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WHAT SHOULD BE THE LOW BOUND OF BP IN PATIENTS WITH DIABETES AND HYPERTENSION? [9-1]

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"Lower The Better" Is Not Better

9-1 ASSOCIATION OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE AND ALL-CAUSE MORTALITY IN PEOPLE WITH NEWLY DIAGNOSED TYPE-2 DIABETES.

This retrospective cohort study examined the effect of BP achieved in the first year of treatment on all-cause mortality in a large primary-care cohort of patients with newly diagnosed type-2 diabetes (**DM-2**).

Clinical guidelines recommend maintaining BP below 140/90 in people with hypertension in the general population. And a further lowering of BP to a treatment goal below 130/80 in high risk patients, including people with diabetes, cerebrovascular disease, or kidney disease. And initiation of anti-hypertension therapy in high risk groups, even if their BP is in the normal range.

The lower target in patients at high risk of cardiovascular disease (**CVD**) was based on early randomized trials, which showed marked reduction in CVD outcomes in groups receiving tight control of BP vs those receiving conventional control. Evidence from epidemiological studies suggested that CVD risk starts to increase above BP of 115/75. This evidence led to the consensus that there is no lower threshold for BP lowering. Ie, the "lower the better".

Aggressive targets for BP treatment in DM-2 have recently been questioned because recommended targets are well below those found in the trials on which the guidelines are based. The ACCORD trial did not show further CVD benefits of anti-hypertension treatment reducing systolic BP to below 130 in people with diabetes.

To date there is little evidence indicating a cardio-protective effect of BP lower than 130/80. Too aggressive lowering in high risk patients could do harm.

STUDY

1. Extracted records of all adult patients with a new diagnosis of DM-2 from a large database. (1990-2005; n = 126 092)
2. Principle outcome = all-cause mortality. Patients were followed until date of death, or end of study.
3. Covariants included: Age at diagnosis; sex; socioeconomic status; smoking; body mass index; BP; total cholesterol; HbA1c.
3. Categorized into 2 groups: 1) previous CVD (stroke or myocardial infarction; 10% of cohort); and 2) no previous cardiovascular event.
4. Categorized into 3 groups according to mean systolic and mean diastolic BP:

    <130/<80 (tight control)

130-139/80-84 (usual control)

140+/85+ (uncontrolled)

5. The cohort was further categorized into 10 and 5 mm Hg segments, resulting in 7 BP groups. (Systolic <110 to 160+; diastolic <70 to 95+)

RESULTS

1. Over a mean follow-up of 3.5 years, 25 495 deaths were recorded (20% of cohort).
2. Overall mortality was 28% in those with CVD, and 19% in those without CVD.

   Those with CVD were more likely older, male, ex-smokers, and to have lower BMI, HbA1c, and cholesterol than those without CVD. And more likely to receive anti-hypertension drugs (thiazides, ACE inhibitors and angiotensin II blockers), lipid lowering, and anti-platelet drugs, during study period.
3. BP control according to CVD status:

   At diagnosis of DM-2, patients with established CVD had significantly lower mean BP than those without CVD.

   In both groups, the mean value of systolic and diastolic decreased significantly during the first year after diagnosis. BP was significantly lower in those with CVD

   Patients with CVD were more likely to have tight BP control and reduced rates of uncontrolled BP.
4. All-cause mortality after adjustment for baseline characteristics:

   (Hazard ratio—observed BP vs usual control BP [130-139/80-84])

Patients with CVD	HR
Systolic < 110	2.79
Diastolic 70-74	1.32
Diastolic < 70	1.89
People without CVD:	
Systolic 110-119	1.58
Systolic <110	2.42
Diastolic 70-74	1.17
Diastolic < 70	1.54

5. After restricting analysis to patients who received medical treatment for hypertension, there were

similar HRs for mortality when comparing tight control (<130/<80) with usual control (130-139/80-84)) and comparing uncontrolled BP (140+/85+) with usual control in both people with and without CVD.

