Reduction of mortality following better detection of hypertension and alcohol problems in primary health care in Spain

Reducción de la mortalidad mediante una mejor detección de la hipertensión y los problemas con el alcohol en la atención primaria de salud en España

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Abstract

Through a simulation study, we estimated the potential effects of better detection of hypertension and improved screening for alcohol problems with subsequent interventions. Results showed that if 50% of Spanish males between 40 and 64 years of age who are currently unaware of their hypertension become aware of their condition and receive the usual treatment, and 50% of these males with hypertension are screened for alcohol and are treated for hazardous drinking or alcohol use disorders, then the percentage of uncontrolled hypertension among men with hypertension decreases from 61.2% to 55.9%, i.e. by 8.6%, with about 1/3 of the effect due to the alcohol intervention. For women, likewise, these interventions would decrease the percentage of women in the same age group with uncontrolled hypertension by 7.4% (about 40% due to the alcohol intervention). The reduction of blood pressure in the population would avoid 412 premature CVD deaths (346 in men, 66 in women) within one year. Therefore, better detection of hypertension and screening for alcohol with subsequent interventions would result in marked reductions of uncontrolled hypertension and CVD mortality.

Keywords: Blood pressure; Hypertension; Alcohol use; Alcohol use disorders; Primary health care; Screening; Detection; Intervention, simulation.

Resumen

Se estudian mediante una simulación los potenciales beneficios que puede comportar una mejora en la detección y tratamiento de la hipertensión y de los problemas relacionados con el alcohol. Los resultados muestran que si el 50% de los varones españoles entre 40 y 64 años que desconocen que padecen hipertensión fuesen detectados y recibiesen tratamiento; y si en el 50% de los varones hipertensos se realizase el cribado de consumo alcohólico y recibieran consejo para la reducción de consumos o tratamiento cuando procediera, el porcentaje de hipertensión no controlada descendería del 61,2% al 55,9% (una reducción del 8,6%). Un tercio del efecto es atribuible a la intervención sobre el alcohol. De forma similar, las mismas intervenciones en mujeres de los mismos grupos etarios implicarían una reducción del 7,4% de la hipertensión no controlada (40% debido a la intervención sobre alcohol). La reducción de la presión arterial en la población permitiría evitar 412 muertes prematuras por patología cardiovascular (346 varones y 66 mujeres) anualmente. Una mejor detección de la hipertensión y el cribado de consumos alcohólicos con las consiguientes intervenciones resultarían en una marcada reducción de la hipertensión no controlada y de las muertes de origen cardiovascular.

Palabras clave: Presión arterial; Hipertensión; Consumo de alcohol; Trastornos por consumo de alcohol; Atención primaria de salud; Cribado; Detección; Intervención; Simulación.

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The major non-communicable diseases caused more than half of the deaths worldwide in the year 2012 (38 million out of the almost 56 million; World Health Organization, 2014; based on Global Health Estimates by the World Health Organization: http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html). To reduce this burden, a global action plan has been implemented, which foresees the overall target of a 25% relative reduction in risk of premature mortality from cardiovascular diseases, cancer, diabetes, or chronic respiratory diseases (World Health Organization, 2013), plus specific targets for the major risk factors. Both hypertension and the harmful use of alcohol are among these targets, with expected reductions of 25% and 10%, respectively. Both risk factors are closely associated in a dose-response fashion; i.e., the higher the alcohol consumption, the higher the blood pressure (Briasoulis, Agarwal, & Messerli, 2012; Taylor et al., 2009). The effect of alcohol has been shown to be causal: increases and decreases in alcohol consumption have been shown to result in subsequent changes in blood pressure in observational studies and controlled clinical trials (for overviews: O'Keefe, Bhatti, Bajwa, DiNicolantonio, & Lavie, 2014; Xin et al., 2001; see also Saunders, 1987, for an early review including clinical recommendations). The dose-response relationship is not linear, as the association gets stronger (steeper) in the higher drinking levels, and thus heavy drinking and alcohol use disorders have a large impact on elevated blood pressure and hypertension (Rehm et al., 2015b; Saunders, Beevers, & Paton, 1979; Saunders, Paton, & Beevers, 1981; Taylor et al., 2009).

