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**When people live with  
multiple chronic diseases:**  
a collaborative approach to an  
emerging global challenge



Escuela Andaluza de Salud Pública  
CONSEJERÍA DE SALUD







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# When people live with multiple chronic diseases: a collaborative approach to an emerging global challenge

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Published by ESCUELA ANDALUZA DE SALUD PÚBLICA

ISBN: 978-84-693-2470-7

DL: Gr-2653/2010

Printed in Granada: Alsur, S.C.A.

Layout and graphic design: Carmen F. Sigler. [www.transversal.tv](http://www.transversal.tv)

How to reference

Jadad AR, Cabrera A, Martos F, Smith R, Lyons RF. When people live with multiple chronic diseases: a collaborative approach to an emerging global challenge. Granada: Andalusian School of Public Health; 2010. Available at: <http://www.opimec.org/equipos/when-people-live-with-multiple-chronic-diseases/>

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## Prevention and health promotion

This chapter is continuously evolving at [www.opimec.org](http://www.opimec.org)

### Vignette: How it could be

*It is the year 2020. Carlos is 85 years old. He has diabetes and heart disease, but he still manages to live remarkably well on his own with the support of technology. When he was younger, there was little interest in prevention in his community. Carlos smoked, ate a poor diet and exercised little in adolescence and early adulthood. But for the past 15 years Carlos has placed much more emphasis on prevention, in keeping with the development of a health promoting environment in his community and his country.*

*El Dorado, the community where Carlos lives, has changed dramatically over the past 35 years. It has become a much healthier place to live. Many shops used to sell processed and fast foods, but now it is easier to buy fresh fruit and vegetables. Also the shops in his neighbourhood used to sell cigarettes, and the bars and cafes were full of smoke. Nowadays all public places are smoke-free and it is unusual to see a person smoking. Exercising was difficult in the past because the streets were jammed with traffic. Now traffic congestion has declined and cycling has increased. In fact, Carlos himself cycled up until five years ago.*

*At the national level, the government has also worked hard to develop policies that can reduce social and health disparities in this region. These disparities were some of the main reasons why people in the country were experiencing multiple chronic diseases (e.g. poor housing; poor air quality, food and water; and children not having a healthy start in life).*

*From the age of 60 onwards, Carlos was regularly screened for risk of heart disease and stroke, abdominal aortic aneurysm (ballooning of the main artery from the heart), bowel cancer, diabetic eye disease and high blood pressure. The screening results indicated that he was at high risk of heart disease and stroke and at age 50, in addition to improving his health behavior, he began taking*

*a polypill (a pill which contains drugs that lower blood pressure and blood lipids, and the likelihood of blood clotting).*

*The local community health services have also become much more geared towards people with multiple health issues. From the age of 60, Carlos was contacted regularly by a community health worker. From the age of 70 onwards he was visited by a nurse, who came more often if he was having problems. Since then, advances in technology have enabled him to send regular reports on the various tests he has self-administered and a nurse has contacted him if necessary. He also has a community health worker, who often comes to offer emotional and social support, to help him and to keep him cheerful and hopeful. The combination of the nurse, the community health worker and technology, used in a coordinated way, has allowed him to stay at home, despite being very limited in what he can do. Carlos's family is engaged in helping to manage his health and they are supported by the health and social care system to ensure he keeps as healthy as possible.*

*Creating the conditions that have helped Carlos to stay healthy, despite his limitations, and to live at home, has depended, to a large extent, on the building of a culture of health in his community and on the efforts of local planners and authorities, and health service managers. Many of the services he is entitled to are provided in a cost-effective manner, which is achieved by ensuring that health professionals use their practical abilities to the full and that care is coordinated, and by providing the appropriate skill mix which is needed for optimal health outcomes.*

## Summary

- It is important to understand the health trajectory and life conditions that result in multiple co-morbidity and complex chronic disease in order to determine the most effective individual and populational approaches to prevention.
- Prevention can be categorised in the following four ways, which may provide a useful framework for thinking about prevention and poly pathology: primordial, primary, secondary and tertiary prevention.
- Three preventable risk factors contribute to a large extent to chronic disease: tobacco use, poor diet and physical inactivity. These risk factors need to be addressed at all levels of society, from governments to the individual, paying particular attention to populations which are at the highest risk of developing chronic disease.
- All individuals should be encouraged and supported by their communities to avoid smoking, eat a healthy diet and exercise regularly. In some cases there may be a level of risk where drug treatment is justified.



- One radical and controversial strategy for preventing heart attacks and strokes is for everybody at the age of 55 to start taking a single pill, which combines drugs that lower blood pressure and blood lipids, and the likelihood of blood clotting (known as a polypill).
- Screening populations for early signs of disease can play an important role in prevention, but it is important that a number of criteria are met, including the use of a reliable test, effective treatment, the possibility of early detection of pathology long before serious disease manifests itself and cost effectiveness.
- Guidelines are increasingly used for managing patients with chronic conditions, but they are usually designed for treating patients with single conditions. Combining guidelines designed for patients with single conditions to treat patients with multiple conditions may be not only ineffective but also dangerous.
- Information and communication technologies, particularly those which promote tele-monitoring and tele-consultations, have been conclusively shown to improve outcomes for patients with chronic conditions and to lower costs, mainly by reducing hospital admissions.

## Why is this topic important?

Clearly when patients with complex chronic conditions are so common and they experience so many complications and inappropriate hospital admissions, prevention and health promotion are important.