6. As the systolic rose incrementally over 160 and the diastolic over 95, there was no statistically significant increase in all-cause mortality.[1]

DISCUSSION

1. This observational study related the levels of systolic and diastolic BP during the first year after diagnosis of diabetes to the risk of all-cause mortality in a large cohort of patients with newly diagnosed DM-2.
2. In patients with DM-2 and CVD, systolic below 110 and diastolic below 75 were significantly associated with increased risk of death.
3. In patients with diabetes without CVD. systolic below 120 and diastolic below 75 were associated with a significant increased risk of mortality.
4. These associations persisted when restricted to patients who received treatment for hypertension.
5. Despite the known benefits of lowering BP, and the benefits of medical treatment to reduce BP, the optimal goals of treatment to reduce BP are still not clear in patient with diabetes.
6. Additional benefits of lowering BP below 130/80 have not been consistently supported by trial evidence.
7. Because of the observational nature of this study, the increased risk related to tight control des not imply causality.
9. Maintaining diastolic BP above a critical level is especially important to ensure coronary flow during diastole.
10. The study was not able to ascertain the causes of death and assess CVD mortality in relation to BP levels.
11. Guidelines recommend that patients at high risk of CVD should maintain BP below 130/85. But, there is no convincing evidence from clinical trials that maintaining a low BP in patients with DM-2 provides additional cardiovascular benefits.
12. Conclusions and policy implications:

    In this large observational study, BP below 130/80 was <u>not</u> associated with decreased risk of all-cause mortality in patients with newly diagnosed diabetes with or without known CVD.

    Low BP, particularly below 110/75 was associated with increased risk.

Although no causality can be implied from these results, the "lower the better" approach night not apply to BP control beyond a critical level in high risk patients.

Since there is no current robust evidence available for lowering BP below 130/80 in people with diabetes, it might be advisable to maintain BP between 130-139/80-85

BMJ2012;345:e5567 Based on data from the United Kingdom General Practice Research Database 1990-2005

A short summary appeared in BMJ September 22, 2012; 345:18 First author Eszter Panna Vamos, Imperial College, London, UK

This is an important clinical point. How should primary care clinicians respond to this information? I believe it would be prudent to set the lower bound of treated BP to the 130s/80s for all patients, not only those at high risk. In general treatment of hypertension should be "low and slow", starting with a low dose of one drug and gradually increasing dose moderately, especially in elderly patients. Then adding a second drug at low dose and increasing dose moderately. I believe adding a third or even a 4th drug to reach a goal of 130 would do more harm than good.

1 This certainly needs confirmation.

See also: "Diabetes and Hypertension: A Bad Combination" Lancelet August 11, 2012; 380:601-10 First author Ele Ferronnini, University of Pisa, Italy

High BP is reported in over 2/3 of patients with DM-2. Its development coincides with the development of hyperglycemia. Many physiological mechanisms underlie this association including: the stimulatory effect of hyper-insulinemia on sympathetic drive, smooth muscle growth, sodium-fluid retention, and the excitatory effect of hyper-glycemia on the rennin-angiotensin-aldosterone system.

The combination confers an enhanced risk of CVD

A BP lower than 140/85 is a reasonable therapeutic target.

Patients with controlled diabetes have a CV risk similar to patients without diabetes, but with hypertension.

A rennin-angiotensin-aldosterone system blocker combined with a thiazide diuretic might be the beet initial anti-hypertension treatment for patients with diabetes.

"Newer Guidelines Are Likely To Suggest A Goal For Patients With DM Of Less than 140 Based On The Totality Of Evidence."

9-2 USE OF A SINGLE TARGET BLOOD PRESSURE LEVEL IN TYPE-2 DIABETES MELLITUS FOR ALL CARDIOVASCULAR RISK REDUCTION

For more than 15 years, all major clinical practice guidelines have recommended a target BP of less than 130/80 for patients with diabetes. This is based almost exclusively on retrospective analyses of primary outcome trials

The first prospective trial to randomize patients with type-2 diabetes (DM-2) was the United Kingdom Prospective Diabetes Study (UKPDS 38). In that trial, the group randomized to tighter BP control had a mean BP of 142/82. This group demonstrated significant reductions in DM-related deaths and complications compared with the control group, whose mean systolic BP was 10 mm Hg higher.