In light of the strong impact of heavy drinking on hypertension, it does not come as a surprise, that screening, monitoring and subsequent interventions for this risk factor has been recommended already in the 1980s in the management of hypertension (Saunders, 1987); and reduction of drinking is now part of the recommended lifestyle changes in hypertension treatment (Mancia et al., 2013a; Mancia et al., 2013b). However, screening of alcohol consumption does not seem to be a routine part of the general practice in hypertension management in primary health care yet. In fact, alcohol consumption in general or heavy drinking in particular are relatively rarely broached as issues in primary care, independent of hypertension (Brotons et al., 2012; Drummond et al., 2013; for Spain see also http://www.papps.es/suplemento_ap_09.php). Despite current practice, primary health care seems to be the natural setting for screening and intervening with alcohol-related hypertension problems, since the majority of the population seek treatment for all kinds of medical conditions on a yearly basis (Miller, Anton, Egan, Basile, & Nguyen, 2005; Rehm et al., 2014). Moreover, hypertension is one of the most common, if not the most common diagnosis in primary care in many high-income countries (e.g., Minas, Koukosias, Zintzaras, Kostikas, & Gourgoulianis, 2010; Ministry of Health and Social Policy, 2010; Wändell et al., 2013), and is a chronic illness for which many patients may see their providers regularly.

Thus, it was the aim of this contribution to model what could happen if:

- the rate of awareness of for hypertension increased (see Banegas et al., 2012; Catalá-López, Ridao, Sanfélix-Gimeno, & Peiró, 2013; Llisterri et al., 2012 for current level of awareness and control of hypertension in Spain).
- screening for alcohol would be introduced, with brief interventions for hazardous and harmful drinking, and formal treatment for alcohol use disorders (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001; Room, Babor, & Rehm, 2005).

The consequences modelled comprise the distribution of systolic blood pressure and the risks for cardiovascular diseases linked to hypertension (Singh et al., 2013).

Methods

Exposure of hypertension in Spain

The blood pressure distributions among people with hypertension in Spain was modelled based on the results of Banegas and colleagues (Banegas et al., 2012; also see Catalá-López et al., 2013; Llisterri et al., 2012). In the Banegas study (Banegas et al., 2012), BP was measured by certified trained personnel, using standardized procedures, with validated automatic devices. Two sets of BP readings were made separated by 90 minutes. In each set, BP was measured 3 times at 1- to 2-minute intervals, after resting at least 3 minutes in a seated position. In the analyses, BP was calculated as the mean of ≥3 of the last 5 readings. We restricted our modelling to ages 40-64, as this is the age group, where there is already a considerable prevalence or hypertension, with less awareness than in older age groups (Banegas et al., 2012). In addition, in this age group prevalence of hazardous and harmful drinking and alcohol use disorders is high (Rehm et al., 2015a; Rehm et al., 2014): in a representative study of more than 13,000 patients of primary health care in 6 European Union countries, the following prevalence was found: hazardous drinking and other alcohol problems indicating the need of a brief intervention: women 14.1%-16.1%; men 14.2%-19.8%; alcohol dependence indicating the need for a therapy: women 3.9%-5.8%; men 11.1%–16.7 %).

Modelling the distribution of blood pressure: The "belly curve"

In order to estimate the change in blood pressure distribution among the sub-population of people with hypertension, a new distribution was designed as an alternative to a simple normal distribution. This distribution which we refer to as the "belly curve" is an attempt to model the asymmetric distribution of blood pressure among people with hypertension (Pater, 2005)

1. The belly curve was designed according to the following rules about its shape:
2. The shape of the belly curve is made up of one half of a normal distribution to the right and left of its modus.
3. The standard deviation of the normal distribution making up the right half of the belly curve is twice that of the other.

The two normal distribution halves are multiplied by constants so as to yield a continuous distribution.

Based on these assumptions, it is possible to reverse engineer the required normal distributions if the overall mean and standard deviation of the final belly curve are known, therefore it is possible to obtain a belly curve fitting the mean and standard deviations found in surveys or other data.

