Pattern of declining blood pressure across replicate population surveys of the WHO MONICA project, mid-1980s to mid-1990s, and the role of medication

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Abstract

Objective Declining mean systolic and diastolic blood pressures were observed in most populations of the World Health Organization MONICA (monitoring trends and determinants in cardiovascular disease) project from the mid-1980s to mid-1990s. We tested whether pooled results would show mean change associated with decline in high readings only, resulting from better antihypertensive medication, or with similar falls in low, middle, and high readings, implying other causes.

Design Independent, random sample, cross sectional population surveys, each end of the MONICA decade.

Setting 38 populations in 21 countries across four continents.

Participants Design target in each survey of 200 participants in each 10 year age and sex group from age 35 to 64

Main outcome measures Changes in the population in mean systolic and diastolic blood pressure, and in low, middle, and high readings—the 20th, 50th, and 80th centiles—and the differences between these changes.

Results Individual populations differed considerably, but pooling the 38 population results gave mean changes in systolic blood pressure of −2.2 mm Hg in men, −3.3 mm Hg in women, and in diastolic blood pressure of −1.4 mm Hg in men and −2.2 mm Hg in women (overall average −2.26 mm Hg, population median −1.55 mm Hg). Antihypertensive medication, associated with high readings, rose by 0.5% to 11.4%. However, average falls in low and middle blood pressure readings were so similar to those in high readings and in the mean that no effect from improving treatment of hypertension was detected. Results in contrasted subgroups were consistent.

Conclusions Blood pressure fell across 38 MONICA populations at all levels of readings, with no differential fall in high readings attributable to better control of hypertension. Despite the importance of medication to individuals, in that decade other determinants of blood pressure lowering must have been more pervasive and powerful in whole populations.

Introduction

The World Health Organization MONICA (monitoring trends and determinants in cardiovascular disease) project took place from the mid-1980s to mid-1990s. Across 38 populations in 21 countries in men and women aged 35-64, emphasising standardisation and quality control, the project related trends in mortality due to coronary disease, and event rates, to trends in coronary care, and risk factor levels in the population. Risk factor levels were measured through independent random sample surveys in each population, at both ends of that decade. Most MONICA centres reported declining mean values in the populations for systolic and diastolic blood pressure; increases were exceptional.[1 2]

Epidemiologists identify two methods for changing continuous risk factors such as blood pressure. "High risk" targets the top of the population distribution bell curve, lowering blood pressure selectively in individuals where it is high. By contrast, through dietary, lifestyle, or environmental factors, "mass population" interventions (figure next page) deliberately or accidentally move the whole curve downwards, also lowering middle and low readings.[3 4] Both change the population mean value. Can we apportion responsibility by pooling the 38 MONICA population results? Did blood pressure fall or was it pushed? Did the blood pressure bell curve swing or was it dented?

Methods

Blood pressure measurement

In every population, investigators targeted 200 or more participants from each 10 year age and sex group, from age 35 to 64, in a random sample survey at the beginning of the MONICA decade, replicated independently at its end.[1 2] Blood pressure data were forwarded to the MONICA data centre in Helsinki for analysis and quality assessment.[5]

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Supplementary data, explanations for the tables, and a methodological appendix are on bmj.com

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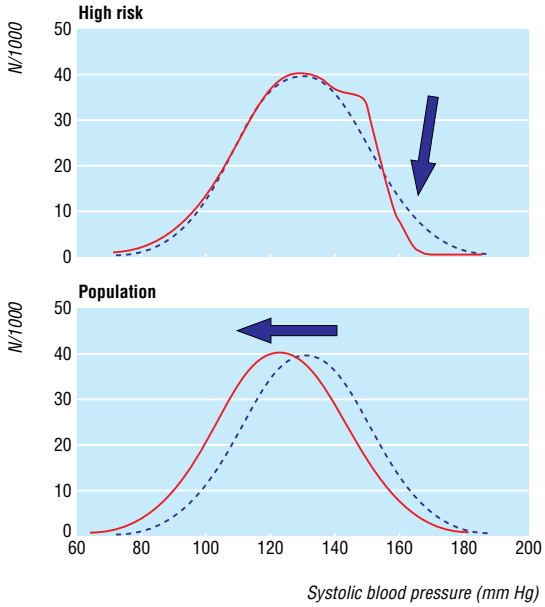

