

Authors' Responses to Reviews

All acceptable manuscripts require some revision based on reviewers' comments and medical editor guidance. Authors will receive a letter outlining the comments and recommendations. Authors should respond to this letter by indicating the changes made or actions taken as a result of each recommendation (see sample below).

Do's:

1. List each response, and then describe how you've addressed it.
2. If you have a good reason for not following a certain recommendation, please say why. If the medical editor in charge of your manuscript wants you to do something further, they will let you know.
3. If you're presented with seemingly contradictory recommendations (e.g., one reviewer says to make it longer, the other says to make it shorter), please ask the medical editor handling your manuscript for guidance.
4. Upload this "response to reviewers" as a Word document in Editorial Manager.

Don'ts:

1. Don't simply say "I've made all recommended changes." Say HOW you've done so. That way, the medical editor can judge whether the changes are appropriate. Otherwise, it's difficult to note what's different without doing a line-by-line comparison of both versions of the manuscript.
2. Don't list "Done" after each recommendation, unless the explanation is self-evident, such as when the recommendation was to delete a certain section or spell out an abbreviation.
3. Don't fail to respond to each comment, which might result in your response letter being returned to you for elaboration, which will delay the editing and publication of your manuscript.

Sample Response Letter:

The following sample letter shows the reviewers' and medical editors' recommendations and the appropriate way for authors to respond. In this sample, the author's responses are in bold, preceded by the word "RESPONSE." The format is not important; simply make your responses to each point obvious.

Ref.: Ms. No. 09-4955 [*manuscript number specific to your manuscript*]
Global Coronary Heart Disease Risk: Assessment and Application [*title of your manuscript*]

POINT-BY-POINT RESPONSES TO REVIEWS

COMMENTS FROM DR. SEXTON:

Overall, this is an excellent article on an important topic. I only have a few comments to add to Dr. Siwek and the reviewers. Please carefully review their comments, especially Reviewer #3. My only contradiction would be to

avoid adding more details of the studies as suggested by Reviewer #3. We have space limitations that should be reserved for explaining your recommendations.

RESPONSE: We agree that adding more details of the studies would add to the length without adding substantially to the overall message of this paper. We did add one sentence about the effects of global CHD risk +/- counseling reducing predicted CHD risk from 0.2-2%.

In the section about the evidence behind global risk calculation, please briefly define in parenthesis "receiver operator characteristic".

RESPONSE: We have added a brief parenthetical description "(graphical techniques to assess the accuracy of tests)" of this term.

In the section on evidence of effectiveness, the last paragraph should be rewritten in the third person per AFP style.

RESPONSE: We changed to third-person style.

I agree with Reviewer #3's concern about potentially endorsing CRP testing. Please further clarify the role of CRP in global risk assessment, if any.

RESPONSE: We have removed the sentences on the potential use of CRP for reclassifying people at intermediate risk and added a sentence on the lack of evidence that using CRP to guide statin management is better than global CHD assessment alone.

I agree with Dr. Siwek's comments about adding a table for physicians to better understand and explain risk reduction/interventions in the section on presenting the information to patients. Again in that section please do not use first person "our systematic review".

RESPONSE: We have added the new table (see also under Dr. Siwek's comments). We changed "our..." to "a recent systematic review...."

In the uncertainties section you mention the role of diabetes as a CHD equivalent, but what about chronic kidney disease? How does this play a role in risk assessment? Should we be doing a CKD calculation too?

RESPONSE: CVD is highly prevalent in patients with CKD and may account for 50% of all deaths. The Dialysis Outcomes Quality Initiative (DOQI) publication on the evaluation, classification, and stratification of CKD states that a reduced GFR identifies individuals at greater risk for CVD and death. This risk is the result of traditional and nontraditional CVD risk factors. AHA guidelines recommend treating patients with CKD as highest risk. We have added this information to the paper (and the reference).

Also, please consider writing a patient education handout to accompany your article. Dr. Siwek has provided further details below. Before you write it, please take a look at the section on "health calculators" on familydoctor.org. You can click on <http://familydoctor.org/online/famdocen/home/tools/calculators.html> which then links you to revolution health <http://www.revolutionhealth.com/calculators/heart-attack-risk>. If there is too much overlap, please let me know. Otherwise, creating a unique handout on this topic will be a great addition to the family doctor site.