More recently, the ACCORD-BP trial randomized over 4500 high risk patients with DM-2 to systolic BP less than 120. After 4.7 years, there was no difference in non-fatal stroke, non-fatal MI, fatal MI, or all-cause mortality. The lower BP goal was associated with fewer strokes, but with more serious adverse events. While the trial achieved a mean systolic of 119, there was no overall CV risk benefit.

The main conclusion of the ACCORD trial was that a target of less than 120 does not reduce CV risk to a greater extent that a target less than 140.

A subgroup analysis of 6400 patients with DM, hypertension, or coronary artery disease from the INVEST trial showed no benefit in patients having a target of less than 130 compared with 130-139. Patients with levels below 115 trended toward increased CV risk.

One could argue that the data do not support a target goal less than 130.

An exception is the ADVANCE trial, which randomized 11 000 patients with DM-2 to drug treatment vs placebo. After 4 years, the mean systolic was 135 in the therapy group and 140 in the controls. There were fewer CV outcomes among those with BP under 130.

The issue of the optimal BP goal in patients with DM-2 remains unresolved.

But all agree that more intensive therapy is associated with increase in serious adverse effects.

A new meta-analysis of randomized trials appears in this issue of Anarchies [1] sought to determine the effectiveness and safety of treating BP to intensive targets (upper limit systolic 130) vs standard targets (upper limit 140-160) in patients with DM-2. The use of intensive BP targets was not associated with a significant decrease in risk for mortality or MI. It was associated with a small decrease in risk for stroke.

The meta-analysis reported that no conclusions about any specific BP target level can be drawn. The study did not support lower, more aggressive target BP levels for overall CV risk reduction.

Newer guidelines are likely to suggest a goal for patients with DM of less than140 based on the totality of evidence.

Physicians need to understand and discuss these goals with their patients.

Archives Internal Medicine September 24, 2012; 172: 1304-05 "Commentary", first author Pantelis A Saragides, Aristotle University of Thessaloniki, Greece.

1 Archives Internal Medicine September 24, 2012; 173: 1296-303 "Intensive And Standard Blood Pressure Targets In Patients With Type-2 Diabetes Mellitus", first author Kerry McBrien, University of Calgary, Calgary, Canada

Conclusion: "Although the use of intensive compared with standard BP targets in patients with DM-2 is associated with a small reduction in risk of stroke, evidence does not show that intensive targets reduce the risk of mortality or myocardial infarction."

I believe these data can be extrapolated to non-diabetic patients as well, although they will be less likely to experience adverse CV events.

Any BP lowering will benefit. The question is: how low and how quickly?

I believe that treatment of hypertension and other non-urgent conditions should "start low and go slow", especially for the elderly. We should treat with the lowest effective dose to minimize adverse effects. If a low-dose single drug lowers systolic to 130 and below, good! Adding a second and third drug should be gradual and at low dose. We often should be satisfied with a systolic above an arbitrary target.

If I had to choose between a systolic above 140 and 3 high-dose drugs, I would choose the former.

Lifestyle interventions must be part of any treatment schedule.

I believe that many adverse effects of drugs are due to a high dose. It may be safer to add another drug at a lower dose than to increase the dose of the first drug.

Home BP determinations are essential for good BP control.

Fitness May Be Associated With Compression Of Morbidity In Older Age

9-3 MIDLIFE FITNESS AND THE DEVELOPMENT OF CHRONIC CONDITIONS LATER IN LIFE.

Although physical activity (**PA**) likely represents an important determinant of healthy aging, studies have reported inconsistent results. The incremental contribution of PA to healthy aging beyond other healthy lifestyle characteristics remains unclear.

This study hypothesized that higher fitness levels in midlife would be strongly associated with healthy aging, defined by a low burden of chronic condition (**CC**) later in life.

