PRACTICAL POINTERS

FOR
PRIMARY CARE

ABSTRACTED MONTHLY FROM THE JOURNALS

APRIL 2011

ADOLESCENT BMI AND RISK OF DIABETES AND CORONARY HEART DISEASE IN ADULTHOOD [401]

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This document is divided into two parts

    1) The **HIGHLIGHTS AND *EDITORIAL COMMENTS***

        HIGHLIGHTS condenses the contents of studies, and allows a quick review of pertinent

          points of each article.

        EDITORIAL COMMENTS are the editor's assessments of the clinical practicality of articles

          based on his long-term review of the current literature and his 20-year publication of Practical

          Pointers.

    2) The main **ABSTRACTS** section is designed as a reference. It presents structured summaries of the

      contents of articles in much more detail. And provides the citation.

    I hope you will find *Practical Pointers* interesting and helpful. The complete content of all issues for the past 5 years can be accessed at www.practicalpointers.org

Richard T. James Jr, M.D.
Editor/Publisher.

Prevention Of CHD Should Start At An Early Age

4-1 ADOLESCENT BMI TRAJECTORY AND RISK OF DIABETES VERSUS CORONARY DISEASE

Obesity in adulthood is a risk factor for type-2 diabetes (**DM-2)** and coronary heart disease (**CHD**). It is not clear whether a long history of overweight, starting early in life, poses an additional risk.

The trajectory of weight and height from birth to adolescence is well known. The progression of body index (BMI; kg body weight divided by height in meters squared; kg/m^2) from adolescence into adulthood is less well described. Obese children have high likelihood of obesity in adulthood. Childhood obesity is associated with classic CVD risk factors as is adult obesity.

The study followed over 37 000 healthy young men whose BMI was measured in adolescence and repeatedly in early adulthood in order to identify incident cases of DM-2 and CHD.

All males eligible for the Israeli army are examined at age 17. Height, weight and BMI are determined. All remaining in the army after age 25 are examined every 3 to 5 years. This study included 37 674 male career army personnel. None had known DM-2 or CHD at baseline.

Follow-up and outcome: Participants were followed prospectively from the time of their first army examination at about 25 years of age. Measured height and weight and calculated BMI at age 17 (adolescence) were tracked retrospectively.

BMI and incidence of disease:

Diabetes:

A total of 1173 cases of DM-2 were diagnosed between ages 25 and 45. (Young adulthood). After adjustment for multiple possible confounders, adolescent BMI was predictive of incident diabetes, with a significantly increased risk observed at age 17 in the three highest BMI deciles (22.8. 24.1 and 27.6). Hazard ratio of the highest 3 deciles vs the lowest deciles was 2.76. The risk of diabetes increased by 9.8% for each 1 BMI unit.

Only BMI in adulthood was significantly associated with increased risk of diabetes. *(By the investigator's analysis, this was because individuals with high BMI in adolescence were very likely to maintain high BMI in adulthood. If an individual with a high BMI in adolescence controlled weight and maintained a lower BMI in adulthood, the risk of DM-2 decreased. . The high BMI in adulthood was the reason for the high incidence of DM-2 in adulthood. Ed.)*

CHD:

During a mean of 17 years, 327 cases of angiographic-proven CHD occurred.

The risk of CHD increased by 12% for each 1 BMI unit increase in adolescent BMI.

Both BMI in adolescence and adulthood were significantly and independently associated with risk for CHD. Adolescent BMI remained a risk factor for CHD that was independent of adult BMI.

Diabetes is influenced mainly by recent BMI in adulthood and weight gain whereas, for CHD, both elevated BMI in adolescence and recent BMI in adulthood are independent risk factors. The natural history of CHD (in contrast with that of diabetes) is probably the consequence of gradual increasing atherosclerosis during adolescence and early adulthood that leads to clinically important disease in midlife.

It is noteworthy that these conclusions were deduced from adolescent BMI values that are well within the range of normal (22.8 and 24.1).

