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Strategies for Reducing Risks in Smoking: Opportunity or Threat?

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ABSTRACT

The smoking control policies recommended by the World Health Organisation have achieved a slight decrease in smoking prevalence in developed countries, although associated mortality is still very high. The use of tobacco products other than cigarettes and even medicinal nicotine (known as nicotine replacement therapy [NRT]) has been proposed as a risk reduction strategy. Among the tobacco products with less individual risk than cigarettes would be any type of tobacco without smoke (smokeless) with a low content in nitrosamines and modified cigarettes; both forms included under the PREP (Potentially Reduced Exposure Products) concept. The idea would be to promote these products among patients who cannot quit smoking or wish to reduce their risk without giving up nicotine intake. The possible effects of risk reduction strategies, including PREP, on the decreased prevalence and morbidity and mortality are reviewed, and the possible implications that this measure could have in Spain are analysed. Tobacco control measures in Spain have only been made recently and are still insufficient. Therefore, the current priority in Spain is to develop control policies that have proven to be more than effective. The marketing and advertising of new tobacco products, even with reduced potential risk, seems more a serious threat than an opportunity for developing smoking control policies.

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Estrategias de reducción de riesgos en tabaquismo: ¿oportunidad o amenaza?

RESUMEN

Las políticas de control del tabaquismo recomendadas por la Organización Mundial de la Salud han logrado un discreto descenso en la prevalencia de tabaquismo en los países desarrollados, aunque la mortalidad relacionada sigue siendo muy elevada. Se ha propuesto como estrategia de reducción de riesgos el uso de productos de tabaco distintos a los cigarrillos o bien la nicotina medicinal (conocida como terapia sustitutiva de nicotina o TSN). Entre los productos del tabaco con menos riesgo individual que los cigarrillos estarían algunos tipos de tabaco sin humo (smokeless) con bajo contenido en nitrosaminas y los cigarrillos modificados; ambas formas englobadas bajo el concepto de PREP (Potentially Reduced Exposure Products). La idea sería promover estos productos entre aquellos que no pueden dejar de fumar o bien desean reducir su riesgo sin abandonar el consumo de nicotina. Se revisan los posibles efectos sobre la disminución de la prevalencia y sobre la morbimortalidad de las estrategias de reducción de riesgos, incluyendo los PREP, y se analizan las posibles implicaciones que esta medida podría tener en nuestro entorno. En España, las medidas de control del tabaquismo son recientes y todavía insuficientes. Actualmente, la prioridad en España es, por tanto, el desarrollo de políticas de control que han mostrado su eficacia de forma sobrada. La comercialización y difusión de nuevos productos de tabaco, aún de riesgo potencial reducido, parece más una seria amenaza que una oportunidad para el desarrollo de las políticas de control del tabaquismo.

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Introduction

The current development in public smoking control policies recommended by the International Framework Agreement, promoted by the World Health Organisation, is fostering an average descent in smoking prevalence of 0.5 to 1% in developing nations, while still increasing in impoverished countries. The world mortality rate due to smoking is currently estimated at 5.4 million people/year, a figure that could surpass the 8 million mark in 2030 if the same trend is maintained.¹

Due to the difficulties in implementing these control policies, their effects could be insufficient in reducing the morbidity and mortality related with tobacco consumption in the following decades. This reality, together with the fact that nicotine addiction is on occasion difficult to break, has induced institutions such as the Royal College in the United Kingdom and some experts to advocate, as a new risk reduction strategy, the use of tobacco products other than cigarettes, or of medicinal nicotine, known as nicotine replacement therapy (NRT). Among the tobacco products with less individual risk than cigarettes would be some types of smokeless tobacco with a low content in nitrosamines and modified cigarettes, both forms included under the PREP (Potentially Reduced Exposure Products) concept. At present, with the exception of NRT, the tobacco products with less toxic content are marketed by the tobacco industry. The idea would be to promote these products among those who cannot quit smoking or wish to reduce their risk without giving up nicotine intake.2

Given the huge implications this would have with smoking control policies, a previous detailed analysis seems reasonable. This article makes a brief revision of the risk reduction strategies, including the PREPs and their possible effects, both on the decrease in prevalence as well as in morbidity and mortality from tobacco consumption. Lastly, the possible implications that this measure could have on our surroundings are analysed.