RESPONSE: Thank you for inviting us to write a patient handout. We did not think there was too much overlap. We do, however, think that the www.med-decisions.com website is better than the revolutionhealth site because it allows people to "see" the average risk reductions potentially achievable by instituting therapy (and also does not have advertising). We have included this information in the patient handout. (We did not include the address to the NCEP calculator because it also does not provide information on risk reduction.) Let us know what you think.

COMMENTS FROM DR. SIWEK:

Overall, this is a well-written, professionally prepared manuscript. Many thanks for sending it to us. It makes an important point about assessing global risk, and using risk calculators. And, you provide some handy references/links to get them into the hands of any reader who doesn't already have one.

RESPONSE: Thank you Dr. Siwek.

Page 3: in the introduction, you do a good job of telling readers to treat absolute risk, rather than just risk factors. Anything you can do to emphasize this point would be helpful. There is evidence that clinicians spend too much time treating individuals who have risk factors but relatively low risk, while not being aggressive enough with individuals who have high risk, some of whom have modest levels of "risk factors." One concrete example that drives this point home is that people who have already had a cardiovascular event (MI or CVA) are those at highest risk for recurrence; yet too often those people aren't treated aggressively enough.

RESPONSE: We added a sentence emphasizing the important point that treatment should be based on a person's absolute CHD risk rather than just his or her risk factors. We did not add the specific example of a person with a previous event only because that gets into secondary prevention, for which Framingham calculations would not be applicable. As pointed out, they are "automatically" in the highest risk group. We added a sentence in the first paragraph of the introduction reminding the reader of this fact.

Page 4: "Because the risk-benefit ratio of taking aspirin for primary prevention transitions from harmful to helpful at a 10-year CHD risk of between 6% to 10%, 13 clinicians need to be able to estimate risk with relatively fine gradations in order to effectively counsel patients and make recommendations." Good, concrete example.

RESPONSE: Thank you.

Page 7: "Clinicians should also provide information about what constitutes an actionable level of risk (e.g., 10% for aspirin, 20% for cholesterol reduction, and any risk level for hypertension treatment and smoking cessation) according to current practice guidelines." Please create a table that shows thresholds for intervention, based on absolute risk. Also, please be specific/explicit: what does "10%" refer to?? There's no context, and for someone not used to using these calculators, they're left in the dark guessing. Please be specific about "hard" endpoints--risk of death and MI, and total CHD risk, including, for example, angina. Be explicit when setting thresholds for intervention--what is the percentage, and what is the endpoint? Pretend you're telling someone who's never used one of these calculators how to put it into practice. If this, then that etc.

RESPONSE: We created a new table with this information.

Page 7: "For example, a male, hypertensive smoker who has a 20% CHD risk over 10 years can reduce his risk to 10% (a 50% relative risk reduction) by smoking cessation." Please specify that this is global (if indeed that's what you're referring to).

RESPONSE: Yes, that is what we are referring to. Changes made.

Also, I just noticed that global CHD risk does not seem to be defined in the text of the manuscript, but only in the abstract. Please define it in the text, since this is such an important point (does CHD risk mean heart attack, cardiovascular death, both, other?).

RESPONSE: Another excellent point. We added definition as first sentences of 2nd paragraph.

Page 8: "Finally, risk is a difficult concept, and there remains much to be learned regarding best methods of presenting risk to patients, particularly those with low literacy or numeracy skills." Here's another opportunity to distinguish between risk (where the money is), and risk factors. Emphasize to readers that they should be treating a person's actual risk (for example, 20% risk of CHD in the next 10 years), rather than an isolated risk factor (elevated LDL, which might translate into significant risk in some people, but not in others).

RESPONSE: We added a concluding sentence as suggested.

There seems to be some evidence that patients find it helpful when risk and benefit are presented using boxes illustrating outcomes with treatment and without treatment, as exemplified here:

In AFP:

http://www.aafp.org/afp/20090415/668.html?aafpvlogin=5929344&aafvpw=&URL_success=http%3A%2F%2Fwww.aafp.org%2Fafp%2F20090415%2F668.html

In the primary source:

<http://nntonline.net/visualrx/examples/>

<<in response to the following NICE guidance:

"People should be offered information about their absolute risk of CVD and about the absolute benefits and harms of an intervention over a 10-year period. This information should be in a form that:

- * presents individualized risk and benefit scenarios
- * presents the absolute risk of events numerically
- * uses appropriate diagrams and text."