These conclusions highlight the clinical importance of considering BMI history when assessing the risk of CHD vs the risk of diabetes in overweight or obese young men.

An elevated BMI in adolescence predicts CHD in early adulthood independently of the BMI in adulthood. The upper decile of adolescent BMI is related to seven times the risk of CHD as the lowest deciles.

These results may be explained by the fact that diabetes represents a more functional patho-mechanism than CHD, which relies on anatomical changes (atherosclerosis). Even clinically established diabetes is readily reversible in response to changes in lifestyle interventions, whereas atherosclerosis is responsive to diet interventions only if the intervention takes place before the "clinical horizon" of the disease is reached.

Conclusion: BMI in adolescence is an independent predictor of CHD in young adulthood even when it is well within what is now defined as the normal range of BMI. (Atherosclerosis begins at an early age.) Incident diabetes was mainly due to high BMI in adulthood.

Abstracting this study was a challenge. I think it is important for public health. Atherosclerosis begins at an early age. Prevention should start at an early age.

Adolescent BMI-adult BMI	Risk of DM-2	Risk of CHD
High-high	*Highest*	*Highest*
High-low	*Low*	*Still high*
Low-high	*High*	*Not as high*
Low-low	*Lowest*	*Lowest*

"There Are Few Healthcare Interventions More Impactful Than Helping Smokers Quit"

4-2 SMOKING CESSATION INTERVENTIONS: A Primer for Physicians

A suggested approach to cessation:

A. Follow the 5 A's (See the full abstract)

Set a quit date

Refer to a smoking cessation program or telephone quit line (1-800-QUITNOW)

B. Initiating drug treatment:

On the quit date, begin nicotine replacement therapy using a long-acting nicotine patch, approximating the current daily nicotine intake for 8 weeks. (Eg, a patch delivering 21 mg for a patient smoking a pack a day). Consider adding short-acting nicotine therapy (gum, lozenges, or inhalers) for acute craving, not to exceed an additional 12 mg/day of nicotine. Then taper the patch dose over a period of 4 weeks.

C. Alternative drug treatment (1):

Begin sustained release bupropion 1 to 2 weeks before the target quit date, using 150 mg every morning for 3 days, and then 150 mg twice a day for 7 to 12 weeks.

D. Alternative drug treatment (2):

Begin varenicline 1 week before target quit date at 0.5 mg twice daily for 4 days. Then 1 mg twice daily for 3 to 6 months.

Practical Pointers has abstracted a number of articles dealing with smoking cessation in the past. I found this article helpful, giving up-to-date information.

Please read the full abstract for more details.

If your patient is a smoker, ask if he is ready to quit every time you see him in consultation. If he says he does not want to stop, ask again later. Don't give up. We don't give up trying to control BP and weight.

Which treatment schedule to start? This would depend on the patient's individual choice.

Cost ; My pharmacy quotes:

Nicotine is available over the counter without a prescription

Varenicline 1 mg twice daily costs $182 for a 30 day supply

Bupropion sustained release is generic, but cost is high: $75 for a month's supply

The A,B,C,Ds Of Drug Treatment For Hypertension

4-3   ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS IN HYPERTENSION

First-line antihypertension drugs are classified as A,B,C,D. Drugs classified as A include angiotensin converting enzyme inhibitors (**ACE**) and angiotensin II receptor blockers (**ARB**). B drugs are beta-blockers (**BB**); C are calcium antagonists; D are diuretics. A,B,C,D is a helpful mnemonic to use in initial treatment as well as adding a second drug when needed. It is used in UK guidelines to manage hypertension in primary care.

Beta blockers have fallen out of favor as single agents for treatment of hypertension when the BP is the only problem. This leaves A, C, and D as the main drugs to start treatment.

Patients with normal or raised plasma renin levels (eg, many young adults with essential hypertension) do better with A and B drugs. Those with low renin levels (patients of African descent and older patients) respond well to C and D.