Risk Reduction Strategies

The concept of risk reduction emerges in the 1980s in the context of parenteral drug consumption, as a reply to two particular factors: firstly, the appearance of the AIDS epidemic among heroin users and secondly, the growing suspicion that the strategies adopted to face drug use had not been sufficiently effective.³

In the case of smoking, the initial risk reduction strategies were proposed in the area of clinical practice as a measure to reduce diseases associated with cigarette consumption or as an intermediate step to definitive abstinence. Similarly, as the perception of the risks involved in smoking increased, the tobacco industry enlarged the market with new products other than cigarettes, presented to the consumer as a reduction in damage, aimed at reassuring the smoker and maintaining consumption.

The different risk reduction proposals that have appeared throughout the history of cigarettes are commented herewith, both in the clinical domain as well as those carried out by the tobacco industry.

Clinical Strategies

The proposals included here are born out of the health care sector aimed at decreasing use to reduce the risk, either as an end or as an intermediate step to the complete suppression of tobacco.

Reduction in Number of Cigarettes

Reducing the number of cigarettes has been the usual strategy used by smokers to decrease the risk or to try and advance in the process of quitting. It was also a proposal used in the past by some professionals as a "realistic" solution for those patients who cannot or will not give up smoking completely. There is no scientific evidence that a reduction in the number of cigarettes truly reduces the health risks, an apparently paradoxical fact. The main explanation for this is that when smokers reduce tobacco consumption, they develop unconscious compensatory practices (smoke to the butt, inhale much deeper, etc.) to obtain the same amount of nicotine as before the reduction. The result is a slight decrease in the amount of nicotine inhaled and, consequently, of the accompanying tar and toxins, decrease that is not proportionate to the number of cigarettes eliminated. For some diseases such as ischaemia heart disease, a decrease of 10 cigarettes in a 20-cigarette per day smoker involves a risk reduction of less than 10%; that is, 5 times less than that expected due to the compensatory effect in the manner of smoking.4

The possible benefits of the reduction in the number of cigarettes have been assessed by several follow-up studies. Godtfredsen et al⁵ analysed the mortality rate by diseases related to tobacco use in smokers of over 15 daily cigarettes, compared with a group that had reduced the amount by half and with those who had given up smoking completely. Among those who reduced the number of cigarettes smoked, no decrease in the mortality rate was observed. However, those who quit smoking completely experienced a 35% reduction in the risk of death 15 years after the study. Neither were there significant differences found in relation to respiratory disease and cardiovascular mortality among the over 15 daily cigarette smokers and those who had reduced the number. Another recent study carried out in Norway assessed 50,000 participants, male and female, over a period of 15 years and concluded that a reduction in consumption (e.g. from 30 to 20 cigarettes) did not significantly reduce the risk of cancer, lung disease, heart attack or brain infarction;6 table 1 displays this study's data. A recent review of a total of 31 publications concludes that a substantial reduction in the number of cigarettes has a slight marginal health benefit, much less than that expected.7

Moreover, it is generally thought that smoking few daily cigarettes is not an excessive health risk. However, there are studies that proved that very small amounts of tobacco produce harmful effects on the health.⁸

Gradual Reduction of Tar and Nicotine

Described in 1979, the gradual reduction of tar and nicotine, via a weekly change in the brand of cigarettes smoked, is conceived as a transition and preparation strategy towards total abstinence, although many therapists have applied it with the aim of reducing consumption. A number of studies have shown its effectiveness as just another technique, within the psychological treatments to quit smoking, above all within the framework of multi-component programs.⁹