The smiley face diagram made its first appearance in the BMJ in an article communicating risk; since then we changed the colours of the faces to red, yellow and green as red and purple are not easy to distinguish for those who are colour blind, and it seemed that traffic light colours might be more familiar to users.

There is also an interesting recent article on communicating risk by David Spiegelhalter in the Annals of Family Medicine in which he refers to Visual Rx as one of the ways of trying to make risks accessible to patients. Links to many further examples are available here. >>

RESPONSE: Thank you for this suggestion also. We added a Cates Plot as a new figure (along with the website link to VisualRx) as well as information in the text and in the "best practices" for communicating risk table.

References: if reference 20 is not accepted by the time of publication of this manuscript in AFP, then we won't be able to list it (journals do not list "under review" papers in reference bibliographies). If this is the case, then please renumber all references accordingly. If, as you request, we delay publication of this article until that one is accepted (in which case, we would list it as "in press") or published, that's okay, provided that it is likely to get accepted. We wouldn't want to hold this one indefinitely (no longer than a year from acceptance).

RESPONSE: The systematic review article has been accepted for publication by Archives of Internal Medicine. The current citation is: Sheridan SL, Viera AJ, Krantz M, Ice CL, Steinman LE, Peters K, Kopin L, Lungelow D. Does giving global coronary risk information to adults improve outcomes? A systematic evidence review. Arch Intern Med [in press].

Please review, and cite as appropriate, this article: A Practical and Evidence-Based Approach to Cardiovascular Disease Risk Reduction. Arch Intern Med 7/26/04 (especially if they have any tables or figures you might want to adapt).

RESPONSE: Thank you for this reference article. We did not include it since it addressed secondary prevention. There were no tables or figures to adapt.

Please see this reference on the issue of (over)treating risk factors, instead of actual risk.

<http://www.bmj.com/cgi/content/extract/333/7576/988>

As well as the issue of targeting risk, not just risk factors:

<http://www.bmj.com/cgi/content/extract/324/7353/1570?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=1&title=risk+factors&andorexactitle=and&andorexactitleabs=and&andorexactfulltext=and&searchid=1&FIRSTINDEX=50&sortspec=date&fdate=1/1/2000&resourceype=HWCIT>

RESPONSES: Thank you for these references as well. We particularly like the Law & Wald paper and use it in one of the lessons in our MD-MPH course on prevention.

* Citations for all tables and figures: Please provide complete citations for all tables and figures (or mark them as original).

RESPONSE: Done.

Table 3: to better highlight those tools that can be downloaded to a PDA, in the column "Type of Tool", please list "PDA" under "Web" for each such tool.

RESPONSE: Done.

Table 3: in a footnote, please mention that CHD risk calculators are sometimes included with other medical PDA programs. (I access mine via Epocrates, for example).

RESPONSE: Done.

The tables are great, and will be nice additions to the literature. All the URLs listed in your manuscript will be hot-linked in our online version. So, please be sure to verify that each URL works and takes you to the specific web page desired/referred to.

RESPONSE: All links have been verified. We will verify again prior to publication.

Figure: is there a typo in the original publication? In the top right column (Benefit 2), the last number (>20) seems incorrect. Maybe they meant >200? Please check this, and see if they ran any corrections. I don't think it makes sense for us to publish this as >20. Also, as a technical point, even if we get permission, I'm not sure how we might go about reproducing this table. The version you sent is not adequate (pixel-wise) for printing. We'd either need to get the original or (gulp) try to recreate it ourselves. Do you have any other versions to use, just in case? I remember using a similar one years ago (pre-internet) that was in black and white, and had similar grids to select among various risk factors. I think it was based on Framingham, and might still be available if you Google around.

RESPONSE: We did not see a correction that was run. On rethinking it, the New Zealand charts may not be the best to use anyway since they use 5-year predicted risk and our article really spends a lot of time talking about 10-year risk (not that there is anything wrong with using 5-year risk, but just trying to be consistent to try not to confuse readers). What about getting permission to use the charts (and hopefully can get originals for the right pixels for printing) from the 1998 Wilson paper published in Circulation?

* Patient Education: To help our readers and their patients, I'd like to ask you to develop a patient education handout to accompany your article. If you'd like to do so, please prepare a handout of two to four double-spaced pages in length. What would complement your article nicely is a piece on: "Estimating your risk of having a heart attack." Please see the enclosed materials that provide guidelines on format and writing tips for a lay audience, as well as a sample handout.