The standard deviation of the normal distribution on the left of the modus of the belly curve s_{left}, the modus of the belly curve, the mean of the of the belly curve, μ, and the standard deviation of the belly curve, s_{belly}, are linked through the following expressions:

$$Modus = \mu - \sqrt{\frac{2}{\pi}} \cdot \sigma_{left}$$

$$\sigma_{belly}{}^2 = \mu^2 + Modus^2 + 2 \cdot Modus \cdot \sqrt{\frac{2}{\pi}} \cdot \sigma_{left} + 3 \cdot \sigma_{left}{}^2 - 2 \cdot Mean \cdot \left(Modus + \sqrt{\frac{2}{\pi}} \cdot \sigma_{left} \right)$$

We validated the curve by reproducing the actual distributions of blood pressure among people with hypertension (controlled and uncontrolled) in Finland (Koskinen, Lundqvist, & Ristiluoma, 2012; Laatikainen et al., 2013), Germany (Neuhauser, Thamm, & Ellert, 2013), Spain (Banegas et al., 2012; Catalá-López et al., 2013; Llisterri et al., 2012) and the UK (Joffres et al., 2013).

Modelling the effects of treatment and intervention

The above expressions allow us to derive a belly curve for any given mean and standard deviation. To estimate the effects of interventions, 1'000'000 samples were created from the belly curve and a proportional decrease in blood pressure is applied to a subset of the samples, as given by the percentage of patients with hypertension receiving the respective intervention.

Overall, three steps are required for a comparison of the current status with an ideal scenario where all patients with hypertension are screened and receive blood pressure interventions (mainly medications), and where the people with alcohol problems receive additional interventions either in form of brief interventions (Kaner et al., 2007) or formal treatment including pharmacotherapy.

1. An initial belly curve is created using the current known mean and standard deviation of high blood pressure among people with hypertension.
2. The effects of systematic screening are assessed by attributing the mean blood pressure of the group of patients who had been aware and in treatment for their blood pressure (based on empirical information including those, where the intervention did not lead to a control of hypertension) to all people with hypertension.
3. Finally, the effect of brief interventions and formal treatment for alcohol use disorder was assessed by decreasing blood pressure of a randomly sampled subset of the belly distribution from step 2. The subset was chosen to reflect the prevalence of people with hazardous alcohol drinking and alcohol use disorders among people with hypertension (Rehm et al., 2014) specified above. The size of the decrease was modelled based on the meta-analysis of (Xin et al., 2001): using the mean effect of all interventions used in Xin and colleagues (2001) for hazardous drinking, and using the effect specified for formal therapies for the effect of therapies of alcohol dependence.

The main analysis assumes a reduction of people unaware of their hypertension by 50% and coverage rates of alcohol interventions by 50% as well. We also performed two sensitivity analyses: in the first we assumed coverage rates of alcohol interventions by 100%; and in the second coverage rates for hypertension and alcohol by 100%. While the latter goals seem hard to reach, it gives us the maximum effect which could be reached with the interventions suggested.

Modelling the effect of the changed distribution of blood pressure on cardiovascular diseases

To estimate the amount of deaths avoided with the interventions described here, we have to compare the blood pressure distributions before and after the interventions in combination with the relative risk functions associated with blood pressure. It is further assumed, that people without hypertension have a relative risk of 1.

In the case where the blood pressure distributions are known before and after the interventions, the avoided deaths can be computed as follows:

$$DeathsAvoided = \frac{\int P_{HT_{AfterInt}}(BP) * RR(BP)\, dBP - \int P_{HT_{BeforeInt}}(BP) * RR(BP)\, dBP}{P_{normotensive} + \int P_{HT_{BeforeInt}}(BP) * RR(BP)\, dBP}$$

Where $P_{normotensive}$ is the proportion of people that do not have hypertension, $P_{HTAfterInt}$ (BP)is the blood pressure (BP) distribution after all the interventions, $P_{HTBeforeInt}$ (BP) is the blood pressure distribution before any intervention and RR(BP) is the relative risk of dying of a given disease for a blood pressure BP.