Nicotine Substitution Treatment

NRT has been traditionally used as a therapy to quit smoking, although some smokers use it transitionally for long distance trips, hospital stays or while they are in smoke-free environments. Recent

Table 1Relative risk of mortality by several causes for every 10 cigarettes of reduced consumption⁶

		Heavy smokers		All smokers
Cause of death	No. deaths	RR (CI of 95%) for every	No. deaths	RR (CI of 95%) for every
		10 cigarettes less		10 cigarettes less
All the causes	1,809	0.97 (0.90-1.04)	4,042	1.00 (0.94-1.05)
Cardiovascular disease	650	0.90 (0.79-1.03)	1,479	0.98 (0.89-1.08)
Ischaemia heart disease	447	0.85 (0.73-1.01)	989	0.97 (0.87-1.10)
Tobacco related cancer	453	0.91 (0.79-1.06)	935	0.99 (0.89-1.11)
Lung cancer	253	0.97 (0.80-1.18)	497	1.01 (0.87-1.17)

evidence shows that temporary reduction strategies with fast-acting NRT (gum) in smokers who initially do not want to give up smoking may increase the rate of quitting in the mid-term.¹⁰ In either case, NRT or "clean" pharmacology is the only product with scientific evidence for a temporary risk reduction strategy¹¹ and, as such, it is acknowledged in our country.¹²

Tobacco Industry Strategies

These proposals are not truly aimed at reducing risks, rather than commercial interests. However, given that at the time they were presented as such, above all with *light* cigarettes, and frequently many smokers have adopted them with the idea of reducing damage, they are included in this study.

Cigars or Pipe Smoking

Cigars and pipe smoking are different methods of smoking tobacco, although they have always been in the minority. The tobacco industry widely promoted cigars in the 1990s with the aim of increasing market share. The risks associated with these products are less than for cigarettes because those who consume them tend to not inhale the smoke, although they do absorb a great deal of nicotine through their nasal mucous. The results are a lower rate of emphysema, lung cancer and larynx cancer in cigar smokers, but these have a higher risk of mouth and oesophagus cancer than those who smoke conventional cigarettes.¹³ The largest study carried out on the effects on health of cigars was developed in a group of 17,774 males aged between 30 and 85. In the analysis, those who smoked cigars (1,546), in comparison with the nonsmokers (16,228) presented, independently of other factors, a higher risk of heart disease (27% more), of chronic obstructive lung disease (45%) and of oesophageal and lung cancer (twice as high). The risks increased significantly when over 5 daily cigars were smoked.14

Filter Cigarettes

Filter cigarettes appeared on the market in the 1950s. With the addition of filters, the industry's aim was not to protect the health of smokers, but to calm them and protect their own business benefits, which were endangered in 1954 with the first epidemiology studies showing that, without a doubt, tobacco was a cause of lung cancer. At first, it was thought that the addition of filters could reduce the risk of some cancers related to tobacco, by markedly reducing the amount of nicotine. However, a number of cohort studies carried out in the USA and United Kingdom showed that lung cancer kept increasing from 1950 to 1980, despite the widespread use of filter cigarettes.¹⁵

Cigarettes Low in Tar and Nicotine (Light Cigarettes)

With the incorporation of *light* cigarettes in 1970, many smokers switched to brands low in tar and nicotine believing that they were reducing the damage. This perception of reduced risk was widely promoted by the tobacco industry and gave rise to the decision of many smokers to put off quitting. Indeed, the rate of abstinence of *light* cigarette smokers is less than that of conventional cigarettes smokers (27 versus 53%; p < 0.01), which proves the potential of these products of efficiently delaying cessation.¹⁶ In the European Union (EU), the designation of *light* for these cigarettes has been prohibited since 2003, but these products are still being sold with other names or external signs on their packaging.