* Please mention one or more national self-help groups or national medical organizations that can provide further information, such as NHLBI and AHA.

Please include this link, which is a risk calculator from NCEP, designed for the public:

<http://hp2010.nhlbihin.net/atp/iii/calculator.asp>

RESPONSE: Thank you for allowing us to provide a patient handout. We included the link to the www.med-decisions.com calculator rather than the NCEP one because it uses several of the principles we discussed in the article (including presenting a comparison to someone of same age & sex, strategies to reduce risk).

COMMENTS FROM REVIEWER #1:

1. what is the new information here? all references are several years old.

RESPONSE: Our experience suggests that most physicians working with patients to reduce their cardiovascular disease risk do not use global risk to guide discussions and recommendations. This is despite

the fact that the recommendations to do so were made a number of years ago. (We are currently beginning a national survey to learn how often and to what extent family physicians, general internists, and cardiologists use global risk scores.)

2. key recommendation statements are both level C. Not compelling to change clinical practice.

RESPONSE: We believe that decisions about preventive therapy ought to be rational and made after consideration of the likelihood that such therapy will help a person (and have greater likelihood of helping than harming). Treating “risk” rather than risk factors is a very sound principal (Law MR, Wald NJ. Risk factor thresholds: their existence under scrutiny. BMJ 2002;324:1570-6.). Evidence that using global risk calculations is beneficial is accumulating – we cite our recent systematic review on some of the outcomes on which it seems beneficial. However, because these outcomes are not the distal, most patient-oriented health outcomes, the level of evidence remains a C.

3. availability of multiple CHD risk calculation tools is noted but there is no statement in text as to which is best/most accurate, and evidence to support.

RESPONSE: We do not state that one tool is best/most accurate because there isn’t one tool that is best/most accurate. We provide a list of several available tools and present the idea that a clinician can choose a tool based on resources and preferences. We also cite a systematic review (Sheridan 2003) that examined the accuracy of several Framingham tools and provided an extensive list.

4. CHD risk calculators based on Framingham data appear to have serious limitations due to lack of racial/ethnic diversity in that all white cohort, and inability to develop accurate risk estimates in other populations.

RESPONSE: We have mentioned the limitations in the paper. To reiterate, participants in the Framingham Heart Study from which the equations were derived were 2439 white men and 2812 white women, ranging in age from 30 to 74 years. However, the Framingham risk equations have also been shown to predict well in African American men and women. We acknowledged that they tend to overestimate CHD risk in Hispanic and Japanese-American men, Native American women, and in Chinese men and women and underestimate risk in diabetics.

5. authors overlook any substantive mention of smoking and make only superficial mention of obesity. Together these two potentially modifiable risk factors are addressed in only the most minimal fashion.

RESPONSE: Smoking cessation counseling clearly should be offered to any smoker with strong recommendations for complete abstinence. We feel that this article does not need to spend very much time on the topic of smoking beyond that. Similarly, all obese patients ought to be counseled to lose weight (although such counseling is not as effective as counseling to stop smoking). Neither recommendation however need be based on any kind of risk calculation. Pharmacotherapy, particularly statins and aspirin, however, should be guided by risk.

6. section on balancing risk and benefits of treatment (p 4) is potentially interesting but under-developed.

RESPONSE: We added more information on specific risks of aspirin.

7. as summarized in concluding paragraph there is not enough objective information from which to develop evidence-based recommendations for clinical practice regarding the use of global CHD risk assessment for CHD primary prevention.

RESPONSE: We agree that there are unanswered questions and issues worthy of further exploration. However, we believe global CHD risk assessment is useful and should be part of clinical practice. Otherwise we would not have written the article. Upcoming guidelines (e.g., JNC8 and ATP) will also place more emphasis on global risk.

8. table 3 is confusing regarding which risk calculator is preferred.

RESPONSE: There is not one that is preferred. Choice should be based on clinician resources and preference.

COMMENTS FROM REVIEWER #2:

This article presents a very nice review of the tools available to accurately quantitate a person's future risk of a clinical event due to coronary artery disease. The author makes the point that simple guesstimates of coronary risk are often incorrect and lead to misapplication or non-application of indicated therapies. The argument is well-presented and the solution to the problem (the available risk calculators) are well-described and referenced. Unfortunately, as the author points out, there still is a huge gap of undertreatment of known cardiovascular risk. The application of the available risk calculators would go a long way towards closing that gap.