High risk interventions compared with mass population interventions: impact on an idealised population distribution or bell curve for systolic blood pressure

Statistical methods

We extracted published information on numbers of participants and response rates, use of antihypertensive medication (see bmj.com), scores assigned in quality assessment of blood pressure data,[5] and summary statistics on numbers, blood pressure means, standard deviations, and previously defined low, middle, and high readings used for tracking change—the 20th, 50th, and 80th centiles.[6] Results for the age range 35-64 were standardised to the world standard population. We added selected analyses from the MONICA database.

We used differences obtained between surveys in individual populations to produce simple mean pooled values. The number of populations, generally 38 or 19, was used to calculate the standard errors of these pooled means.

Our hypothesis was that hypertension control would selectively depress the top end of the population bell curve, resulting in pooled results showing differential falls in the 80th centile compared with the 20th centile; the mean compared with the 50th centile; and the mean compared with the average change in these three centiles, so we obtained these differences by subtraction. Null hypotheses of no treatment (but a mass population) effect would be disproved by significant values for these differences. In order to test the robustness of the results obtained from pooling all 38 populations together, we then compared the findings in contrasting subgroupings.

Results

Tables listing, by individual population, numbers surveyed, participation rates, use of antihypertensive medication, overall quality scores for blood pressure trends, and changes in systolic blood pressure and diastolic blood pressure for men and women are shown on bmj.com. Data book tabulations are available,[6] and our derived spreadsheets are on bmj.com. Change in mean systolic and diastolic blood pressure in men averaged −2.2 mm Hg and −1.4 mm Hg (ranges −10.6 to +4.5 mm Hg and −9.5 to +3.5 mm Hg); in women −3.3 mm Hg and −2.2 mm Hg, (ranges −13.5 to +8.1 mm Hg and −10.7 to +3.9 mm Hg). Changes in the mean and the different centiles vary considerably within and between populations. The overall drop in blood pressure after averaging falls in systolic and diastolic blood pressure and both sexes across populations was −2.26 mm Hg, but the median population value was −1.55 mm Hg (see appendix on bmj.com). Despite the variation between populations, on taking all 38 populations together, the pooled average values of the changes in the mean and the changes in those centiles chosen for comparison, are remarkably similar (see bmj.com).

The table explores the null hypotheses. Changes in mean blood pressure are substantial and significant. Differences entailed in the null hypotheses are inconsistent between the sexes, between systolic and diastolic blood pressure, and mostly approximate to zero, with non-significant positive or negative values. Older age groups are similar in results to age 35-44, where medication was rare.

The 38 populations were partitioned to show whether null hypothesis differences remained non-significant when contrasting populations by level of antihypertensive medication, by change in medication, by size of blood pressure fall, by quality assessment score, by population sample size, and by national gross domestic product per head (see bmj.com). Findings remained essentially unchanged.

The mean change from the table, by averaging systolic and diastolic blood pressure and the two sexes is −2.26 mm Hg. The difference from subtracting change in the 80th from that in the 20th centile is +0.01 mm Hg; that for the mean and the 50th centile is +0.05 mm Hg; and for the mean and the centile average is +0.04 mm Hg. Overall change in mean blood pressure is significantly negative. The null hypothesis differences are tending non-significantly positive. Treatment benefit should have produced significant negative values. A contribution from improving control of hypertension to the overall population decline in blood pressure seems undetectable.

Discussion

Absence of a detectable contribution to the decline in blood pressure over the MONICA decade from improving control of hypertension was unexpected. Although this finding does not contradict trial evidence that antihypertensive medication limits cardiovascular risk in individuals,[7] it implies that other factors, potentially of great public health interest, were more pervasive and powerful in lowering blood pressure across whole populations at that time. This short discussion is supplemented by a methodological appendix of frequently asked questions (see bmj.com).