The tar content of cigarettes is measured with machines that "smoke" artificially; a large part of the reduction observed is due to the dissolution of the smoke through the holes made in the filters by the manufacturers. In real life, smokers unavoidably cover these holes with their fingers, leading to a much higher tar inhalation. On this basis, the tar/nicotine proportion of *light* cigarettes is in fact similar to that of conventional cigarettes.¹⁷ Indeed, the absorption of tar and nicotine is higher than the amount indicated on the cigarette packet and the ISO standards.^{18,19} The *Centro de Investigación y Control de la Calidad* (Centre for Research and Quality Control) ascribed to the Spanish Institute of Consumer Affairs of the Spanish Ministry of Health and Consumer Affairs²⁰ is the only certified body for the evaluation of tobacco products.

It was initially believed that *light* cigarettes could contribute to reducing the risk of lung cancer.²¹ However, in the decades following the appearance of *light* cigarettes onto the market, overall mortality by lung cancer in the USA, in both sexes, did not cease to increase, going from 98.5 to 153.3 cases per 100,000 people from 1979 to 1997, which contradicts the initial idea of lower risk.²² Despite all of the above, nowadays there are still a great deal of smokers who feel protected by smoking filter and low tar cigarettes.²³

Potentially Reduced Exposure Products

Conceptually, PREPs are defined as those products that contain nicotine, but with lower quantities of tar and other habitual toxins than conventional tobacco (mainly nitrosamines), definition which includes some types of *smokeless* tobacco, as well as modified cigarettes.

Smokeless Tobacco

Several types of tobacco are included under the denomination of *smokeless* (paste, powder, *snus*, etc.) with the common feature of being consumed orally or nasally but without combustion and therefore, without smoke. In general, it is considered that they pose

a lower health risk than cigarettes. *Smokeless* tobacco has traditionally had widespread consumption in some Asian countries. In developed countries, *smokeless* tobacco is infrequent, with the exception of Sweden, where the so-called *snus* has been consumed since 1637. *Snus* is a bag of moist tobacco powder placed under the upper lip and absorbed through the oral mucous. The risk level of this type of tobacco is low compared to cigarettes, but it is also a cause of cancer. The low prevalence of lung cancer observed in Sweden in comparison to other developed countries,²⁴ has contributed to some experts focusing on this product as a possible alternative for a viable risk reduction strategy.

Several studies have evaluated *snus* as a "protective" factor from the consumption of cigarettes. On the one hand, it would delay the start in younger people and, on the other hand, increase cessation in cigarette smokers. In Sweden, it was been observed that 47% of the young who experimented with tobacco became cigarette smokers, while this only occurred in 20% of those who started consuming *snus*. In the Swedish experience, 66% of those who used *snus* quit smoking, while 47% did so with nicotine gum and 32% with patches.²⁵ By contrast, in the USA, where it is also consumed although to a lesser degree, it has been noted that youths who start consuming *snus* tend to initiate easier with cigarette smoking than those who do not (27% versus 12.9%).²⁶ In addition, adult smokers who use *snus* try to give up smoking more frequently but have lower levels of abstinence than those who do not use it (12% versus 21%).^{27,28}

Modified Cigarettes

Modified cigarettes are devices shaped like conventional cigarettes which liberates nicotine without combustion, but through a heating process (electronic or chemical),²⁹ therefore, they are sometimes known as electronic cigarettes (*e-cigarettes*). At present, several tobacco companies have marketed these alternative cigarettes in a number of countries, including Spain. Its legal status in the EU is unclear because it is not a tobacco product, but it has not passed the pharmaceutical product tests, despite it containing nicotine, given that it is not clear that it will be marketed with medicinal aims.³⁰