STUDY

1. This study was based on data from the Cooper Center Longitudinal Study linked with Medicare claims. Included 18 670 healthy participants (baseline median age 49; 21% women). All survived to receive Medicare coverage (beginning at age 65) from 1999 to 2009. Follow-up = a median of 26 years.
2. Measured fitness levels at baseline by a treadmill time and estimated fitness levels in metabolic equivalents (**METs**).
3. Defines 8 common chronic conditions which may develop in later life, and associated them with degree of midlife fitness: congestive heart failure, ischemic heart disease, stroke, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, Alzheimer disease, and colon or lung cancer.
4. Determined CC prevalence from Medicare records.

RESULTS

1. Baseline (midlife) characteristics by fitness quintiles (Male)

	Q1	Q2	Q3	Q4	Q5
Number	2632	2986	3290	3093	2866
Treadmill time (min)	11	14	16	18	23
Fitness (METs)	8.5	9.9	10.9	12.0	14.1

2. After 120 780 person-years, there was considerable variation in the CC burden by attained age. As age increased 70; 75; 80; 85. the prevalence of each CC increased. Higher levels of BP, total cholesterol, BMI, glucose, and smoking were associated with a higher risk of developing CC outcomes.
3. As midlife fitness increased, there was decreasing incidence of CCs later in life

   Rate of CC burden by midlife fitness measurement in men:

Q1	Q2	Q3	Q4	Q5

Rate (No.) of CC burden	28	22	20	17	15
No. of conditions	4797	4376	4263	346	1830

4. The death rate over the years was lower in those with higher midlife fitness.
   Higher fitness was associated with a delay in the development of CCs
5. Compared with participants with lower midlife fitness, those with higher fitness spent a greater proportion of their final 5 years of life with a lower burden of CCs.

DISCUSSION

1. Higher fitness measured in midlife was strongly associated with lower incidence of CCs decades later. Higher fitness was also associated with a delay in onset of CCs, suggesting a compression of morbidity later in life.
2. A modest increase in fitness could translate into a marked reduction in CCs in older age.
3. Previous PA interventions have achieved mean fitness gains of 1 to 2 METs using a 6 month program of 150 minutes per week of moderate intensity exercise.
4. The healthy nature of the cohort and the long follow-up make the presence of undiagnosed CCs at study entry unlikely.

CONCLUSION

Midlife fitness was associated with a lower risk of common chronic health conditions in men and women older than 65 years enrolled in Medicare. Higher midlife fitness may be associated with compression of morbidity in older age.

Archives Internal Medicine September 24, 2012; 172: 1333- 40 Original investigation, first author Benjamin L Willis, Cooper Institute, Dallas Texas

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This cohort was healthier than most.

The study did not consider other healthy habits, which would increase longevity, and compress morbidity later in life. Certainly adopting other healthy habits would also bring benefits in old age.

The authors suggest that beginning to increase PA in middle age would benefit. (30 minutes a day; 5 days a week)

In my opinion, living a healthy old age is more important than living longer.

The Evidence Does Not Suggest Marked Health Benefits From Consuming OF

9-4 ARE ORGANIC FOODS SAFER OR HEALTHIER THAN CONVENTIONAL ALTERNATIVES?

In the US, billions are spent on organic foods (**OF**) every year. They are expensive, costing up to twice as much as conventional foods.

Organic certification requirements and farming practices vary worldwide.[1]

OF are generally grown without synthetic pesticides or synthetic fertilizers and without use of antibiotics and growth hormones. OF are processed without irradiation or chemical food additives and are not genetically modified.

Organic livestock are fed organically produced feed that is free of pesticides and animal byproducts. They are provided access to the outdoors, direct sunlight, fresh air, and freedom on movement.

Consumers purchase OF for different reasons, including concerns about the effects of conventional farming practices on the environment, human health, and animal welfare. There are perceptions that OF are tastier.

This study synthesized the publishes literature on the health, nutritional, and safely characteristics of OF vs conventional foods.

STUDY

1. Extensive literature search selected reports of comparisons of OF vs conventional foods. Seventeen studies in humans and 233 studies of nutrient and contaminant levels in foods met inclusion criteria.