Prevention within the context of polypathology, however, should be about creating the conditions for patients that will avoid them developing further disorders and prevent them from presenting complications of existing pathologies. Many of these patients will be elderly and approaching the end of their lives as well as having coexisting psychological and social problems. Indeed, their personal, family and social concerns may have little to do with their diseases and it is essential that preventive care should be person centred, not disease centred. For example, it may be inappropriate to press as hard to stop such a patient smoking, as would be the case for a younger person, if the elderly patient places a high value on smoking.

Policy makers will be very interested in prevention and polypathology because small percentage reductions in hospital admissions and complication rates can translate into

considerable savings, which is important for the whole healthcare system. All stakeholder groups should be interested in prevention and health promotion in polypathology because we know a lot about the prevention of individual chronic conditions, but little about prevention and health promotion amongst people with complex chronic conditions. Yet, as we have been describing, these patients account for much of the work and cost for the healthcare system.

## What do we know?

Despite the size of this chapter, there is very little evidence of the best approaches for the prevention of polypathology, as we are still at the stage where we are getting to grips with understanding this population and the determinants that contribute to it.

One useful way to think about prevention is to divide it into primordial, primary, secondary and tertiary prevention and to consider these different levels in the context of Complex Chronic Disease (CCD). The following definitions of these terms are taken from the WHO's book on basic epidemiology (1).

Primordial prevention is concerned with creating economic, environmental and social conditions that are conducive to health and that minimise the likelihood of developing disease. An example would be reducing poverty. Heart disease and stroke are often more common among poorer people.

Primary prevention addresses specific causal factors, like tobacco use, poor diet and physical inactivity in the case of chronic disease, in order to reduce the chances of people developing disease. Examples include raising taxes to reduce tobacco consumption and providing smoking cessation programmes. Another example would be policies designed to reduce the salt content of processed food.

Secondary prevention is concerned with targeting people with a disease which is established but usually at an early stage, in order to limit the exacerbation of the disease and the development of complications. An example would be treating diabetic patients to control their blood sugar and hypertension to minimise and delay such complications.

Tertiary prevention is concerned with patients with well-established disease and its aim is to minimise suffering and complications. Tertiary prevention is akin to treatment and rehabilitation and is perhaps most directly relevant to patients with complex chronic disease. An example of tertiary prevention would be a disease management programme,

where case managers follow patients, perhaps by phone, and prompt them to take preventive treatments and attend for screening.

Dividing prevention into these categories is no more than a device for thinking about polypathology and the different levels frequently merge and overlap. The Australians have a phrase: «healthy planet, healthy places, healthy people» that expresses how these levels overlap (2). It is very difficult for individuals to be healthy if they live in unhealthy places where, for example, the water and air are polluted, smoking is common, high fat and high salt foods are readily available when fruit and vegetables are not, and where it is hard to find space to exercise. And, as the whole planet becomes unhealthy through climate change, pollution and urbanisation, so it becomes increasingly difficult to create healthy places.

This chapter will discuss all the prevention categories, except tertiary prevention, which will be covered elsewhere in Chapter 6.

## Primordial and Primary Prevention

### Social Determinants of Chronic Disease

The social, environmental and economic circumstances of people's lives are central to determining their health and chances of developing chronic disease. Life expectancy varies by as much as 40 years between countries and by more than 10 years within countries. Income, education, housing, employment, social networks and many other factors are all influential and intertwined, as the WHO has recognised in its crucial report on the social determinants of health (3). Access to health care is also a social determinant of health. Any strategy designed to reduce chronic disease must recognise the importance of these social determinants and strategies that ignore them will have only limited impact.

Chronic disease has three main preventable causes: tobacco use, poor diet (including excessive alcohol consumption) and physical inactivity. The discussion that follows is an exploration of what we know about reducing tobacco consumption, and promoting healthy eating and physical activity.

## Tobacco Consumption

Tobacco consumption kills five million people a year globally and that number is set to rise to eight to 10 million by 2030 (4). Half of all smokers die prematurely as a result of smoking and yet, if people stop smoking, they can return to having the same risk as non-smokers within 10 to 15 years.

The world has largely recognised the extreme dangers that tobacco poses and, consequently, the WHO, for instance, has created the Framework Convention on Tobacco Control, which commits countries to regulating tobacco sales, reducing consumer demand for tobacco, improving the environment and health of tobacco workers, and encouraging research. A total of 168 countries out of a possible 192 have signed the convention, the United States and Indonesia being the largest countries not to follow suit.

We know a great deal about public health measures that are effective in reducing tobacco consumption. The WHO has put together the MPOWER package of six policies which are known to be effective (4).

They include the following:

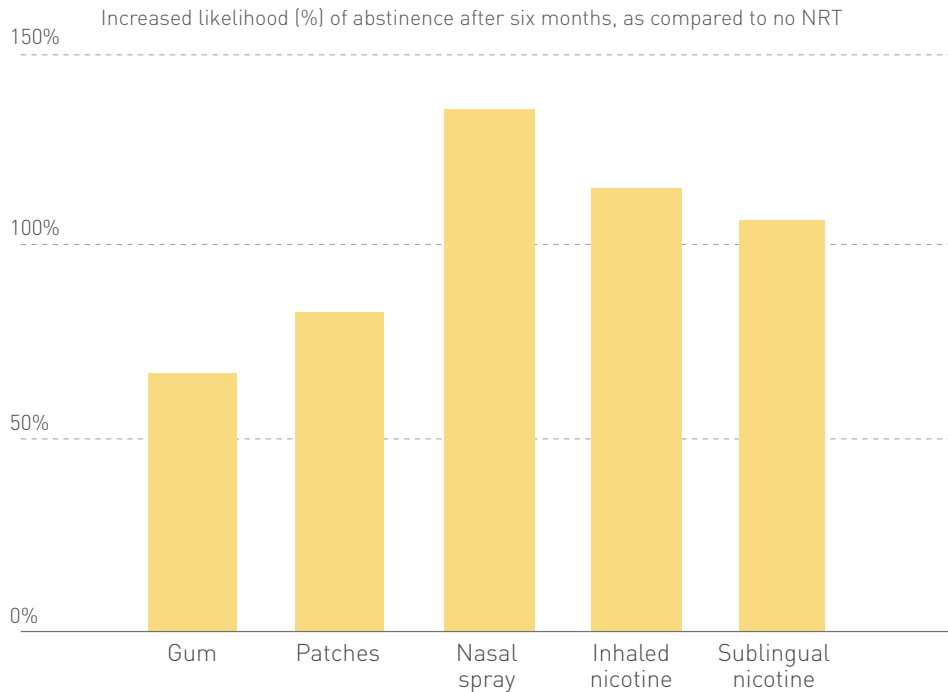
- Monitor tobacco use and prevention policies.
- Protect people from tobacco smoke.
- Offer help to quit tobacco use.
- Warn about the dangers of tobacco.
- Enforce bans on tobacco advertising, promotion and sponsorship.
- Raise taxes on tobacco.