Brand names such as Ruyan® and Similar® have recently appeared on the Spanish market; the former uses an electronic system to heat and liberate the nicotine, while Similar® uses a chemical system. In our country, it is sold in some cinemas, petrol stations and airlines, although its commercial extension is still quite limited. With some brands (such as Eclipse®, sold in the US by RJ Reynolds), it has been proven that, although they release less tar than conventional cigarettes, they produce more carbon monoxide, making the risk of heart attack even higher.31 Shiffman et al32 point out that the idea that these modified cigarettes reduce the risk can have an adverse effect, since they prevent the definitive quitting of tobacco consumption or can even induce ex-smokers to try these new products. For the time being, there are no studies proving that modified cigarettes are safer than conventional ones.³³ It is for several reasons that the promotion of these products could undermine some of the effectiveness policies demonstrated in tobacco control.³⁴

Advantages and Disadvantages of the Risk Reduction Strategies

To evaluate the reduction in damage from tobacco use, the individual impact should be dealt with separately from the general population impact. From an individual viewpoint, it is possible that,

in certain circumstances, total abstinence is not a realistic objective and a strategy of damage reduction could be posed. The therapeutic option would be NRT or "clean" nicotine, given that it is the only product that has proven scientific evidence for a temporary risk reduction strategy. NRT, although it is a freely available product, is subject to regular pharmaceutical regulation.

From a general population viewpoint, the traditional clinical strategies (cigarette reduction, etc.) have not proven to be effective and those proposed by the industry have only served to maintain the epidemic. As far as reduced toxicity products or PREPs, on which the current debate is centred, there are several drawbacks.³⁵ Firstly, smokeless tobacco has not proven to reduce risks to the general population, given that it is unclear if the introduction of new forms of dispensing nicotine contribute to decreasing tobacco consumption among the population. By contrast, the data indicates that the tobacco industry could make the most of the liberation of *snus* to attract adolescents and young adults to nicotine consumption³³. The strategy that should be followed in the young is to not encourage them to consume *snus*, as an alternative, but to develop preventative and treatment programs,^{36,37}

The promotion of *snus* and other forms of smokeless tobacco could reduce the risks in the general public of smokers, but at the expense of increasing the use of tobacco in the totality of the population, which would clearly not be a benefit, but and added risk. In fact, In Norway, where *snus* is also sold, its consumption has increased 11% in all males and up to 18% in the 16 - 24 year age bracket, with no evidence of a descent in the prevalence of traditional smoking.³⁸

A recent review summarises the evidence on smokeless tobacco in relation to the observations made in Sweden, Norway and USA³⁹ (table 2). The data leads us to believe that the Swedish model is not reproducible in other countries.⁴⁰

Another limitation for its use would be the need for new regulations. For the time being, the European Directive for tobacco products⁴¹ prohibits the commercialisation of new types of tobacco in the EU, including the oral tobacco such as *snus*, except in those countries where its use is traditional such as Sweden and Norway. If the commercialisation of these products was permitted, it would be difficult to avoid the reappearance of advertising from brands whose main line of business is traditional cigarettes and not *snus*. Given that the tobacco companies are faced with a world control on advertising by the Framework Agreement, it seems that they would use these new products to weaken and elude the current regulation. In this sense, there is data highlighting the interest that legislation be passed in favour of the commercialisation of these new tobacco products mistakenly classified as "healthier".⁴²

Table 2 Evidence for smokeless tobacco³⁵

It is toxic and carcinogenic

Its promotion has increased global sales of tobacco products in some countries The increase of its consumption has especially increased among adolescents and young adults

Its use is not associated with a reduction in the start in the consumption of cigarettes or its prevalence

It does not play a role in quitting and in Sweden, its effect is contradictory The countries with a lower prevalence of tobacco also consume less smokeless tobacco

There is no data of its effectiveness as a method to give up

The prevalence of smoking is high among smokeless tobacco consumers It is generally used as a partial substitution of cigarettes more than total substitution

The evidence for promoting it as a public health strategy is weak and inconclusive

Implications of the Use of Products of Potentially Reduced Exposure in our Surroundings

The main argument from the supporters of promoting PREPs is that it would be an effective measure in reducing health risks among smokers, which on the other hand is still considered to be too high.