In our case, the final BP distribution has been estimated using 1 million samples. The integral was therefore replaced by the mean value of the relative risk function applied to each sample. The mortality data for Spain were taken from the WHO Global Health Estimates for 2012 (http://www.who.int/healthinfo/global_burden_disease/en/).

Results

Main result for reduction of uncontrolled hypertension

Table 1 gives the results on the proportion of people with controlled and uncontrolled blood pressure after the two interventions described above. If 50% of Spanish men between 40 and 64 years of age currently not aware about their hypertension, could be made aware of their condition and received interventions to change their blood pressure distribution; and if 50% of people with hypertension who have alcohol problems or alcohol use disorders, receive interventions (either brief interventions for hazardous or harmful drinking or therapy for alcohol use disorders), the percentage of uncontrolled hypertension among men with hypertension would decrease from 61.2% to 55.9%, i.e. by 8.6%. This is equivalent to a reduction of men aged 40 to 64 with uncontrolled hypertension in the general population by 2.2 percentage points (from 25.7% to 23.5%). Controlled hypertension here is defined as having a systolic blood pressure below 140 mm Hg. Alcohol interventions contributed about one third of this effect.

Similarly, for women, these interventions would decrease the percentage of women in the same age group with uncontrolled hypertension by 7.4%, reducing the proportion of such women in the general population from 17.8% to 16.5%, i.e., by 1.3 percentage points. Alcohol interventions contributed about 40% of this effect.

Reduction in CVD mortality

Overall, within one year, 412 out of 9,912 cardiovascular deaths in the age group 40-64 could be avoided (data are based on 2012). The overwhelming majority of these deaths would be in men, and in ischemic heart disease, followed by stroke.

Sensitivity analyses

We conducted 2 sensitivity analyses in addition to the main analysis to get an idea of how each change affects the bottom line outcome. The first sensitivity analysis assumed that 50% of Spanish between the age of 40 and 64 who were unaware of their hypertension were made aware and changed their blood pressure distribution accordingly, and that all people having alcohol problems or alcohol use disorders received interventions.

The second sensitivity analysis assumed that all Spanish between the age of 40 and 64 unaware were shifted to the distribution of people aware of their hypertension, and furthermore, that all people having alcohol problems or alcohol use disorders received interventions.

For each of the sensitivity analyses, the computations were again split in 2 steps, as for the main analyses. The results are summarized in Table 3.

Table 1. *Shifts in systolic blood pressure among people with hypertension (controlled and uncontrolled) in Spain after two hypothetical interventions (based on (Banegas et al., 2012)*

	Women 40-64 years of age				Men 40-64 years of age			
	Mean systolic blood pressure (BP)	% controlled[&] among hypertensives	Increase in control delta%	Systolic BP ≥ 140 mmHg in population	Mean systolic BP	% controlled[&] among hypertensives	Increase in control delta%	Systolic BP ≥ 140 mmHg in population
Before	146,0	40,4	-	17,8	146,8	38,8	-	25,7
After increasing awareness (50%)	144,8	43,0	2,6	17,0	145,3	42,2	3,5	24,2
After increasing awareness (50%) and alcohol interventions (50%)	144,1	44,8	4,4	16,5	144,5	44,1	5,3	23,5
Proportion of effect due to alcohol intervention	40,5%	40,6%		38,5%	33,5	33,4%		31,8%

Note. & defined as systolic blood pressure ≥ 140 mm HG.

Table 2. *Expected cardiovascular mortality gains within one year from the interventions via the reduction of blood pressure (based on (Singh et al., 2013)*

	Women 40-64 years of age		Men 40-64 years of age	
	Number of avoided deaths	% of all deaths	Number of avoided deaths	% of all deaths
Ischemic heart disease	20	2,5%	180	4,2%
Hypertensive heart disease	9	9,9%	33	14,3%
Rheumatic heart disease	1	0,7%	1	1,2%
Inflammatory heart disease	1	0,7%	13	2,2%
Ischaemic Stroke	6	4,3%	24	6,7%
Haemorrhagic Stroke	25	5,1%	66	7,7%
Other CVD	8	1,5%	36	2,6%
Total	66	3,0%	346	4,5%

Note. The effects were modelled for 2012. They comprise reductions in mortality within one year based on the effect of both interventions on blood pressure.