We need to support research in a number of areas: tobacco control, surveys of smoking levels, global cigarette consumption, the economic effects on individual countries (tobacco leads to losses not gains, as the costs of damage outweigh income from taxation), smoking costs to employers, economic costs of fires and litter, costs to smokers, tobacco company documents, litigation, the tobacco industry and the recruitment of scientists to the tobacco company cause.

Banning smoking in workplaces and public places, and increasing taxes on tobacco, are two of the most effective interventions (4).

Figure 1

### Effectiveness of Various Forms of Nicotine Replacement Therapy in Helping People to Stop Smoking



Source: Silagy C, Lancaster T, Stead L, Mant D, Fowler G, «Nicotine replacement therapy for smoking cessation», *Cochrane Database System Review 2004; (3); CD000146.*

Figure 1 shows data from a Cochrane Review on smoking cessation rates after various forms of nicotine replacement therapy (4, 5). The vast majority (between two thirds to three quarters) of ex-smokers stop smoking completely with no assistance (6, 7). This data comes from nations which have experienced two decades of major promotion of nicotine replacement therapy, using budgets that dwarf public campaign expenditure on smoking cessation.

Most smokers (by far) quit after being exposed to mass-reach policies, campaigns and the changing culture of smoking. They do not use drugs, go to counselling or even phone quitlines. This is an important and very positive message.

Nearly all the trials on nicotine replacement therapy have been conducted in wealthy countries. These nations differ substantially from low and middle-income countries in their culture of smoking control (smoking is far more accepted in most low and middle-income countries; there is scant tobacco control in most of them, including few motivational campaigns urging cessation). It is unwise to assume a similar interest, on the part of the population, in nicotine replacement therapy in the countries where most of today's smokers live.

Countries that have implemented comprehensive bans on advertising (meaning bans on media and point-of-sale advertising) have seen much greater falls in tobacco consumption than countries that have not introduced such bans (4, 8). There are clearly issues around causation here, but the evidence on the effectiveness of comprehensive bans is strong. Reducing taxes on tobacco leads to higher consumption and raising them reduces consumption (4, 9). This sensitivity to price has been seen repeatedly in many countries at different times and is well established.

Much of the evidence on reducing the harm tobacco causes concentrates on cigarettes, but in many regions of the world, such as South Asia, other forms of smoked tobacco like bidis and smokeless, oral tobacco consumption are common, particularly among women and young people.

What we know much less about is the effect of these policies, including nicotine replacement therapy, in patients with complex chronic conditions. Indeed, of some 40 Cochrane reviews on smoking cessation none involve patients with established chronic disease. Often a whole range of trials exclude or control for polyopathy.

It is also important to acknowledge that the control of tobacco use is made much more difficult by the presence of a powerful tobacco industry which is focused on promoting tobacco sales worldwide. These companies are increasingly concentrating their energies on low and middle-income countries, where the number of smokers and potential smokers is substantial and controls may be weak. These countries often depend on tobacco for economic development.

## Diet and Physical Activity

The goal of tobacco reduction is very clear: to reduce its use as much as possible in individuals and populations, and ideally to create a smoke-free world. The aim with respect to diet and physical activity is less clear and there continues to be intense debate over what should be recommended in both cases; the same applies to determining what actions will produce the greatest benefit, for whom and under what conditions.

The WHO recommends the following guidelines for individuals who wish to improve their diet (10):

- Achieve energy balance and a healthy weight.
- Limit energy intake from total fats and shift fat consumption from saturated fats to unsaturated fats and towards the elimination of trans-fatty acids.
- Increase consumption of fruits and vegetables, and legumes, whole grains and nuts.
- Limit the intake of free sugars.
- Limit salt consumption from all sources and ensure that salt is iodised.

With respect to physical activity, the WHO recommends «at least 30 minutes of regular, moderate-intensity physical activity on most days» (10).

This level of activity is expected to reduce the risk of cardiovascular disease, diabetes, colon cancer and breast cancer. More activity may be required for weight control. A recent Cochrane review of 43 randomised trials with 3,476 participants found that exercise increased weight loss compared with no treatment, but dieting was more effective (11).

Exercisers lost 0.5 to 4.0 kg, whereas subjects randomized to no treatment groups gained 0.7 kg or lost 0.1 kg. Exercise had more effect on risk factors for heart disease than on weight and more intense exercise led to more weight loss. The effects of exercise seem to be different in men and women, with women needing to reduce their calorie intake more actively to lose weight (12). Many people with multiple chronic conditions will not be able to exercise for 30 minutes on most days, although, counter to general opinion, the Diabetes Prevention Program showed that people aged 60 or older were more likely than younger people to follow advice to exercise more and improve their diet (13).