This article focused on use of ACE or ARB when starting treatment.

ACE and ARB relax blood vessels and promote excretion of sodium, reduce cardiac preload and afterload, and lower BP especially in patients in whom the renin-angiotensin-aldosterone system is activated.

The article discusses:

How do ACE and ARB compare with other antihypertensive drugs?

How well do ACE and ARB work?

Combination treatment with ACE and ARB

How safe are A drugs? (Adverse effects)

What are the precautions when starting ACE or ARB?

How cost-effective are ACE and ARB?

How are ACE and ARB taken and monitored?

This is an excellent review and reference article for primary care. Please read the full abstract. It presents general comments about treatment of hypertension, as well as detailed information about ACE and ARB

Since most hypertensive patients in primary care are over age 55, C and D drugs are the preferred drugs.

"Nothing About Me Without Me".

4-4 SUPPORTING PATIENTS TO MAKE THE BEST DECISIONS: Must be a Core Component of What it Means to be a Health Professional

"Imagine an intervention to improve patient care that systematic reviews have shown to be effective, does not seem to have any serious unwanted effectors, has been a central component of health policy for more than a decade, is popular with patients, and which in principle is embraced by most clinicians."

Such an intervention does exist.

It is shared decision making. This is a process in which patients are encouraged to participate in selecting appropriate treatment or management options on the basis of the best available evidence. A defining mantra has become a central part of the current health reform: "Nothing about me without me".

Patients involved in shared decision making are bettered informed than those who are not involved, and are less likely to be undecided about the best course of action. They are also more likely than the doctor to defer or decline surgical intervention, with no measurable adverse impact on health outcomes or satisfaction.

Clinicians are often poor at eliciting the patient's agenda. One in three patients in primary care, and one in two patients in the hospital would have liked greater involvement in decisions about their care.

Shared decision making is a concrete manifestation of a more substantial social process, a re-conceptualization of the roles and responsibilities of patients and health professionals.

The interaction is increasingly being framed as a meeting between two experts. The clinician brings an understanding of the effectiveness, benefits, and harms of specific actions. The patient brings an understanding of preferences and attitudes to illness and risk.

Promoting shared decision making is increasingly seen as something that is needed to keep pace with changing social expectations.

The challenge for practitioners is to change attitudes and introduce new skills. Time and difficulty in access of high quality evidence are barriers.

Most fundamentally, the ability to share decisions must be seen as a core component of what it means to be a health professional.

Medicine's most glaring failure has been our inability to convince the public to take better care of their health.

I was trained in the era of medical authoritarianism and paternalism. Often that was because patients and their physicians lacked choice of therapy. There was only one therapy or none. If no therapy was available, other choices had to be negotiated.

Now, the availability of choice and the ethical principle of autonomy have become the basis of the social change in medicine. There can be different approaches to a disease and its therapy, leading to the requirement of a choice based on shared decision making.

Shared decision is a process of negotiation. In primary care practice, negotiating a shared decision may at times be impossible. Not all patients are capable of understanding. Some are illiterate. Many may not realize they have a choice. There may be ethnic differences and language difficulties. Some are old, feeble and demented. They may not have a competent surrogate.

Not every consultation will involve shared decision making. The subject may not come up in many routine office visits in primary care, especially for short term care. The doctor's advice is often not controversial and is automatically accepted. The problem becomes more acute when decisions about end -of-life care, and cancer and other long term illnesses are debated. And when surrogates are responsible for decision making.

Physicians negotiate on the basis of probabilities and statistical reasoning, which the patient may not understand. Probabilities are based on randomized, controlled trials. Participants in RCTs often differ from the individual patient seen in consultation. Evidence may be conflicting. Pragmatic trials are rarely available The expertise required to apply the treatment suggested by RCTs may not be available locally. Drugs may be too expensive. Compliance may be too difficult for some. The probabilities cited by "the evidence" may not be applicable to the individual in his present situation.