RESPONSE: Thank you.

COMMENTS FROM REVIEWER #3:

Thank you for the opportunity to review this article. Use of appropriate screening, therapies and finding ways to motivate patients and doctors in the prevention of CHD is very important. As a general review of CHD risk calculators, where to find them, and a summary of the evidence behind them the article is good. Overall, I find the article argues too strongly in favor of global CHD calculators without acknowledging the lack of patient oriented evidence to tell us which strategies are most effective. This article attests to the potential for risk calculators to produce benefit, but doesn't contain any new patient oriented information or present evidence that global CHD is really superior to conventional risk factor identification.

RESPONSE: We cite two systematic reviews that highlight what is currently known about the benefits of this approach. These benefits include greater likelihood of prescribing risk-reducing medicines to high risk patients and greater likelihood of patients' initiating therapy. We also acknowledge that more research is needed.

The article (Page 1) suggests that conventional risk factor approaches overlook many patients who would benefit from therapy. It's not that there's anything empirically wrong with the risk factor approach. Smoking status, blood pressure, and lipids aren't necessarily overlooked, but there are barriers to treatment. The problem may be the doctor who watches a blood pressure of 142/80 and borderline lipid levels instead of treating. So the question is whether using the global CHD to restate risk as a percent chance of MI compared to an ideal patient is better at overcoming those barriers or selecting the best therapy. The article suggests that calculating a Global CHD 10 year risk (death, coronary event, and coronary disease) using Framingham Criteria is superior to treatment of individual risk factors in primary prevention of heart disease. AHA guidelines based on the consensus of experts also recommend this. The evidence for this approach lacks adequately powered, high quality, prospective studies to show a clear benefit of decreased mortality, coronary events, quality of life, costs, or other outcomes that matter to patients. The authors correctly point out that this recommendation is expert opinion (SORT class C).

RESPONSE: We mostly agree. Where we differ is with the idea that there is nothing wrong with the risk factor approach. As we describe in the paper, a person's "levels" (e.g., LDL) can be high yet his risk actually be quite low. Whether to take a statin (given the cost, possible side effects, hassle, etc) ought to be an informed choice. On the other hand, a person's "levels" can be only modestly elevated, even "borderline", yet his risk might be quite high. (Part of the reason is that age is such an important driver of risk.) That person should be offered treatment to reduce his *risk*, not his *risk factor levels*. (Of course the choice would still be his).

The systematic review (Sheridan SL BMC Health Services Research) does suggest that physicians are more likely to prescribe cardiovascular medications when using a global CHD. And no harms were found to this approach. However, this is not a patient oriented outcome. I feel the article might give more depth about the studies in the review. Which medicines were more prescribed? Did the doctors prescribe the cardiovascular medication that, if effective, might produce the biggest risk reduction on the global CHD calculator? E.g. if a patient has borderline

HTN and borderline lipids, which cardiovascular medication, antihypertensive or statin, might be expected to produce a larger risk reduction on the calculator? Does this hold up in prospective, controlled trials? As a review article, summarizing this would be helpful to primary care physicians.

RESPONSE: Interested readers can certainly take a look at the references. The BMC article is available free online. As suggested by Dr. Sexton, we did not expand much on this in this paper.

The authors (page 4) state that using global CHD reduces harm. Yet no evidence is given. While it is established that aspirin may cause harm in low CHD risk populations, the paper does not show controlled evidence that use of global CHD results in better prescribing of aspirin much less reduction in actual harms.

RESPONSE: We changed the phrasing to "...and may help to avoid harm...." We were surprised to find no such studies on aspirin when conducting our systematic review.

The authors cite a systematic review (NAMES WITHELD FOR BLINDING, Does Giving adults global coronary risk information improve clinical outcomes? Under review) showing that providing patients with their global CHD risk calculation improved clinical outcomes. The outcomes mentioned are accuracy of risk perception and intent to start therapy. While encouraging, these outcomes fall short of even surrogate markers of improved cardiovascular health (med compliance, improved BP, smoking cessation, or improved lipid profile) much less reductions in events. I could not review this source to see if these were prospective trials or included outcomes or harms that matter to patients.

RESPONSE: This will be published in Archives of Internal Medicine.