Increasing physical activity may be more beneficial than improving diet in that, as well as reducing the chance of developing chronic disease, it also improves quality of life, which may be particularly important in people with complex chronic disease (14).

The WHO recently completed a systematic review of the evidence as to what works in increasing physical activity and improving diet (15). It examined the evidence using the following categories: policy and environment, mass media, school settings, workplace, community, primary health care, older adults and religious settings (Table 1).

Table 1

**A Systematic Review of Interventions Designed to Improve the Diet and Promote Physical Activity (15)**

CATEGORY	Total number of peer-reviewed studies	Total number of interventions	Interventions focused on disadvantaged communities	Interventions in low or middle-income countries
Policy and environment	30	23	3	2
Mass media	36	24	2	3
School settings	107	55	14	1
Workplace	49	38	5	1
Community	75	65	22	3
Primary health care	67	29	5	0
Older adults	18	17	3	3
Religious settings	13	10	10	0
<b>Total</b>	<b>395</b>	<b>261</b>	<b>64</b>	<b>13</b>



The reviewers identified 395 studies that met their inclusion criteria, but only 13 were related to low or middle-income countries and only 18 were concerned with older adults. The review considered psychosocial, behavioural and clinical outcomes and classified interventions as effective, moderately effective, promising but based on limited evidence, minimally effective, based on insufficient evidence or not shown to be effective, or with outcomes which were not measured or reported. Taking into consideration the limitations of the studies that were included in the analysis, the main findings of the review are summarized as follows:

- **Policy and environment:** Three interventions were found to be effective:
  - 1) government regulation that supports healthier staple foods; for example, replacing palm oil with soya oil, thus reducing dietary fatty acid content; 2) building, planning and transport policies that reduce the barriers to physical activity; and 3) point of decision prompts that encourage the use of stairs. Moderately effective interventions include pricing policies, point of purchase prompts to support healthier choices and multi-targeted approaches to encourage more walking and cycling.
- **Mass media:** Campaigns to encourage physical activity are effective if they are combined with community based support programmes or associated with policies to reduce environmental barriers to physical activity. Moderately effective interventions include intensive campaigns that concentrate on one simple message (like increasing consumption of low fat milk), national health brands or logos that signal healthier foods to consumers and long-term, intensive campaigns that promote healthy diets.
- **School settings:** High intensity school programmes can work if they are comprehensive and have many components, including teaching provided by trained individuals, supportive school policies, a physical activity programme, a parental/family component and access to healthy food options in schools. Focused programmes and assessments of the needs of schools and their cultural context are moderately effective.
- **Workplace:** Multi-component workplace programmes that include the provision of healthy foods and space for exercise, involving the staff in planning and implementation, incorporating family interventions and helping individuals to change, and monitoring, are effective.

- **Community:** Three interventions have been shown to be effective in the community. Firstly, multi-component diet education programmes that target high-risk groups. Secondly, community development programmes that either involve intersectorial cooperation or have a single goal, for example, reducing the risk of a cardiovascular event. Thirdly, community-based programmes for a homogenous group. Several interventions have been shown to be moderately effective: using existing phone-in services to provide dietary advice; community interventions performed as part of a national or global campaign; programmes that target the poor or illiterate and include dietary advice; computer-based interventions that provide personalised feedback to high-risk groups; supermarket tours to support the purchase of healthier foods; and walking school buses.
- **Primary care:** Primary care interventions that target individuals at risk of chronic disease can be effective if they include people who are inactive, eat less than five portions of fruit or vegetables a day, consume a lot of fat, are overweight or have a family history of chronic disease; if they include at least one session with a health professional who negotiates reasonable goals with follow-up provided by trained staff; and if they are supported by targetted information. Interventions which are linked with actions taken by other stakeholders, for example, sports organisations or the mass media, can also be effective. Programmes that identify patients with raised blood cholesterol levels and provide follow-up are moderately effective, as are weight loss programmes that include telephone or internet consultations over a period of at least four weeks and a self-help programme with self-monitoring.
- **Older adults:** Although the systematic review found 18 studies of 17 interventions in older adults, it did not identify any effective interventions in this particular age group, which is very relevant to our focus on people with multiple chronic conditions. Moderately effective interventions included those encouraging physical activity in a group setting that used an existing social structure or meeting place, and home-based interventions in which older adults are given increased access to fruit and vegetables using an existing infrastructure.
- **Religious settings:** Culturally appropriate and multi-component dietary interventions, which are planned and implemented in conjunction with religious leaders and include group education sessions and self-help strategies, are effective. Culturally appropriate interventions that target weight loss, healthy diets and increased physical activity are moderately effective.

This review identifies many interventions in which there is evidence to show that they are effective and then notes characteristics that seem to be shared by interventions that work. These tend to be: multi-component in design, adapted to the local context culturally and environmentally, appropriate use, existing social structures and involving participation by stakeholders throughout the process.

The authors of the review also note that most of the studies are short-term, meaning that most of the outcomes are psychosocial rather than clinical and that we have little evidence about programme sustainability. Few of the studies provided evidence about cost effectiveness or examined unintended consequences.

The limited evidence from low and middle-income countries makes it clear that involving communities in all stages of planning, implementation and evaluation is important for success.

With respect to polypathologies, there is a real need for a review that takes these concepts and approaches and examines their relevance to prevention, as well as the trajectory that leads to polypathology. If X practices and policies were in place, could we reduce the incidence of CCD and delay its onset and impact? What populations are at the highest risk for CCD? Should we focus on high-risk populations in terms of population health intervention and policy? What efforts are required to effect change in these populations? What analyses are required?