RESULTS

1. Only 3 of the human studies examined clinical outcomes:
   No differences between populations by food type for allergic outcomes (eczema, wheeze, atopic sensitization) or symptomatic Campylobacter infection.
2. Two studies reported significantly lower pesticide levels among children consuming OF vs conventional diets.
3. Studies of biomarkers and nutritional levels in serum, breast milk, and semen did not identify clinically meaningful differences—no difference in vitamin content; some evidence that organic milk and organic chicken may contain more beneficial omega-3 fatty acids.

4. All estimates of differences in number and contaminant levels in foods were highly heterogeneous except for phosphorous, which was significantly higher in conventional produce, although the difference was not clinically significant.
5. Contamination with detectable pesticides was lower in OF. But risk for exceeding maximum allowed limits in conventional foods were small.
6. E coli contamination did not differ between OF and conventional foods. And risk of bacterial resistance to 3 or more antibiotics was higher in conventional than in organic chicken and pork.

DISCUSSION

1. Despite widespread perception that OF are more nutritious, this study did not find robust evidence to support this perception.
2. Studies measuring nutrient levels among humans consuming OF vs conventional foods did not find consistent differences. Of all the nutrients evaluated, only one nutrient (phosphorus) had a higher content in conventional foods. This is not likely to be of clinical significance.
3. Slightly higher levels of total phenols were found in organic produce, and higher levels of omega-fatty acids were found in organic chicken. These findings however, were highly heterogeneous.
4. Three additional key findings:
    1) Conventional foods had a 30% higher risk of pesticides contamination. However, the clinical significance of this is not clear because the difference in risk for contamination exceeding maximum allowed limits may be small.
    2) No difference in the risk for contamination of produce or animal products with pathogenic bacteria. Both organic and conventional animal products were commonly contaminated by Salmonella and Campylobacter species. A recent study found that produce from organic farming using manure for fertilization was at significantly higher risk of contamination with E coli.
    3) Conventional chicken and pork had a higher risk for contamination with bacteria, which were resistant to 3 or more antibiotics. This may be related to the routine use of antibiotics in conventional animal husbandry.
6. There have been no long-term studies of health outcomes in populations

consuming OF vs conventional foods.

7. The results of this study should be interpreted with caution because summary effect estimates were highly heterogeneous. Variations in organic practices (even if certified under the same standard) may also explain heterogeneity.

CONCLUSION

This study of the published literature on conventional foods vs OF on comparative health outcomes, nutrition, and safety identified limited evidence for superiority of OF. The evidence does not suggest marked health benefits from consuming OF vs conventional foods although organic produce may reduce exposure to pesticides, and organic chicken and pork may reduce exposure to antibiotic-resistant bacteria.

Annals Internal Medicine September 4, 2012; 157: 348- 366 Original investigation, first author Crystal Smith-Spangler, Stanford University, Stanford. California

1 European Economic Community, US Department of Agriculture. International Federation of Organic Agriculture Movements

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This is a detailed study quoting 298 references. I abstracted the article chiefly to learn more about OF. I believe this is the best analysis possible given the heterogeneity of data.

I doubt this study will change any minds. Enthusiasts on both sides will find some points in their favor.

I would not dissuade any advocates of OF from their position. I would not encourage persons who consume conventional foods to switch to OF.

When calculating the benefit / harm-cost ratio of OF vs conventional, I would favor conventional

Careful washing and peeling fruits and vegetables will remove most of the pesticides.

I applaud the proponents of OF for their gentleness toward animals.

Not Significantly Associated With Major Vascular Outcomes Across Various Patient Populations.

9-5 ASSOCIATION BETWEEN OMEGA-3 FATTY ACID SUPPLEMENTATION AND RISK OF MAJOR CARDIOVASCULAR DISEASE EVENTS

Treatment with marine-derived omega-3 polyunsaturated fatty acids (**O-3PUFA**) for prevention of major cardiovascular events (**MVE**) has been supported by a number of randomized clinical trials, and refuted by others.