Table 3. *Shifts in systolic blood pressure among people with hypertension (controlled and uncontrolled) in Spain after two hypothetical interventions (Banegas et al., 2012) – sensitivity analyses*

Assumption: 50% of unware -> aware;
100% of people with alcohol problems get interventions.

	Women 40-64 years of age				Men 40-64 years of age			
	Mean systolic blood pressure (BP)	% controlled[&] among hypertensives	Increase in control delta%	Systolic BP ≥ 140 mmHg in population	Mean systolic BP	% controlled[&] among hypertensives	Increase in control delta%	Systolic BP ≥ 140 mmHg in population
Before	146,0	40,4	-	17,8	146,8	38,8	-	25,7
After increasing awareness (50%)	144,8	43,0	2,6	17,0	145,3	42,2	3.5	24,2
After increasing awareness (50%) and alcohol interventions (100%)	143,3	46,4	6,0	16,0	143,6	45,9	7.1	22,7
Proportion of effect due to alcohol intervention	55,6%	56,7%		55,6%	53,1%	51,4%		50,0%

Note. & defined as systolic blood pressure ≥ 140 mm HG

Assumption: 100% of unware -> aware;
100% of people with alcohol problems get interventions.

	Women 40-64 years of age				Men 40-64 years of age			
	Mean systolic blood pressure (BP)	% controlled[&] among hypertensives	Increase in control delta%	Systolic BP ≥ 140 mmHg in population	Mean systolic BP	% controlled[&] among hypertensives	Increase in control delta%	Systolic BP ≥ 140 mmHg in population
Before	146,0	40,4	-	17,8	146,8	38,8	-	25,7
After increasing awareness (100%)	143,7	45,5	5,1	16,2	143,7	45,8	7.0	22,8
After increasing awareness (100%) and alcohol interventions (100%)	142,2	49,0	8,6	15,2	142,1	49,3	10.5	21,3
Proportion of effect due to alcohol intervention	39,5%	40,7%		38,5%	34,0%	33,3%		34,1%

Note. & defined as systolic blood pressure ≥ 140 mm HG.

Discussion

Overall, it could be shown, that alcohol interventions in primary care patients with hypertension, i.e. brief interventions for harmful and hazardous drinking and treatment or referral to specialized treatment for alcohol use disorders (Babor et al., 2010; Babor et al., 2007) promises public health gains in terms of reducing blood pressure levels and subsequent cardiovascular disease (see also Gual, Zarco, Colom, & Rehm, 2015). With respect to reducing blood pressure levels it could be shown, that up to 17% of existing hypertension in men and 15% in women could be controlled, if unawareness is reduced maximally and if alcohol interventions are initiated (see results sensitivity analysis 2). In this scenario, the current differences between men and women would also disappear (for recent assessments of gender differences in Spain see (Banegas et al., 2008; Gijón-Conde & Banegas, 2012; Ortiz Marrón et al., 2011).

The impact of the interventions on cardiovascular mortality was also pronounced. More than 400 cardiovascular deaths could be avoided by the main scenario within one year (see Table 2 for details), mainly in men. In addition, and not explicitly modelled here, reduction in alcohol consumption will be associated with sizable short term reduction of morbidity and mortality for many disease outcomes (Rehm & Roerecke, 2013; Rehm, Shield, Rehm, Gmel, & Frick, 2013; specifically for Spain: Rehm, Rehm, Shield, Gmel, & Gual, 2013; Soler González, Balcells Oliveró, & Gual Solé, 2014; for a complete listing of alcohol-attributable diseases see Rehm et al., 2010). To give a sense of the magnitude of such reductions for formal treatment: if alcohol consumption was reduced, including, but not limited to reaching abstinence, the risk for all-cause mortality will be reduced by about 60% overall within 9 years (results based on a comprehensive meta-analyses of all treatment studies with the relevant information - Roerecke, Gual, & Rehm, 2013). These effects included the effects on cardiovascular diseases via hypertension, however.

