Appendix 3 for

Simulating and Evaluating Local Interventions
to Improve Cardiovascular Health
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High and Borderline Risk Analysis in the Cardiovascular Health System Dynamics Simulation Model (CVH-SD)

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Appendix 1 describes our procedures for risk calculation in the CVH-SD model, based on NHANES data on risk factors, AHA data on CV events, the Framingham-based Anderson risk calculator, and literature on the effects of secondhand smoke and particulate air pollution. The NHANES data differentiate high risk from lower risk for blood pressure (SBP/DBP) based on a threshold of 140/90, and for cholesterol (LDL) based on a threshold of 130. Based on this approach, an elimination of all high risks (BP, cholesterol, diabetes, smoking: “BCDS”) for females age 30-64 would be predicted to reduce CHD events about 50%. This is less than the 75% of CHD that Magnus and Beaglehole (1) estimate is explained by B, C, and S. The authors suggest that some of the reason for this apparent discrepancy (75% vs. 50%) is that borderline BP and cholesterol contribute to risk.

If we think (a) that interventions (e.g., changes in nutrition and activity environments) might end up reducing both high and borderline risks, and (b) the borderline risks contribute significantly to CV events as the authors suggest, then we may want to consider modeling both high and borderline risks, rather than only high risks as we do currently. This would likely mean separating the high from the borderline. because high risks are the ones that get addressed through medication while borderline risks generally do not. It may be worth the extra effort to add this additional structure to the model, if indeed the contribution of borderline risks is significant. We can use the procedures for risk calculation described in Appendix 1 to make such a determination; that is, in a sense to check for ourselves the Magnus and Beaglehole claim.

NHANES data identify the prevalence of borderline conditions, using standard cutpoints (e.g., setting the threshold for borderline SBP/DBP at 130/85 and the threshold for borderline LDL at 110). The present analysis does not attempt to differentiate risk based on the person’s prior diagnosis or lack thereof, but rather looks only at whether the person’s risk level is currently low (below borderline), medium (within the borderline zone), or high (beyond the high threshold). Table 1 below shows the prevalences of high or medium BP and cholesterol, uncontrolled and total diabetes, and current smoking from

NHANES 1988-1994 vs. NHANES 1999-2004, for males vs. females, and for ages 30-64 vs. ages 65+. It also shows percentage changes in prevalence from the earlier survey to the later one. Some identical directional trends are seen for all age-sex combinations, such as the decline in high cholesterol, increase in medium cholesterol, increase in total diabetes prevalence, and decrease in smoking. Other trends have exceptions: BP risk has generally increased, but not for elderly males; and uncontrolled diabetes prevalence has generally increased, but again, not for elderly males.

In the current model, we have examined the reduction in CV risk that would correspond to taking people from the high risk category down to non-high risk, where non-high risk includes what we would call low risk or medium risk. With the NHANES figures in Table 1, we can now also examine the reduction in CV risk that would correspond to taking people from either the high or medium risk category down to the low risk category. The purpose, then, is to compare these two approaches and determine how much more CV risk reduction one could expect by not only reducing high risk down to non-high risk, but by reducing high and medium risk down to low risk.

The first step in the new analysis is to determine the input values for the Anderson risk calculator. In this calculator, one must specify the person's age. For the age 30-64 group, we select age 48 as a representative midpoint. For the age 65+ group, actuarial life expectancy tables show that in 2001, US males had an expected remaining life of 16.4 years, females of 19.4 years. Based on this, we use age 73 for males and age 76 for females as estimated means for the 65+ population and as inputs to the Anderson calculator. In the calculator, one must also specify inputs of log(SBP) and log(TC / HDL). The NHANES analysis has given us mean values of these log-transformed variables.

Second, we used the Anderson calculator to estimate 4-year relative risks for each risk factor (B, C, D, S) separately, and for all for risk factors combined, and calculated the synergy exponents, as described in Appendix 1.

Third, we have taken those calculated relative risks and combined them with the high (or high+medium) risk prevalences seen in Table 1 below to get estimates of *relative event rates based on risk factor prevalences*. (Note that we have considered a person to have diabetes for this purpose only if their diabetes is uncontrolled, meaning that their HbA1c level is greater or equal to 7.0.) As described in Appendix 1, this estimate involves calculating for each risk factor an event multiplier combining prevalence and relative risk, multiplying the four multipliers together, and then raising their product to the synergy exponent.

Having calculated a relative event rate based on prevalences, it is a straightforward matter to estimate how much of the total risk is due to the difference between lower and higher risk along our 4 risk factors. In particular, if the relative event rate is "x" and the explained fraction is "y", then $y = (x-1)/x$. Thus, if $x=2$, then $y= 50\%$; whereas if $x=4$, then $y= 75\%$. The explained fractions or "y" values are presented below in Table 2.

For each CV event type in Table 2, the first row of results is the fraction of events explained by the 4 risk factors, based on “higher risk” being defined strictly as high risk, and “lower risk” as the combination of low and medium risk. The second row is based on “higher risk” being defined as the combination of high and medium risk, and “lower risk” defined strictly as low (below borderline) risk. *Thus, the first row shows the contribution of high BP and cholesterol risks strictly speaking, while the second row shows the contribution when borderline BP and cholesterol risks are included.*

The second row value is always greater than the first row value, as expected; in most cases the difference is 15 to 20 percentage points. The absolute values and the amount of increase differs by event type, by age-sex category, and also in some cases by survey period. For example, focusing on CHD in age 65+ females, the fraction explained rises, when borderline conditions are included, from 52% to 72% in the older NHANES and from 46% to 60% in the new NHANES. As in this example, the explained fractions tend to be somewhat smaller for the newer NHANES than they do for the older NHANES, perhaps a reflection of the fact that cholesterol and smoking prevalences are lower than they used to be, making the Framingham relationships a little less useful for explaining CV events now than they used to be.

This analysis suggests that there is significant potential benefit to be had from reducing both high and borderline risk prevalences, and not only reducing high risk prevalences. Strong enough interventions, whether preventive or control-oriented, could do just that, and are worthy of study and modeling.

References

1. Magnus P, Beaglehole R. The real contribution of the major risk factors to the coronary epidemics: time to end the "only-50%" myth. Arch. Intern. Med. 2001;161(22):2657-60.