The World Health Organisation recently passed 6 policies to reduce and prevent tobacco consumption, summarised in the plan of measures known as MPOWER, which do not include the reduction of risks. This report also highlights that only 5% of the world population is protected by global tobacco control policies, and that few tobacco consumers receive the necessary help to quit smoking.⁴³ In Spain, only 12% of smokers seek professional help to give up smoking, while in the United Kingdom, with the highest percentage of people seeking help, the figure reaches 41% of the smokers and the EU average is 18%.⁴⁴ This is paradoxical given that, although there is insufficient evidence to assess the results of breaking the tobacco habit in the long term,⁴⁵ the treatment of smoking is cost-efficient and is widely recommended.⁴⁶

The smoking control measures are quite recent in Spain and still insufficient. The priority in our country is, therefore, the development of control policies that have proven their effectiveness more than enough (table 3). All in all, the debate should centre not so much on the possible good points in the reduction of risks, but in the opportunity, to thus avoid the division between clinical professionals, more worried about individual health and those with a wider outlook towards public health.⁴⁷ That is, what is the point of reducing risks when basic elements of proved efficiency such as smoke-free area, physicality of tobacco or the treatment of smokers are starting to make their way, still with a huge amount of difficulties, in the majority of nations?⁴⁸

The background shows how the tobacco industry has been able to periodically develop new products and place them on the market as "safer", which stops the process of quitting among a lot of smokers. Nowadays, the commercialisation and diffusion of new tobacco products in Spain, even those with reduced risk potential, seems to be more a serious threat than an opportunity for the development of smoking control policies.

Table 3 Effective smoking control policies

- 1. Annual increase in tobacco taxes (placing the price above the CPI). Removing the price of tobacco from the CPI basket
- Regulate tobacco additives without including carcinogenic products per se or substances that directly or indirectly increase its addictive capacity
- Regulate labelling and packaging, making them less attractive and using generic packaging without attractive logos
- Limiting the sales points to official sales points (tobacconists), prohibiting expending machines and "second channel" distribution (restaurants, newsstands, etc.)
- Total prohibition of advertising, promotion and tobacco sponsorship. Indirect promotion compensation methods on film and television without prior censorship (declaration of subsidies for product placement, health warnings, etc.)
- 6. Completely smoke-free public places without exception or ambiguities
- Information and education on the risks of active and passive smoking, continually (similar to the prevention campaigns for road accidents as far as investment and intensity)
- 8. Public subsidies for treatments to break the habit of smoking (including medication) and liberalisation of the sale of nicotine substitution treatments
- Health warnings with images, changing and with a combination of negative and positive messages on the cigarette packets or generic brands
- 10. Inspection system of tobacco regulations with state, regional and local development. Deterrent sanctions with speedy procedures and executions