A comprehensive analysis of neighbourhoods and diabetes in Toronto, Canada (ICES, 2007) provides very valuable insights into the social and physical context as a determinant of chronic illness and who is most at risk, and into approaches that may be useful in reducing its incidence. This research is a good example of new approaches to studying polypathology and its prevention (16).

## Primary Prevention: Treating Populations or Individuals?

Primordial prevention focuses on population health, but, once we move to primary prevention, then individuals and their families can be targeted. Most health workers in contemporary society are concerned with treating individuals and their families.

People with established disease are at high risk by definition, but risk can also be measured in people who have no established disease. There is controversy over how best to measure risk and at what level to treat people. The WHO recommends measuring cardiovascular risk by using charts that combine risk factors including age, smoking

status, whether or not people have diabetes and systolic blood pressure (17). Charts for well resourced countries also include blood cholesterol levels, but there are charts that exclude cholesterol for places where it is impossible or prohibitively expensive to access laboratories to measure cholesterol. The point of using these charts is that they give a much more accurate estimate of risk than using any one factor alone, although some argue that age is such a powerful determinant of risk that it can be used alone (Nick Wald, personal communication; publication pending).

These charts are developed using data from the famous studies in Framingham in the USA, where a large population was followed up for years. Some experts argue that it is inadequate to use the Framingham data for other countries, where the makeup of the population may be very different. The United Kingdom, for example, which probably has a population which is less different from that of Framingham than many other countries, has used electronic records to generate a new risk assessment tool called QRISK, which has been shown to be a better predictor for the UK than the Framingham tool (18, 19).

Figure 2

### Overlap among Women and Men who will Experience a Cardiovascular Event in the next 10 Years and who are Predicted to Do so by the QRISK and Framingham Risk Assessments

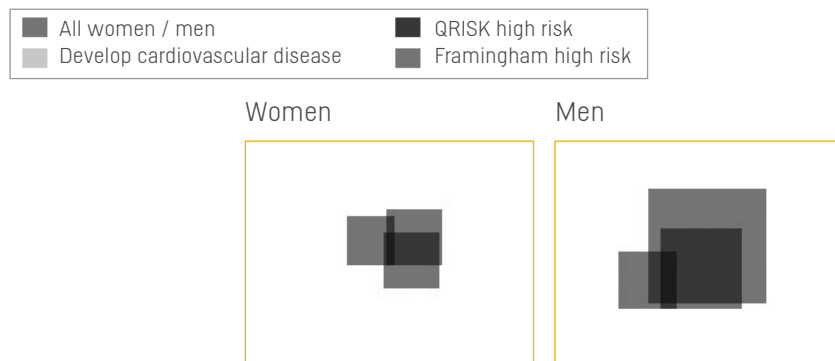


Figure 2 shows, however, that neither tool is very good at measuring risk at the population level. QRISK identifies 10% of men as «high risk» (having a 20% chance of having a cardiovascular event within the next 10 years) but only 30% of cardiovascular events will occur in those men (18). In other words, 70% of cardiovascular events will occur in men defined as being at low risk because they make up 90% of the population. For

women it is worse: QRISK identifies 4% of women as being at high risk, but only 18% of cardiovascular events occur in this group (19).

The WHO recommends lifestyle improvements for people at all levels of risk, as well as regular monitoring for those with a 10-20% risk, and pharmacological treatment for patients with a risk above 20%. The National Institute of Health and Clinical Excellence in England and Wales recommends the same measures (20). The American Heart Association recommends low dose aspirin for patients who have more than a 10% chance of a major cardiovascular event in the next 10 years (21). A recent systematic review suggests that this advice may be misguided (22).

But there is an argument that a 20% chance of a cardiovascular event in the next 10 years is an unacceptably high risk of something that might well result in death or severe disability. People spend large amounts of money every year to insure their houses, which pose nothing like a 20% chance of being burnt down or suffering severe damage in the next 10 years. The risk of potential harm must, of course, be measured against the risk carried by treatment and that is why the authors of the recent systematic review argued against the use of aspirin in people at low risk (22): aspirin will undoubtedly reduce the chances of a thrombosis leading to a heart attack or stroke, but it also increases the risk of a gastrointestinal or cerebral bleed, with the risk of treatment cancelling out any potential benefit.

## The Polypill

But supposing there were a treatment that posed a much lower risk, then it might be reasonable for people to take it, if they had a lower risk of experiencing a major cardiovascular event. Such a treatment could also reduce the overall numbers of heart attacks and stroke because many more people who would have had heart attacks or strokes would be treated. Giving up smoking, losing weight, exercising more and eating a healthier diet will all reduce the chances of a heart attack or stroke and do not carry risks, but slow progress is being made with these measures. Indeed, a cynic might say that, while a relatively small number of relatively wealthy people in developed countries are improving their lifestyle, we have a global pandemic of smoking and obesity.

This is the thinking behind the idea of the polypill, a single pill that contains several drugs (anti-hypertensives, a statin, and possibly aspirin and folic acid). The idea was developed by several researchers around the turn of the millennium but really took off with the publication of papers in the BMJ in 2003 (22). Nick Wald and Malcolm Law used

extensive data to argue that, if everybody aged 55 started routinely taking a pill containing a statin, aspirin, folic acid and three anti-hypertensives at low doses (to get 80% of their benefits with only 20% of the side effects), then 80% of heart attacks and strokes would be prevented. Recent studies have questioned the use of aspirin in the polypill and the version currently advocated by Wald and Law does not include it [21]. The inclusion of folic acid has always been controversial and other polypills do not include it. People at the age of 55 have a risk of about 8% of suffering a major cardiovascular event in the next 10 years simply because of their age. The argument of Wald and Law was that the simplicity of everybody being treated with a single pill would save many more lives than the inherent complexity of assessing risk in individuals and tailoring their treatments using different drugs.