Current guidelines issued by major societies recommend their use, either as supplements or through dietary counseling, for patients after a myocardial infarction.

The FDA has approved their administration only as triglyceride-lowering agents in patients with overt hyper-triglyceridemia.

There has been confusion in everyday clinical practice about whether to use these agents for cardiovascular protection.

This present systematic review and meta-analysis determined the association between O-3PUFA and major CVD outcomes.

STUDY

1. The meta-analysis selected 20 randomized clinical trials (N = 68 680 subjects) evaluating the effect of O-3PUFA on all-cause death, cardiac death, sudden death, myocardial infarction, and stroke.
2. No trial was for primary prevention alone.

RESULTS

1. Median age = 68; diet alone trials 2; supplement trials 18; median treatment duration 2 years; primary prevention trials 0; secondary prevention trials 13; mixed primary/secondary trials 4; trials in patients with implantable cardioverter-defibrillator 3. Total deaths = 7044; 3993 cardiac deaths; 1150 sudden deaths; 1873 MI; 490 strokes.
2. O-3PUFA administration through diet counseling (2 trials; N = 5147):
   Showed associations of *opposite* directions that differed beyond chance. (All-cause mortality (RR = 1.15 and 0.73) and cardiac death (RR = 1.27 and 0.67). The investigators could not explain the observed discrepancy.
3. O-3PUFA by supplementation (17 trials; N = 6295 events among 63 279 participants:
   Overall, O-3PUFA were *not* statistically significantly associated with a reduced all-cause mortality (RR =0.96): cardiac death (RR = 0.91) sudden death (RR = 0.87); MI (RR = 0.89); stroke (RR = 1.05)
4. Cumulative meta-analysis:

The investigators arranged 17 trials of O-3PUFA supplements for all-cause mortality arranged by year of publication beginning in 1995 and ending in 2012. This cumulative meta-analysis contained trials published every year, and every 2, 3, 4 years.

The cumulative number of participants 1995-2006 was 13 680; between 2007 and 2012 was 50 595.

All trials (N = 9) 1996-2006 showed statistically significant reductions in all-cause mortality. (RR= 0.30m to 0.87)

All trials (N = 8) 2007 to 2012 showed no significant reductions in all-cause mortality. (RR = 0.94 to o.96)

DISCUSSION

1. This study incorporated the available published randomized controlled trials (RCT) . It showed that O-3PUFA supplementation is not significantly associated with reduction in major cardiovascular risks.
2. The first quantitative meta-analysis of RCTs (2002) showed a strong significant effect across all major CV outcomes. As more randomized evidence accumulated, the effect became weaker and then non-significant.
3. This meta-analysis did not find any association with sudden death, thus rejecting a distinct anti-arrhythmic O-3PUFA effect.

CONCLUSION

O-3PUFA were not significantly associated with major vascular outcomes across various patient populations.

These findings do not justify use of O-3PUFA as an intervention in everyday clinical practice.

JAMA September 12, 2012; 308: 1024-33 Original investigation, firs author Evangelos C Rizos, University Hospital of Loanina, Loanina, Greece.

See also: "N-3 Fatty Acids And Cardiovascular Outcomes In Patients With Dysglycemia" NEJM 2012; 367: 309-18 (Short abstract ANNALS Journal Club JC3-17 September 18. 2012) Conclusion: "In high-risk patients with dysglycemia, N-3 fatty acids did *not* reduce cardiovascular events more than placebo."

These trials included only subjects at high risk for CVD. (Secondary preventing trials)

My pharmacy reports that sales of fish oil continue to be brisk. Certainly they are used by the general population for primary prevention. There is no evidence for benefit of supplements in primary prevention.

The cumulative meta-analysis was interesting. Nine RCTs between 1995-2006 all reported benefit from O-3PUFA. All 8 trials thereafter reported no benefit. Why should this be?

These results remind me of the enthusiasm greeting new interventions that suggest benefit (eg, vitamin D; estrogen; prostate specific antigen). Is there bias in early studies? I suspect so. And bias is repeated until the truth comes out.