References

- Organización Mundial de la Salud. Diez datos sobre la epidemia de tabaquismo y el control mundial del tabaco. Ginebra: OMS; febrero de 2008.
- Anónimo. Adding harm reduction to tobacco control [editorial]. Lancet. 2007:370:1189.
- Socidrogalcohol. Guía sobre reducción de daños. Disponible en http:// socidrogalcohol.psiquiatria.com/enlaces/
- Law MR, Wald NJ. Environmental tobacco smoke and ischemic heart disease. Prog Cardiovasc Dis. 2003;46:31-8.
- Godtfredsen NS, Holst C, Prescott E, Vestbo J, Osler M. Smoking reduction, smoking cessation, and mortality: a 16-year follow-up of 19,732 men and women from the Copenhagen Centre for prospective population studies. Am J Epidemiol. 2002;156:994-1001.
- Tverdal A, Bjartveit K. Health consequences of reduced daily cigarette consumption. Tob Control. 2006;15:472-80.
- 7. Pisinger C, Godtfrensen NS. Is there a health benefit of reduction tobacco consumption? A systematic review. Nicotine Tob Res. 2007;9:631-46.
- 8. Prescott E, Scharling H, Osler M, Schnohr P. Importance of light smoking and inhalation habits on risk of myocardial infarction and all cause mortality. A 22-year follow up of 12 149 men and women in The Copenhagen City Heart Study. J Epidemiol Community Health. 2002;56:702-6.
- 9. Becoña E. Tratamiento psicológico del tabaquismo. Adicciones. 2004;16 Supl 2:237-63.
- Fagerström KO. Can reduced smoking be a way for smokers not interested in quitting to actually quit? Respiration. 2005;72:216-20.
- Stead LF, Lancaster T. Interventions to reduce harm from continued tobacco use. Cochrane Database Syst Rev. 2007;(3):CD005231.
- 12. Jiménez-Ruiz CA, Riesco JA, Ramos A, Barrueco M, Solano S, De Granda JI, et al. Recomendaciones para el tratamiento farmacológico del tabaquismo. Propuesta de financiación. Arch Bronconeumol. 2008;44:213-9.
- 13. National Cancer Institute. Questions about cigar smoking and cancer. 1998. Disponible en: http://www.cancer.gv/cancertopics/factsheet/tobacco/cigars
- Iribarren C, Tekawa IS, Sidney S, Friedman GD. Effect of cigar smoking on the risk of cardiovascular disease, chronic obstructive pulmonary disease, and cancer in men. N Engl J Med. 1999;340:1773-80.
- 15. Thun MJ, Burns DM. Health impact of "reduced yield" cigarettes: a critical assessment of the epidemiological evidence. Tob Control. 2001;10 Suppl:i4-11.
- Tindle HA, Rigotti NA, Davis RB, Barbeau EM, Kawachi I, Shiffman S. Cessation among smokers who used "light" cigarettes: results from the 2000 National Health Interview Survey. Am J Public Health. 2006;96:1498-504.
- Organización Mundial de la Salud. Convenio Marco de la OMS para el Control del Tabaco. Ginebra: OMS; 2003.
- Darrall KG, Figins JA. The blocking of cigarette filter ventilation holes. Laboratory of the Government Chemist Report EH40M007/98. 1998.
- 19. World Health Organization. The scientific basis of tobacco product regulation. WHO Technical Report series n.º 945. Geneva: WHO; 2007.
- 20. Comisión Europea. Disponible en: http://ec.europa.eu/health/ph_determinants/life_style/Tobacco/label_labo_en.htm
- 21. Wynder EL, Hoffman D. Tobacco and tobacco smoke. Semin Oncol. 1976:3:5-15.
- American Lung Association. Epidemiology and Statistic Unit Research and Program Services. May 2005. Disponible en: http://www.lungusa.org/atf/cf/%7B7A8D42C2-FCCA-4604-8ADE-7F5D5E762256%7D/ASTHMA1.PDF
- 23. Warner KE. Tobacco harm reduction: promise and perils. Nicotine Tob Res. 2004;4 Suppl 2:61-71.
- Foulds J, Ramstrom L, Burje M, Fagerström K. Effect of smokeless tobacco (snus) on smoking and public health in Sweden. Tob Control. 2003;12:349-59.
- Ramström LM, Foulds J. Role of of snus in initiation and cessation of tobacco smoking in Sweden. Tob Control. 2006:15:210-4.
- Haddock CK, Weg MV, DeBon M, Klesges RC, Talcott GW, Lando H, et al. Evidence that smokeless tobacco use is a gateway for smoking initiation in young adult males. Prev Med. 2001;32:262-7.
- 27. Tomar SL. Is use of smokeless tobacco a risk factor for cigarette smoking? The US experience. Nicotine Tob Res. 2003;5:561-9.
- Tomar SL. Snuff and smoking in US men: implications for harm reduction. Am J Prev Med. 2002;23:143-9.
- 29. Wayne GF. Potencial reduced exposure products (PREPs) in industry trial testimony. Tob Control. 2006;15 Suppl 4:90-7.
- 30. European Commission. Health & Consumer Protection Directorate-General. Electronic cigarettes ant the EC legislation. Orientation Note. Brussels, 22/05/2008.
- 31. Caraballo RS, Pederson LL, Gupta N. New tobacco products: do smokers like them? Tob Control. 2006;15:39-44.
- 32. Shiffman S, Pillitteri JL, Burton SL, Di Marino ME. Smoker and ex-smoker reactions to cigarettes claiming reduce risk. Tob Control. 2004;13:78-84.
- 33. McNeil A. ABC of smoking cessation. Harm reduction. BMJ. 2004;328:885-7.
- 34. Stratton K, Shetty P, Wallace R, Bondurant S, editors. Clearing the smoke: assessing the science base for tobacco harm reduction. The National Academy Press, 2001. Disponible en: http://www.nap.edu/catalog/10029.html
- 35. Champan S. Dead customers are unprofitable customers: potential and pitfalls in harm reduction and product regulation. En: Public Health Advocacy and Tobacco Control, editor. Making smoking history. Oxford: Blackwell Publishing; 2007.

