

A healthy lifestyle which has been defined as above appears not to be associated with any undesirable side effect. During the conduct of the Caerphilly Study, estimates of a number of aspects of "well-being" were made when the men in the study were aged 75–89 years. Thus 89% of those who had followed a healthy lifestyle (four or five of the behaviors) claimed that they were "in good health" as assessed by the General Health Questionnaire[6] compared with 53% of the subjects who had been following an unhealthy behavior (none or a single behavior) (P < .005). A "satisfaction with life" score[7] was 28 in those following a healthy lifestyle and 26 in those following an unhealthy lifestyle (P < .06), and "positive attitudes"[8] were shown by a greater proportion (P < .001) of those who were following a healthy lifestyle.

3 | STATINS

Over 40% of adult subjects in the USA take a statin,[9] and it is estimated that "one third of the 5.5 million people over age 75 in the UK
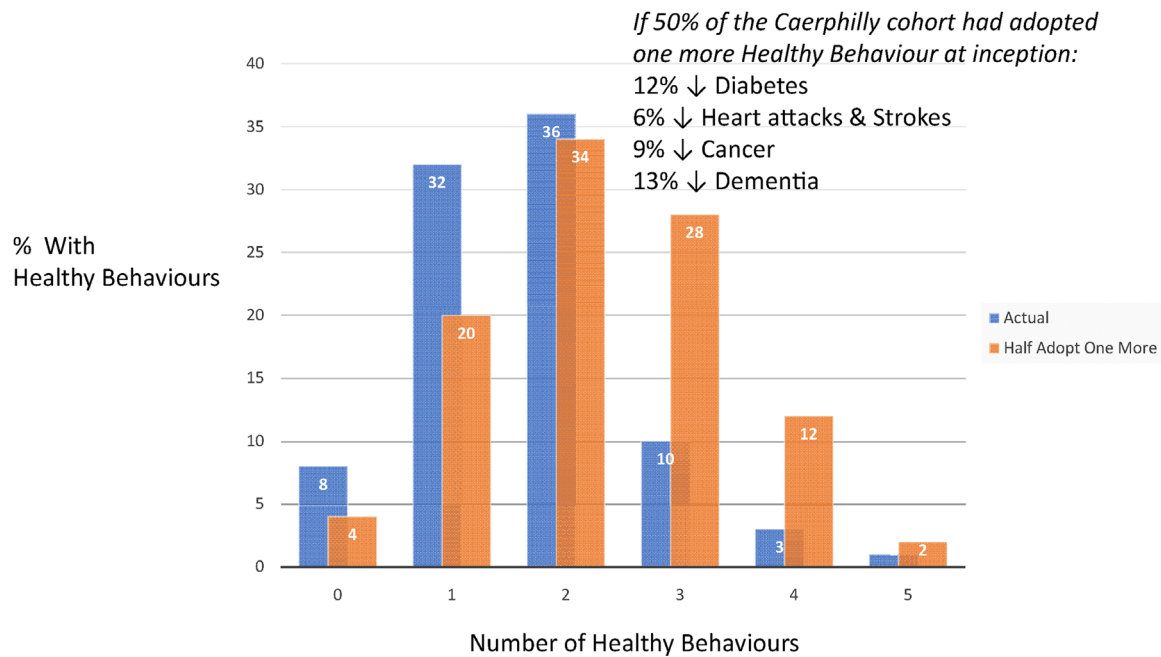
If 50% of the Caerphilly cohort had adopted one more Healthy Behaviour at inception:
12% ↓ Diabetes
6% ↓ Heart attacks & Strokes
9% ↓ Cancer
13% ↓ Dementia

FIGURE 1 Modeling impact of 50% of Caerphilly cohort adopting one more healthy behavior

take statins."[10] In fact, the National Institute for Health and Care Excellence has issued guidelines within which almost all men aged over 60 and women over 75 in England qualify for statin use.[11]

Efficacy of statins against vascular disease has been shown in numerous randomized trials and although their use in healthy subjects is somewhat controversial, the marked reduction shown in the table has been taken from a randomized trial based on 17,802 "apparently healthy men and women."[12]

Statins however are a frequent cause of muscle cramps, estimated to affect one in every 10 persons taking the drug, and rarely muscle necrosis,[13] and these side effects lead to poor long-term compliance with taking the drug.[14] More importantly, there is evidence consistent with an increase in diabetes in subjects taking the drug, estimated to amount to between about one new case in every 50 (Ref. [13]) and one in every 223 patients taking a statin.[15]

4 | ASPIRIN

Almost 20% of adults in the USA take aspirin daily or on alternate days,[9] and a survey in Wales found that about 30% of men and 20% of women over age 50 take daily aspirin, with a significant bias in favor of the more privileged social classes.[16]