In sum, the impact of better awareness and alcohol interventions could be marked. What keeps the current system from not achieving them? First, awareness of hypertension is still seen as a problem of the elderly. Clearly, the older the population, the better the awareness (Banegas et al., 2012): whereas two thirds of the people younger than age 45 in Spain was not aware of their hypertension, the majority of the population older than 65 (again about 2/3) was aware of this disease condition. For primary health care physicians, screening for hypertension in younger people, especially in younger males with heavy alcohol use (Org et al., 2011), is worth the effort. Second, screening for alcohol use and applying brief interventions or treatment could make a marked difference in the control of hypertension. Primary health care centres would be the ideal point where to apply these screenings and early interventions: not only do primary health care physicians recognize heavy drinking and alcohol use disorders (Rehm et al., 2015a), but in this environment both brief interventions and treatment for less severe alcohol use disorders are possible (Rehm et al., 2016; Rubio, Jiménez-Arriero, Martinez, Ponce, & Palomo, 2010; Segura Garcia, Gual Solé, Montserrat Mestre, Bueno Belmonte, & Colom Farran, 2006). Third, if such interventions are given, also the rate of treatment resistant hypertension (for a definition Boswell, Pascual, & Oliveras, 2015; for Spain: Oliveras & de la Sierra, 2014) could probably be reduced (Calhoun et al., 2008; Denolle et al., 2014). In addition, alcohol interventions may have an effect on medication intake (Miller et al., 2005), not only in people with hypertension (Grodensky, Golin, Ochtera, & Turner, 2012), and alcohol reduction will reduce the risk and severity of other co-morbidities (Diaz et al., 2014; Rehm, Manthey, Struzzo, Gual, & Wojnar, 2015d; Rehm & Roerecke, 2013).

No modelling is without limitations. First, we based our prevalence data and means of a large study with careful assessment of hypertension by trained personnel (Banegas et al., 2012). However, the chance of "white coat" or "isolated office/study hypertension" could only be excluded if 24-hour ambulatory blood measurements, for example as stipulated in UK guidelines of the National Institute for Clinical Excellence, were taken (Mayor, 2011). While our data may overestimate the real prevalence of people with hypertension, this effect seems to amount to not more than 10% (Banegas et al., 2015, based on an older sample). Second, while the belly curve has been shown to portray the distribution of blood pressure in Spain fairly well, any model is a simplification with some bias. Thirdly, the results of the meta-analyses between blood pressure and cardiovascular outcomes (Singh et al., 2013) were used for Spain, thus assuming that the risk relations hold true. This assumption is standard in global burden of disease modelling (Ezzati, Lopez, Rodgers, & Murray, 2004; Rehm et al., 2009); it should be checked with local data wherever possible (e.g., Roerecke et al., 2015). We found no data for Spain detailing the increase in risk for the various cardiovascular risk categories examined, and thus had to use the global risk relations (Singh et al., 2013). The error introduced does not seem to be too large, as most of the underlying studies were from high income countries, and as the relationships are mainly based on biological mechanisms.

Overall, the modelling and the sensitivity analyses clearly show that interventions to increase awareness of hypertension and to screen and intervene for alcohol problems and alcohol use disorders will lead to public health-relevant reductions of people with blood pressure values above 140 mm Hg systolic blood pressure. The best place for these interventions seems to primary health care, where hypertension is controlled in most cases anyway. For an implementation, three requirements should be in place: firstly, primary care physicians should be trained to do these alcohol interventions (Rehm et al., 2016); secondly, they should be given enough time in their daily schedule to carry out brief interventions and formal treatment for alcohol dependence, and thirdly, there should be appropriate incentive structures (Anderson et al., 2014; O'Donnell et al., 2014).

Conflicts of Interest and Source of Funding

Dr. Rehm reports grants, personal fees and other (membership Nalmefene board) from Lundbeck, outside the submitted work. CS reports personal fees from Lundbeck, outside the submitted work. AG reports receiving grants and personal fees from Lundbeck, grants and personal fees from D&A Pharma, and personal fees from AbbVie, outside of the submitted work. No financial remuneration was obtained for the preparation of manuscript.

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