Another side of the coin may present itself in primary care. Patients may forcefully present their autonomy. They may request (indeed insist upon) a new drug they saw advertised, ("Ask your doctor if X is right for you".) Here the doctor's autonomy comes forth. Doctors have autonomy too. If the drug is not appropriate, the primary care clinician should not prescribe it. Often, however, indication may be debatable, and the doctor may finally agree after informing the patient that adverse effects of new drugs may not be evident for years.

One negotiating point I have enjoyed is the "if" prescription-- for example, when a patient with a sore throat or bronchitis (which is most likely viral) insists on treatment with an antibiotic. The prescription is given with the restriction that it not be filled for a few days to give the illness time to settle. Many times the prescription will not be filled. It works.

How should the primary care clinician respond when the patient asks directly: What would you do? The question can be asked in two different ways.

1) What would you do if you had my illness?

2) What would you do if you were me?

It makes a difference.

See the following abstract—The Salzburg Statement

4-5 THE SALZBURG STATEMENT ON SHARED DECISION MAKING

In December 2010, 58 persons from 18 countries attended a Salzburg Global Seminar to discuss the role patients can and should play in healthcare decisions. They agreed on a statement that calls on patients and clinicians to work together to be co-producers of health.

We call on clinicians to:

- Recognize that they have an ethical imperative to share important decisions with patients.
- Stimulate the two way flow of information and encourage patients to ask questions, explain their circumstances, and express their personal preferences.
- Provide accurate information about options and the uncertainties, and benefits and harms of treatment.
- Tailor information for individual patient's needs and allow them sufficient time to consider their options.
- Acknowledge that most decisions do not have to be taken immediately, and give patients and their families the resources and help to reach decisions.

We call on clinicians, researchers, editors, journalists, and others to:

- Ensure that the information they provide is clear, evidence based and up to date and that conflicts of interest be declared.

We call on patients to:

- Speak up about their concerns, questions, and what's important to them.
- Recognize that they have a right to be equal participants in their care.
- Seek and use high quality health information.

We call upon policymakers to:

- Adopt policies that encourage shared decision making, including its measurement, as a stimulus for improvement.
- Amend informed consent laws to support the development of skills and tools for shared decision making.

Why?

- Much of the care patients receive is based on the ability and readiness of individual clinicians to provide it, rather than on widely agreed standards of best practice or patient's preferences for treatment.
- Clinicians are often slow to recognize the extent to which patients wish to be involved in understanding their health problems, in knowing the options available to them, and in making decisions that take account of their personal preferences.
- Many patients and their families find it difficult to take an active part in health care decisions. Some lack the confidence to question health professionals. Many have only a limited understanding about health and its determinants and do not know where to find information that is clear, trustworthy, and easily understood.

BMJ April 8 2011; 342:794

This may be a way to encourage patients to better care for their own health

The Goal Focuses On Quality Of Life And Symptom Management.
4-6 GLYCEMIC CONTROL IN FRAIL OLDER PATIENTS WITH DIABETES

More than 40% of adults with diabetes are older than 65. Many are frail with functional disabilities that limit their ability to live independently. Many live in nursing homes. Many are community-dwellers depending on others for care.

Large randomized trials examining the effects of glycemic control exclude elders. This has led to uncertainty regarding their appropriate level of glycemic control. Different guidelines recommend different targets. Guidelines generally agree on a target HbA1c of less than 7% for most adults. For frail older patients (**FOP**), The American Geriatric Society recommends a target less than 8%; the V.A. recommends 8% to 9%; the ADA recommends "less stringent glycemic control", not specifying the goals.

Most frail patients over age 65 with diabetes have competing risks for mortality that limit life expectancy and make vascular outcomes less important.

In FOPs, tight control often leads to substantial burdens (dietary restrictions, insulin injections, finger sticks, polypharmacy, and hypoglycemia).

The goal of care for FOPs focuses on quality of life and symptom management. Many of the interventions required for tight control are not consistent with these goals. Tight glycemic control imposes immediate substantial burdens with little chance of benefit.