Validity of analyses

We are confident that our analyses are valid. Alternatives, analysing those on and off medication

Pooled blood pressure results from 38 populations: mean change between surveys, and the three differences used to test the null hypotheses, in mm Hg (with 95% confidence intervals)

All 38 populations	Mean	80th–20th centile	Mean–50th centile	Mean–centile average
Ages 35-44:				
Systolic blood pressure	−2.72 (−3.93 to −1.51)***	−0.47 (−1.14 to 0.20)	0.03 (−0.32 to 0.38)	0.17 (−0.09 to 0.42)
Diastolic blood pressure	−2.05 (−2.97 to −1.13)***	0.05 (−0.53 to 0.63)	0.04 (−0.22 to 0.30)	0.12 (−0.01 to 0.24)
Ages 45-54:				
Systolic blood pressure	−2.74 (−4.00 to −1.48)***	−0.16 (−1.13 to 0.81)	0.37 (0.01 to 0.73)*	0.01 (−0.21 to 0.23)
Diastolic blood pressure	−1.63 (−2.64 to −0.63)**	0.18 (−0.53 to 0.90)	0.26 (0.04 to 0.48)*	0.09 (−0.06 to 0.24)
Ages 55-64:				
Systolic blood pressure	−2.52 (−4.04 to −1.01)**	0.36 (−0.89 to 1.60)	0.26 (−0.16 to 0.68)	−0.04 (−0.22 to 0.14)
Diastolic blood pressure	−1.54 (−2.68 to −0.41)**	−0.24 (−0.94 to 0.47)	0.12 (−0.13 to 0.37)	0.09 (−0.03 to 0.20)
Men, age 35-64:				
Systolic blood pressure	−2.18 (−3.32 to −1.05)***	−0.09 (−1.00 to 0.81)	0.25 (−0.13 to 0.64)	0.03 (−0.13 to 0.19)
Diastolic blood pressure	−1.38 (−2.34 to −0.42)**	0.21 (−0.42 to 0.84)	0.20 (−0.04 to 0.44)	0.16 (0.02 to 0.30)*
Women, age 35-64:				
Systolic blood pressure	−3.30 (−4.65 to −1.96)***	−0.37 (−1.55 to 0.82)	0.03 (−0.42 to 0.47)	−0.13 (−0.33 to 0.06)
Diastolic blood pressure	−2.17 (−3.20 to −1.14)***	0.29 (−0.42 to 1.00)	−0.29 (−0.52 to −0.06)*	0.10 (−0.10 to 0.30)
Both sexes, age 35-64:				
Systolic blood pressure	−2.74 (−3.95 to −1.53)***	−0.23 (−1.14 to 0.68)	0.14 (−0.20 to 0.48)	−0.05 (−0.19 to 0.08)
Diastolic blood pressure	−1.78 (−2.75 to −0.80)***	0.25 (−0.32 to 0.82)	−0.05 (−0.20 to 0.11)	0.13 (0.00 to 0.26)*

*P≤0.05; **P≤0.01; ***P≤0.001.

separately are not (see bmj.com). There are no equivalent databases in which to replicate our analyses. However, by basing our main analyses on published summary statistics[6] and publishing our spreadsheets (see bmj.com) we have left a transparent audit trail by which others, if they wish, can rework them. We gave equal weight to all populations in pooling results. Our tests of robustness imply that different weightings would produce similar answers.

We are unable to say what caused the blood pressure decline in MONICA. Obesity, a known contributor, moved in the wrong direction.[1] Possibilities, apart from measurement errors, include cohort effects, dietary factors, and other lifestyle and environmental factors.

Use of medication

During the MONICA study, the use of antihypertensive medication in MONICA populations increased by a rounded average of 0.5%, from 10.8% to 11.4% (see tables in bmj.com), but drugs in use changed. For 11.4% medication to be the exclusive cause of an average population-wide fall of 2.26 mm Hg between surveys, the blood pressure fall of people taking medication would need to be an improbable 19.8 mm Hg. Individual data show that medication was concentrated among high readings: 25.5% usage above the 80th centile and 3.4% below the 20th.

Change in medication across populations and change in blood pressure were not correlated. In 21 market economy populations where blood pressure declined, use increased in 11 and decreased in 10, implying no simple association. We and others have published the percentage of people with hypertension in the population identified, treated, and controlled.[8] However, better control in people taking medication could result from underlying population trends in blood pressure—the ground moving under the goalposts, and improvements mistakenly credited to clinical vigilance and improved medication.