We are certainly going to have to wait for POEMs of well done prospective trials to validate use of global CHD to improve outcomes that matter as these trials may take years to show benefit. I am surprised that prospective trials of global CHD have not been done to show impact on short term measures like B.P and lipid lowering and smoking status. Until we know, global CHD certainly is a reasonable tool to use in motivating patients. Again, I frequently use global CHD. But it is speculation that routine use reduces cardiovascular morbidity or is cost effective overall. The article might comment on whether prospective trials are underway.

RESPONSE: Dr. Sheridan and I are certainly interested in developing such studies, but we don't know of prospective trials underway specifically to name in the paper.

I think this article would benefit from a frank discussion of why global CHD calculators have not reached the POEM level and remain expert opinion. I would be interested to read the article that was blinded in this paper (ref 20), especially if the systematic review looked for unpublished data or mentioned ongoing prospective studies. The article might benefit from more in depth discussion of the outcome measures found in that review.

RESPONSE: Again, the review will be available when this is published.

Other approaches where patients learn about increase risk often do not result in behavior change. Knowledge of risk does not always translate into benefit. Screening diabetic patients without known CAD with stress myocardial perfusion imaging and finding out which patients have CAD does not change the rates of cardiac events. Young LH et al. Cardiac Outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes. The DIAD study: A randomized controlled trial. JAMA 2009; 301(15):1547-55. The patients in that study presumably improved their perception of risk, intent to start therapy, and their doctors started cardiovascular medications. Yet, there weren't statistically improved outcomes. The article could mention pitfalls in assuming more information about risk improves outcomes.

RESPONSE: We agree that there is much to learn about "risk" and how to present it to patients. It is clearly not always a motivator. Regardless, though, the risk information informs the way clinicians might work with patients to make decisions about preventive therapies, and that is our premise.

I feel primary care physicians often fall into the trap that more tests used to predict risk are worthwhile- e.g., CRP, homocysteine, coronary calcium score, carotid intimal thickness. I think we need to be cautious about recommending too strongly approaches that better quantify risk before we have evidence of improved management, improved outcomes, or cost effectiveness.

RESPONSE: We agree and have toned down the information on CRP.

The article (page 6) correctly points out that not all Framingham global CHD calculators are the same and no evidence helps us know whether one is better than another. The article also correctly points out (p 6) that addition of other risk factors (BMI, homocysteine.) to conventional markers does not improve prediction of risk much less outcomes; yet, some calculators include these. The article suggests that CRP measurement may improve accuracy of risk estimation. High dose statin therapy based on elevated CRP does seem to improve outcomes. Ridker PM, Danielson E, Fonseca FAH, et al. Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. N Engl J Med 2008; 359: 2195-207. Questions remain about the cost effectiveness and broad application of this approach. But the article should mention this with the CRP discussion.

RESPONSE: We would not want to suggest that the JUPITER trial (which we also now cite) demonstrated that CRP ought to be used to guide therapy. Patients in JUPITER were on average at high enough absolute risk to justify statin therapy without any knowledge of their CRP. That a statin reduced their risk is not surprising at all. What we need to know is whether statins have a different effect based on whether someone has an elevated CRP or not. JUPITER did not tell us that.

Framingham based CHD risk calculators require information about diabetes status. In the article, Table 1 lists diabetes as a risk factor and suggests reduction of hemoglobin A1C below 7% as the primary goal for this risk factor. I couldn't tell whether the article was making the point that without the global CHD score, physicians might be misled to chase blood sugar when they would better chase smoking, cholesterol and BP. Or whether reducing blood sugar is the best approach to reduce overall risk. The relationship between intensive glycemic control and CHD is not clearly established, perhaps even increasing mortality (the ACCORD trial). And, a recent systematic review established that DMII is not an equivalent risk to established CHD. Diabet Med 2009; 26 (2): 142-148 Yet, aggressive use of statins do seem to benefit diabetics without known CHD (Snow V Ann Intern Med 2004; 140:650-58.) So I do accept the premise of the article, using global risk is better: that even if diabetes increases your risk, reducing BP or cholesterol may provide a better approach than reducing glucose. The article might discuss this more clearly.

RESPONSE: Great points. We did not mean to imply lowering glucose reduces CHD risk, and removed that from the table. Thank you also for the great Diabet Med 2009 reference.

Please note that in addition to the revisions based on reviewer and editorial suggestions, we also added a couple sentences about the USPSTF recently updating their recommendations on aspirin prophylaxis for CVD. We did not want to go into too great of detail but felt it was important to include this information.