Aspirin was first shown in 1974 to reduce vascular mortality,[17] and a meta-analysis of six primary prevention trials with a total of 95,000 participants confirmed a significant reduction in serious vascular disease events (relative risk 0.89; 95% CI 0.85-0.93; $P < .001$).[18] More recently, a number of long-term follow-up studies of vascular disease prevention have given evidence of a reduction in cancer incidence and cancer mortality associated with having been ran-

domized to aspirin,[19] and, most recently, evidence consistent with a significant increase in the survival of patients with cancer and a reduction in metastatic spread associated with aspirin has been reported.[20]

Low-dose aspirin taking increases the background risk of a gastrointestinal bleed by about 50%, equivalent to a bleed in an additional one or two persons in every 1000 during the first few years of taking the drug.[19,21] The drug is also rarely associated with intracerebral bleeding, equivalent to about one or two in every 10 000 subjects per year,[22] though identification and treatment of hypertension appears to prevent a cerebral bleed.[23]

5 | DISCUSSION

Evidence on the benefits of lifestyles was selected from the Caerphilly Study in Wales because it had been conducted over a longer period of time than any other similar study, and it was the first to include dementia as an outcome.[4] Due to limited funding at baseline, it had been based on men alone, and questions therefore arise as to the acceptability of extrapolations of the results to the general community. Elsewhere, we examine this point and we show that the results from studies based on men and women in communities within the USA,[24-26] within Europe,[27] and in England[28] are reasonably similar to those we report for men in Caerphilly.[4]

There appear to be no interactions between the three prophylactics—a healthy lifestyle; statins and low-dose aspirin—and they should not therefore be considered as competitive alternatives. There is no reason therefore why two, or perhaps all three of the preventives should not be taken for protection against vascular disease

events. At the same time, it seems unfortunate that there is a marked year-on-year decline in the prescribing of aspirin in the UK in favor of newer and more expensive antiplatelet and antithrombotic agents,[29] for none of which is there evidence suggestive of a reduction in cancer.

Although the three strategies are not alternatives for heart disease protection, the overall evaluation of the value of each should take account of background changes in the relative risks and the relative importance of the diseases relevant to their use. Thus ischemic heart disease has decreased in the UK by about 45% and ischemic stroke by about 20% over the past 25 years.[30] In contrast, the incidence of diabetes has more than doubled in the UK within the last 20 years,[31] and overweight alone appears to explain about 70% of this increase.[4] A major, and growing concern is dementia, and it has been estimated that the number of people with dementia in the UK is likely to double every 5 years.[32] While Table 1 shows that all three prophylactics are associated with a reduction in vascular disease outcomes, yet out of the three only a healthy lifestyle is associated with reductions in diabetes and in dementia.

Rose[1] and others have pointed out that a small shift in a distribution of a factor predictive of a disease can have a large effect on the population incidence of the disease, and the effect can be marked at an extreme of the distribution. Thus: suppose that at baseline in 1979 when the Caerphilly cohort was set up, every subject in the cohort had been urged to take up and follow just one additional healthy behavior—either stop smoking or achieve an acceptable BMI or take regular exercise or chose a more healthy diet or reduce alcohol intake to within the accepted guidelines, and suppose that only half of the subjects had done so other than the <1% of subjects who had consistently followed all five behavior (see Figure 1), then over the next 35 years there would have been within the cohort, about 12% less diabetes; about 6% fewer strokes and heart attacks, about 9% fewer patients with cancer, 13% fewer cases of dementia and an overall increase in well-being.[4]

It has to be accepted however that while the estimates of reduction shown in the table for the two drugs have been obtained from randomized controlled trials,[12,18] the results for the effects of a healthy lifestyle were observational and it has not been possible to adjust the estimates for confounding by factors other than age and social class, and for dementia an adjustment was also made for premorbid cognitive ability.[4] "Lifestyle" is a complex and composite way of life determined in part by attitude to life and to relationships which go beyond the five behavior on which we have data. Nevertheless, although the statistical reductions in disease which are attributed in this report to the five healthy behavior may be somewhat overestimated, clinical and other studies give convincing evidence of strong causal relationships between each of the behavior and disease incidence.

Finally, in the most recent data from the annual National Survey of Wales in 2018,[33] the application of the same criteria of healthy lifestyles as was used in the Caerphilly study[4] to the raw data on behavior collected from 11 000 subjects in 2018 indicate that only 4.8% of the adult Welsh population follow a healthy lifestyle (four or five of the healthy behavior) while 45% follow none, or only a single healthy behavior.

6 | CONCLUSION

Now, with an aging population in the UK, with the sustainability of the National Health Service and other health and social provisions being questioned,[28] and with the huge neglect of healthy living, it would seem to be prudent for the current health promotion activities across the whole community to be substantially increased; for the awareness of the benefits of a healthy lifestyle to health and to well-being to be raised throughout the population, and for new challenging and encouraging health-promotion strategies to be devised and tested.

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