Decreases Subsequent Trauma From Road Crashes.

9-6 PHYSICIANS' WARNINGS FOR UNFIT DRIVERS AND THE RISK OF TRAUMA FROM ROAD CRASHES

Dangerous driving imposes risk to others. Physicians' warnings to potentially unfit drivers are intended to prevent motor vehicle crashes.

However, formal warnings may reduce the patient's quality of life, jeopardize the physician-patient relationship, burden family members, and generate bureaucratic hassles.

In Ontario, Canada, medical warnings were introduced in 1968 as an affirmative duty for physicians. The policy requires physicians to report any patient who is suffering from a condition that may make it dangerous to operate a motor vehicle. However, subsequent data showed low rates of adherence by physicians.

In 2006, Ontario introduced a financial incentive for physicians to provide warnings to patients who are potentially unfit to drive. This new program offered an opportunity to test the effectiveness of medical warnings in reducing road crashes.

STUDY

1. Between 2006 and 2009, identified consecutive patients who received a medical warning from a physician who judged them potentially unfit to drive. All were over age 18, and had universal health insurance.
2. Analyzed emergency department (ED) visits for road crashes during a baseline

interval of 3 years before the payments to physicians began, and a subsequent interval after payments began.

RESULTS

1. A total of 100 075 patients received a medical warning from a total of 6098 physicians.

		%
2. Age	< 30	9
	30-44	14
	45-59	22
	60-74	22
	76 and over	33

3. Selected medical diagnoses: Alcoholism; epilepsy; dementia; sleep disorder; fainting-dizziness; stroke; diabetes; depression without psychosis.
4. During a 3-year baseline interval, there were 1430 road crashes in which the patient was driver and presented to the ED.
5 During the 1-year subsequent interval, there were 273 road crashes resulting in an ED visit. This represents a 45% reduction in the annual rate.
6 The lower rate was observed across patients with diverse characteristics.
7. Medical warning were associated with an increase in subsequent ED visits for depression, and a decrease in return visits to the responsible physician.

DISCUSSION

1. Physicians' warnings to potentially unfit drivers were associated with a reduction in subsequent risk of road crashes requiring ED visits by the patients.
2. The reduction in risk was immediate, substantial, and sustained.
3. This intervention poses an ethical conflict for clinicians who seek to optimize patients' health yet respect their preferences.
4. The data suggest that this intervention is associated with a significant increase in depression, and can compromise the doctor-patient relationship .
5. Clinical judgment is needed in deciding which patients are most likely to benefit from a warning (and when the public will also benefit).
6. Some patients continue to drive. (Patients often overestimate their driving skills.)

Road crashes involving patients as drivers still occur at rates above the population norm after receipt of a warning.

7. The mechanism of risk reduction could include a combination of altered driving behaviors such as traveling shorter distances, driving with greater care, and being more vigilant.

CONCLUSION

Physicians' warnings to patients who are potentially unfit to drive may contribute to a decrease in subsequent trauma from road crashes.

They may also exacerbate mood disorders and compromise the doctor-patient relationship.

NEJM September 27, 2012; 367: 1228-36 Original investigation, first author Donald A Redelmeier, University of Toronto, Canada
Doi:10.1056/NEJMsa1114310

I did not understand the full legal consequences of failing to abide by a warning.

The number of warnings for younger drivers surprised me. As did the number of different conditions resulting in the warning. In the USA, I believe we often think that most persons unfit to drive are elderly, with diminished sight, hearing, and reflexes. The list goes far beyond this.

The authors comment on the ethical consequences of warning drivers. I do not believe a serious ethical dilemma is present. Warnings benefit both the driver and the public.

This important problem persists in the USA. Approaches to control unsafe drivers by governments vary and are confusing.

Primary care clinicians frequently face these decisions. I believe we often will address the patient-driver directly, asking if he still considers himself a safe driver and advise that he stop driving. This may encourage some to stop . The clinician may also enlist the help of family members to continue urging the patient to stop driving. Cessation is best when it is voluntary.