The most appropriate glycemic target for FOPs depends on 2 factors: the degree of frailty and the outcomes that are most important for the patient.

By considering an individual older patient's frailty, life expectancy, and the special outcomes most important to the individual, clinicians can provide patient-centered care that appropriately balances the burdens and benefits of glycemic control.

This is an example of use of good clinical judgment.

I remember, way back when we knew little about diabetes (although insulin was available), one of my professors advocated treatment limited to relief to the classical symptoms of diabetes. (Thirst, hunger, weight loss, polyuria, glycosuria). This might now be a reasonable goal for FOPs.

Recommendations Should Reflect The Patient's Value System In The Light Of The Physician's Knowledge.

4-7 RECONCILING PHYSICIAN BIAS AND RECOMMENDATIONS

In this era of patient-centered care, some argue that physicians should refrain from advising patients or recommending a treatment course, and instead should neutrally present all the options and leave the final decision making exclusively to the patient.

The other option is, in a strong physician-patient relationship, physicians should use their knowledge to make recommendations to help patients make better-informed choices about therapy. Patients may be the ultimate deciders of what treatment to initiate, but they need physician experience and guidance to make the best choice.

A study in this issue of Archives[1] reports that physicians may make choices for patients, which differ from the choices they would make for themselves. Patients often place emphasis on decisions maximizing length of life. Physicians often emphasize quality of life. The weight given to a potential preventable death vs life with a serious lifelong disability may differ considerably depending on whether one is the prescriber or the recipient of the treatment.

Physicians may have a negative emotional reaction to the potential of serious long lasting adverse outcomes that some might view as being worse than death.

These editorialists argue that the cognitive biases expressed by physicians when thinking clinically for their patients are not less, but simply different, from their biases when thinking of themselves in the patient's role. Physicians may have a tendency to favor prolongation of life when making recommendations for their patients, but place more emphasis on quality-of-life when making decisions for themselves.

Given that physicians are human beings and subject to biases in their decision making and recommendations, how can they help their patients make the best possible decisions regarding their treatment?

Physicians must be attuned to the unique values of the patient. If the physician in that role tends to maximize length-of-life concerns and minimize risk of suffering this is fine as long as the patient shares these principles. But a healthy patient -physician relationship should allow the opportunity for the physician to explore the length-of-life and quality-of-life concerns of the patient as well as which complications are acceptable to the patient and which are not.

When making recommendations. physicians should try to fully integrate the values and concerns of each patient, and to carefully present the benefits and risks of treatment options.
If gaps exist between what the doctor would do if he were in the patient's position and what he is recommending for the patient, it is important for the physician to reflect on this disparity and evaluate potential cognitive biases.

As long as the recommendations reflect the patient's value system in light of the physician's knowledge, it is relatively safe to proceed with recommendations.

Archives Internal Medicine April 11, 2011; 171: 634-35 "Commentary", first author Eric Shaban, University of Rochester, Rochester, NY
1 "Physician's Recommend Different Treatments For Patients Than They Would Choose For Themselves." Archives Internal Medicine April 11, 2011; 171: 630-34, first author Peter A Ubel, Duke University, Durham NC

I believe that many patients still leave judgments up to their doctors, trusting their advice and beneficence. I believe that doctors can gently guide patients to make reasonable choices.

Differences may be more acute at the end of the patient's life, especially when surrogates are making the decisions.

At the end, when the life loses all meaning and dignity, physicians can help surrogates to abandon "Life at all costs" and recognize that death is a necessary part of life. And help the patient to make a peaceful transition.

With the help of Hospice, physicians can help surrogates of loved ones who are at the end of life to be more comfortable and peaceful, while discontinuing the many unhelpful drugs these patients receive.

4-8   FDA EXPANDS AGE RANGE FOR SHINGLES VACCINE

Shingles vaccine (Zostavax: Merck; a live varicella-zoster vaccine) is now approved for persons age 50-59 as well as older persons. The FDA made this announcement in late March 2011.