Importantly, because these drugs are no longer subject to patents, the pill might be made for as little as \$1 a month, meaning that treatment might be available to millions in poorer countries, who are at high risk but unable to afford the expense of more traditional treatment. Doctors would not be needed to prescribe the treatment. It could be advocated and dispensed by community health workers.

Some experts welcomed this revolutionary idea with enthusiasm, but many were appalled. For cardiologists the idea promoted inferior treatment, although they acknowledged that most people who will develop heart attacks or strokes are not currently treated because they are not at a high enough risk, are not treated even when they are at risk, are inadequately treated or fail to take their medication. Public health practitioners thought that the polypill would mean that people would not bother to adopt healthy lifestyles. Drug companies saw the potential disappearance of lucrative markets and many found the idea of «medicalising» everybody over 55 years of age offensive.

Although progress has been horribly slow from the point of view of the enthusiasts, the idea of the polypill is gathering momentum and several polypills are now available, most of them manufactured in India. A feasibility trial from India has shown that it is possible to manufacture a pill with all the necessary components, that people will take it and that it will reduce risk factors, although perhaps not enough to reduce heart attacks and strokes by 80% [23].

Some people in India are taking the pill and it may be the case that versions of the polypill will be allowed onto the market in Europe and the USA for secondary prevention. Indeed, there is strong evidence that people who have had heart attacks or strokes should take these pills, although there is also sound evidence that many people are not taking them [24]. A trial to evaluate the effectiveness of the polypill in primary prevention is now being

planned, but it is unlikely to identify the potentially adverse behavioural effects feared by its dissenters (e.g., would those who take the pill feel protected and increase high-risk activities?).

An interesting sideline to this is that combining drugs in one pill may be effective in different circumstances, particularly for people living with multiple chronic diseases, for example, for treating asthma, chronic obstructive lung disease and depression, all at the same time. Polypharmacy has acquired a bad name because it is often an irrational approach, but rational polypharmacy with a number of drugs in one pill may be a much better way forward than spending hundreds of millions to invent new ones that often have only marginal benefits.

## Secondary Prevention

Secondary prevention is concerned with people with established disease, although usually it is at an early stage. Its aim is to limit the extension of the disease and the development of complications. For it to be successful there must be an early stage in the disease that can be identified and an effective treatment for preventing its progression.

Screening, using large-scale tests to identify disease in apparently healthy people, is a form of secondary prevention. Screening for cervical cancer is a good example, as it identifies cancer at an early stage and surgery can remove it. Interestingly, there is now a vaccine against the human papilloma virus, the cause of many cases of cervical cancer, which means that cervical cancer can be prevented through primary rather than secondary prevention, although its use remains controversial.

Perhaps there has been a substantial increase in the demand for screening to ensure the early detection of certain disease conditions because of the well-known phrase «prevention is better than cure». It is necessary, however, to establish the cost-benefit profile of these procedures at the populational level in order to determine the cost for each life which is saved.

Rational screening means that many criteria must be met before mass screening can be introduced and these criteria are shown in table 2. The test itself must be sensitive (good at picking up people with the disease) and specific (unlikely to identify, wrongly, people without the disease as having it). Unfortunately, many potential screening tests have low sensitivity and specificity, meaning that they fail to pick up people with the disease (false negatives) and wrongly identify people who do not have a specific disease as having it (false positives).

Table 2

Requirements for an Effective Screening Programme

Disorder	Well-defined
Prevalence	Known
Natural history	Long period between first signs and overt disease: medically important disorder for which there is effective remedy
Test choice	Simple and safe
Test performance	Distributions of test values in affected and unaffected individuals known
Financial	Cost-effective
Facilities	Available or easily provided
Acceptability	Procedures following a positive result are generally agreed upon and acceptable to both the screening authorities and to those screened
Equity	Equity of access to screening services: effective, acceptable and safe treatment available

Randomised clinical trials are very useful for determining the effectiveness of screening on the mortality and morbidity of specific conditions in populations, particularly in situations where an intervention has been designed to manage the disease on the basis of screening results. Such trials have been conducted to determine the cost of breast cancer screening and systematic reviews show that screening does reduce mortality, despite many women having biopsies of breast lumps that turn out not to be malignant (26).

The cost per quality-adjusted life year (QALY) is about £5,000 in the UK, which is well below the cut-off point of £20,000 to £30,000 used by the National Institute for Health



and Clinical Excellence to decide which interventions should be available as part of the UK National Health Service. [A quality-adjusted life year is a year of life adjusted for its quality or its value; it is a measurement devised by health economists. A year of perfect health is considered to be equivalent to 1.0 QALY. The value of a year of ill health would be discounted. For example, a year in which a person is bedridden might have a value equivalent to 0.5 QALY (26).

It is crucial for any screening programme which is introduced to have a high level of quality assurance. Otherwise it may not achieve its desired results. For years in Britain, for example, cervical screening was not quality assured. The wrong women were screened, the samples were poorly collected and smear reading was not quality controlled. The result was that, before quality assurance was introduced, cervical screening achieved little (28).