- 36. Gómez G, Barrueco M, Aparicio I, Maderuelo JA, Torrecilla M. Programa de prevención del tabaquismo en alumnos de enseñanza secundaria. Arch Bronconeumol. 2009;45:16-23.
- 37. Barrueco M, Gómez G, Torrecilla M, Pérez A, Bartolomé C. Valor de la intervención breve y los tratamientos para dejar de fumar en adolescentes. Arch Bronconeumol. 2007;43:334-9.
- 38. Britton J, Edwards R. Tobacco smoking, harm reduction, and nicotine product regulation. Lancet. 2008;371:441-5.
- 39. Tomar SL. Epidemiologic perspectives on smokeless tobacco marketing and population harm. Am J Prev Med. 2007;33 6 Suppl:387-97.
- European Comission. Health & Consumer Protection Directorate-General. Health. Scientific Commitee. Effects of smokeless tobacco Products. Brussels, February 2008.
- 41. Directiva 2001/37/CE del Parlamento Europeo y del Consejo, de 5 de junio de 2001, relativa a la aproximación de las disposiciones legales, reglamentarias y administrativas de los Estados miembros en materia de fabricación, presentación y venta de los productos del tabaco.

- 42. International Smokeless Tobacco Company. Submission in relation to directive 2001/37/EC to the European Commission. 2004. Disponible en: http://www.ussmokeless.com/regulatory/31.pdf
- 43. WHO Report on the Global Tobacco Epidemic, 2008. The MPOWE Package. Geneve: WHO; 2008.
- 44. European Commission. Special Eurobarometer. Attitudes of Europeans towards tobacco. May 2007. Disponible en: http://ec.europa.eu/health/ph_determinants/life_style/Tobacco/Documents/ebs272c_en.pdf
- 45. Barrueco Ferrero M, Torrecilla García M, Hernández Mezquita MA, Jiménez Ruiz CA, Morales Sánchez A, Alonso Díaz A, et al. Deshabituación tabáquica. Valor del resultado en la fase de acción sobre el resultado en la fase de consolidación. Arch Bronconeumol. 2007;43:136-42.
- 46. Trapero-Bertrán M. Evaluación económica de las intervenciones antitabáquicas: ¿nos dejamos algo en el tintero? Arch Bronconeumol. 2009;45:209-11.
- 47. McDaniel PA, Smith EA, Malone RE. Philip Morris Project sunrise: weakening tobacco control by working with it. Tob Control. 2006;15:215-30.
- 48. Pierce J, Leon M on behalf IARC Handbook and IARC Secretariat. Special Report: Policy. Effectiveness of smoke-free policies. Lancet Oncol. 2008;9:614-5.