Conclusions

Our findings contrast with earlier MONICA collaborative results showing unexpectedly strong links between population trends in medication for coronary care, and declining case fatality and mortality[9]; they result from similar dispassionate analyses of standardised data across 38 different populations from the mid-1980s to mid-1990s. MONICA data from that decade may conceal other surprises. Although medication may contribute more to population changes in blood pressure after the mid-1990s, similar standardised multicentre databases may not be available to show such changes.

The MONICA survey data book is available in the public domain from www.ktl.fi/publications/monica/surveydb/title.htm (accessed 19 February 2006) and in the CD Roms from the monograph; both contain lists of MONICA sites and key

What is already known on this topic

Blood pressure is declining in many industrialised countries, but the mechanism is not known

The impact of treating hypertension on the population distribution of blood pressure is difficult to assess, as is the contribution to change over time

What this study adds

Populations differ in patterns of blood pressure decline

Pooled results from 38 populations show that antihypertensive medication made no detectable contribution to population decline in blood pressure in the mid-1980s to mid-1990s

Other determinants of blood pressure decline must have been more pervasive and powerful in the population as a whole during that decade

These findings are important in understanding blood pressure as a challenge to public health, but they do not deny the importance of antihypertensive medication in the individual

personnel, and significant sponsors. The survey data book originates with WHO MONICA Project investigators and thousands of participants.

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Ethical approval: Responsibility, and effected by, principal investigators in each population. This analysis is of anonymised data.

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Oral protein energy supplements for children with cystic fibrosis: CALICO multicentre randomised controlled trial

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Abstract

Objective To determine whether oral protein energy supplements, used long term in children with cystic fibrosis who are moderately malnourished, improve nutritional and other outcomes.
Design Multicentre randomised controlled trial.
Setting Seven specialist paediatric cystic fibrosis centres and their associated shared care clinics and seven smaller paediatric cystic fibrosis clinics.
Participants 102 children with cystic fibrosis, aged between 2 and 15 years, who were moderately malnourished.
Interventions Oral protein energy supplements in addition to usual dietary advice compared with dietary advice alone, for 12 months.
Main outcome measure Change in body mass index centile over one year.
Results Use of supplements was not associated with a change in body mass index centile (mean difference 2.99 centile points, 95% confidence interval −2.70 to 8.68) or other nutritional and spirometric outcomes in this group of children.
Conclusions Long term use of oral protein energy supplements did not result in an improvement in nutritional status or other clinical outcomes in children with cystic fibrosis who were moderately malnourished. Oral protein energy supplements should not be regarded as an essential part of the management of this group of children.
Trial registration ISRCTN: 95744468.

Introduction

Poor nutrition is common in people with cystic fibrosis and is an important predictor of decline in lung function.[1–5] Oral protein energy supplements are widely prescribed to improve energy intake and nutritional status.[6] However, many people find them unpalatable, particularly when prescribed for long term use. A systematic review of oral protein energy supplements for people with cystic fibrosis identified two eligible trials involving 29 participants.[7] Because of a lack of evidence, the review was unable to reach a conclusion on the efficacy of these supplements.

The aim of the CALICO (calories in cystic fibrosis—oral) trial was to investigate whether oral protein energy supplements improve or prevent deterioration in the body mass index centile of children with cystic fibrosis. The trial also evaluated the effect of supplements on other measures of nutritional status, macronutrient intake, spirometric lung function, activity levels, and gastrointestinal symptoms.

Methods

Study design and participants

The trial was a multicentre randomised controlled trial of oral protein energy supplements for children with cystic fibrosis. We recruited children with cystic fibrosis aged between 2 and 15 years if they met one of the following criteria: body mass index of less than the 25th centile and more than the 0.4th centile, no increase in weight over the previous three months, a 5% decrease in weight from baseline over a period of less than six months. Children were recruited by dietitians at seven specialist cystic fibrosis centres in the United Kingdom, associated shared care clinics, and seven smaller clinics.

Members of Trial Steering Committee and Collaborative Group are on bmj.com

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