Table 3

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**UK Criteria for Appraising the Viability, Effectiveness and Appropriateness of a Screening Programme (updated June 2009)**

Ideally all the following criteria should be met before screening for a condition is initiated:
<b>THE CONDITION</b>
1. The condition should be an important health problem
2. The epidemiology and natural history of the condition, including its development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, disease marker, latent period or early symptomatic stage
3. All the cost-effective primary prevention interventions should have been implemented as far as this is practicable
4. If the carriers of a mutation are identified as a result of screening, the natural history of people with this status should be understood, including the psychological implications
<b>THE TEST</b>
5. There should be a simple, safe, precise and validated screening test
6. The distribution of test values in the target population should be known and a suitable cut-off level should be defined and agreed

<b>THE TEST (continued)</b>
7. The test should be acceptable to the population
8. There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to these individuals
9. If the test is for mutations and if all possible mutations are not being tested, the criteria used to select the subset of mutations to be covered by screening should be clearly set out
<b>THE TREATMENT</b>
10. There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment
11. There should be agreed evidence based policies to decide which individuals should be offered treatment and the appropriate treatment to be offered
12. Clinical management of the condition and patient outcomes should be optimised by all health care providers prior to participation in a screening programme
<b>THE SCREENING PROGRAMME</b>
13. There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an «informed choice» (e.g. Down's syndrome, cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened
14. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public
15. The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment)

THE SCREENING PROGRAMME (continued)
16. The cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced with respect to expenditure on medical care as a whole (i.e. value for money). The assessment of this criterion should take into account the evidence from cost-benefit and/or cost-effectiveness analyses and consider the effective use of available resources
17. All other options for managing the condition should have been considered (e.g. improving treatment, providing other services) in order to ensure that no more cost-effective intervention could be introduced or that current interventions cannot be increased using the resources which are available
18. There should be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards
19. Adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to initiating the screening programme
20. Evidence based information, explaining the consequences of testing, investigation and treatment, should be made available to potential participants to assist them in making an informed choice
21. Public pressure to broaden the eligibility criteria, to reduce the screening interval and to increase the sensitivity of the testing process should be anticipated. Decisions about these parameters should be scientifically justifiable to the public
22. If screening is for a mutation, the programme should be acceptable to people identified as carriers and to other family members

Table 3 shows the criteria used by the UK National Screening Programme to decide which screening programmes to introduce. Screening programmes that have met these criteria include screening for abdominal aortic aneurysm, breast, bowel and cervical cancer, diabetic retinopathy, hypertension and vascular risk. Table 4 shows the programmes which have not met the criteria, often despite popular for them to be introduced.

Table 4

**Systematic Population Screening Programmes which have not been Recommended in the UK**

Alcohol problems	Glaucoma
Alzheimer's disease	Glomerulonephritis
Atrial fibrillation	Haemochromatosis
Cancers: Anal   Bladder   Lung   Oral   Ovarian   Prostate   Stomach   Testicular	Hearing loss
Chlamydia	Hepatitis C
Coeliac disease	Old age
Chronic kidney disease	Osteoporosis
Depression	Postnatal depression
Diabetes	Stroke
Domestic violence	Thrombophilia
Familial hypercholesterolaemia	Thyroid disease

Many disadvantaged populations, for example, people with learning disabilities or chronic mental health problems, are less likely to be screened. This may well be true as well for people with multiple chronic conditions.

Measures to stop people smoking, increase physical activity and improve diet will also be effective as secondary preventive strategies in patients with established cardiovascular disease, but patients also need pharmacological treatments to reduce the chances of recurrence or of complications in the case of diabetes or progression of chronic respiratory disease. Most of these treatments are firmly based on evidence, although there have recently been interesting suggestions from a major trial that tight control of blood sugar in diabetic patients may lead to worse outcomes [29].

## Joining up all the Pieces

Although we have followed the classic epidemiological division of levels of prevention, governments and health authorities must decide on the right mix for their particular circumstances. Some governments will have very few resources for health systems and so may concentrate on social determinants of health. Other governments may operate in political environments where any form of «social engineering» is suspect and so they may concentrate on strategies targetted at sick individuals.

## What do we need to know?

### General

- What are the health trajectories and life conditions that result in multiple co-morbidity and complex chronic disease?
- What are the most effective individual and populational approaches to prevention?
- What are the approaches in terms of conceptualizing prevention in the chronic disease literature that can be applied to poly pathology?
- What is new or different about the poly pathological population?
- What research questions is it important for us to pursue?
- What is the relative contribution of primordial, primary, secondary and tertiary prevention in improving outcomes and satisfaction, and reducing costs in people

living with multiple diseases? What is the best prevention strategy to pursue in any given set of circumstances? Can we produce a guide that could be used in very different circumstances?

The following is a list of research and policy questions for primordial, primary and secondary prevention.

## Primordial and Primary Prevention

- How could healthier communities be promoted, particularly in low to middle-income countries?
- What would motivate more countries, particularly the United States and Indonesia, to sign the Framework Convention on Tobacco Control?
- Is it possible to monitor, by country, research into tobacco control, surveys of smoking levels, global cigarette consumption, the economic effects on individual countries (tobacco leads to losses not gains as the costs of damage outweigh income from taxation), smoking costs to employers, the economic costs of fires and litter, costs to smokers, tobacco company documents, litigation, the tobacco industry and the recruitment of scientists to the tobacco company cause?
- What are the effects of MPOWER policies, particularly nicotine replacement therapy, on people living with multiple chronic diseases?
- What is the optimal diet and level of physical activity for people with multiple chronic conditions? How sustainable, cost-effective and safe are effective interventions?
- Which policies to improve diet and increase physical activity will be effective in patients with multiple chronic conditions?
- How might people in low and middle-income countries, who currently have healthy diets, be encouraged to keep to them rather than switch to unhealthy high fat, high salt, high calorie diets?
- How can we ensure that, with increasing urbanisation and urban poverty, the inhabitants of cities in low and middle-income countries are able to sustain levels of physical activity?
- How best to measure the risk of developing cardiovascular disease, particularly in places where laboratory tests are unavailable or unaffordable?

- Might age alone be used for risk assessment; if so, would the cut-off point be different in different countries?
- What is the right level of risk at which to begin pharmacological treatment?
- Will the polypill be more cost-effective than routine treatment in primary, secondary and tertiary prevention?
- What should the components of the polypill be?
- What is the best strategy for using the polypill in primary prevention: risk assessment followed by treatment or to offer the polypill to everyone above a certain age?
- If the polypill is cost-effective, how can its widespread use be encouraged?
- Might other polypills be useful in other forms of prevention, for example, smoking cessation or chronic lung disease?

## Secondary Prevention

- Can we develop effective screening tests for the many conditions where no reliable test is currently available?
- Is tight control of blood sugar in patients with diabetes dangerous?
- Are patients with multiple chronic conditions less likely to receive screening tests?
- Action research to speed up the implementation of effective technologies.
- Are the gaps in unmet care needs similar across countries and populations?
- Should screening strategies be the responsibility of specific medical specializations or not?
- Can we learn how to improve secondary prevention from the directly observed treatment programme strategy for tuberculosis?

## What Innovative Strategies could Fill the Gaps?

Two broad types of effort could improve the preventive care of patients with multiple chronic conditions: collaborative studies designed to answer outstanding questions (see list above) and technological interventions which aim to promote the more effective implementation of existing knowledge.

The questions that remain unanswered in relation to the prevention of multiple chronic diseases are so diverse and complex that answering them will require large, long-term research efforts that transcend traditional institutional, geographical, cultural, political and linguistic barriers.





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### *Contributors*

Richard Smith, Cristina Rabadán-Diehl, Alejandro Cravioto and Abraham Wall-Medrano wrote the initial draft of this chapter in English. Alejandro Jadad approved the draft before it was made available online, in Spanish and English, through the OPIMEC platform. This draft received important contributions in English from Simon Chapman, Katia De Pinho Campos, Murray Enkin, John Gillies, Rajeev Gupta, Yan Lijing, Beatriz Marcet Champaigne, J Jaime Miranda, Mary Ann Sevick, Ross Upshur, and, in Spanish, from Juan Antonio Guerra, Adolfo Rubinstein and Narcis Gusi. Richard Smith incorporated these contributions into a new version of the chapter, which was revised by Renée F. Lyons and approved for publication by Alejandro Jadad.

Responsibility for the content rests with the main contributors and does not necessarily represent the views of the Junta de Andalucía or any other organization participating in this publication.

### *Acknowledgments*

Carlos Álvarez-Dardet and Angela Cejudo made comments on the chapter in Spanish, and Neil Arnott, Jackie Bender, Gerald Bloomfield and Kerry Kuluski on the English version, which did not lead to changes in its contents.

### *How to reference*

Smith R\*, Rabadán-Diehl C\*, Cravioto A\*, Wall-Medrano A\*, Chapman S, De Pinho K, Enkin M, Gillies J, Guerra JA, Gupta R, Gusi N, Lijing Y, Marcet B, Miranda JJ, Rubinstein A, Sevick MA, Upshur R. [\*Main contributors] Prevention and health promotion. In: Jadad AR, Cabrera A, Martos F, Smith R, Lyons RF. When people live with multiple chronic diseases: a collaborative approach to an emerging global challenge. Granada: Andalusian School of Public Health; 2010. Available at: <http://www.opimec.org/equipos/when-people-live-with-multiple-chronic-diseases/>

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## Abbreviations

AAL: Ambient Assisted Living

BMJ: British Medical Journal

CAM: Complementary And Alternative Medicine

CCD: Complex Chronic Disease

CCM: Chronic Care Model

CIRS: Chronic Illness Resources Survey

CMPs: Case Management Programs

CVD: Cardiovascular Disease

DMPs: Disease Management Programs

EASP: *Escuela Andaluza de Salud Pública*

EPP CIC: Expert Patients Programme Community Interest Company

GRIN: Genomics, Robotics, Informatics and Nanotechnologies

ICCC: Innovative Care for Chronic Conditions

ICD: International Classification of Diseases

ICED: Index of Coexisting Disease

IDS: Individual Disease Severity

MCCs: Multiple Chronic Conditions

MD team: Medical Doctor

MeSH: Medicines Medical Subject Headings

MI: Motivational interviewing

MPOWER: Monitor (tobacco use and prevention policies), Protect (people from tobacco smoke), Offer (help to quit tobacco use), Warn (about the dangers of tobacco), Enforce (bans on tobacco advertising, promotion and sponsorship), Raise (taxes on tobacco)

NHIS: National Health Interview Survey

NHS: National Health Service

OECD: Organization for Economic Co-operation and Development

OPIMEC: *Observatorio de Prácticas Innovadoras en el Manejo de Enfermedades Crónicas Complejas*

PACE: Program of All-inclusive Care

QALY: Quality-Adjusted Life Year

QRISK: Cardiovascular disease risk score

RE-AIM: Reach, Effectiveness, Adoption, Implementation and Maintenance

SNOMED CT: Systematized Nomenclature of Medicine-Clinical Terms

SSPA: *Sistema Sanitario Público de Andalucía*

TCAM: Traditional Complementary And Alternative Medicine

TPE: Therapeutic patient education

VHA: Veterans Health Administration

WHO: World Health Organization

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# When people live with multiple chronic diseases: a collaborative approach to an emerging global challenge

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