The availability of the vaccine for younger persons provides an additional opportunity to prevent the disease.

The FDA based its decision on a multicenter randomized trial of about 22 000 patients age 50-59. Half received vaccine; half placebo. After a year, the vaccine reduced risk of shingles by about 70% compared with placebo.

In the USA, about 200 000 persons age 50-59 develop shingles each year.

Unfortunately, the vaccine can also trigger development of shingles. The cause is not known. The most common adverse effects are redness and pain at the subcutaneous injection site, and headache.

Patients who are immunocompromised should not receive the vaccine. This includes those with AIDs, lymphoma, cancer of the bone or blood, and those undergoing radiation therapy and those receiving corticosteroids.

JAMA April 20, 2011; 305: 1526 "Medical News and Perspective", comment by the JAMA staff.

Shingles provoked by the vaccine can be very severe and disabling. There is no way of predicting.

Children now receive chickenpox vaccine. They will never develop chickenpox, and will not harbor the virus. . Will shingles disappear? The vaccine virus is live.

ABSTRACTS APRIL 2011

Prevention Of CHD Should Start At An Early Age

4-1 ADOLESCENT BMI TRAJECTORY AND RISK OF DIABETES VERSUS CORONARY DISEASE

Obesity in adulthood is a risk factor for type-2 diabetes (**DM-2**) and coronary heart disease (**CHD**). It is not clear whether a long history of overweight starting early in life poses an additional risk.

The trajectory of weight and height from birth to adolescence is well known. The progression of body index (**BMI**) from adolescence into adulthood is less well described. Obese children have high likelihood of obesity in adulthood. Childhood obesity is associated with classic CVD risk factors as is adult obesity.

Given the current pandemic of obesity, it is important to determine whether elevated BMI in childhood, adolescence, or adulthood, or an increase in BMI during transition from adolescence to adulthood, contribute independently to risk of DM-2 and CHD in young adults.

The study used data from the Metabolic, Lifestyle, and Nutrition Assessment in Young Adults (MELANY) study of the Israeli Defense Force, which followed over 37 000 healthy young men whose BMI was measured in adolescence and in early adulthood, in order to identify incident cases of DM-2 and CHD.

STUDY

1. All males eligible for the Israeli army are examined at age 17. Height, weight and BMI are determined. All remaining in the army after age 25 are examined every 3 to 5 years.

2. This study included 37 674 male career army personnel. None had known DM-2 or CHD at baseline.

3. Follow-up and outcome:

    Participants were followed prospectively from the time of their first army examination at about 25 years of age.

    Measured height and weight and calculated BMI at age 17 (adolescence) were tracked retrospectively.

    Follow-up ended at the time of diagnosis of DM-2, CHD, death, or retirement from the service, or on December 31, 2007. Median follow-up was 17 years.

    The outcome definition for CHD was angiography proven stenosis of over 50% of at least one

coronary artery.

RESULTS

1. Characteristics of the study participants.

    Participants were dividend into deciles according to their BMI at age 17. Each decile included about 3700 men.

Cohort characteristics (means)	Decile 1	Decile 10
Adolescent measurements		
Age	17.1	17.1
BMI	17,3	27,6
Adult measurements.		
Age	30.0	30.0
BMI *	21,3	30.6
Change in BMIs	+4.0	+3.0
Systolic BP*	115	123
Fasting glucose*	89.9	93,6
Total cholesterol*	179.1	195.2
HDL-cholesterol**	48.3	43.6
LDL-cholesterol*	107.6	120.5
Triglycerides (Median)*	85	126

    (* Progressively increased between decile 1 and decile 10. **HDL progressively declined.)

2. With increasing deciles of adolescent BMI, the percentage of current smokers increased; the mean duration of physical exercise per week decreased. The prevalence of family history of CHD and diabetes also increased across BMI deciles.

3. BMI and incidence of disease:

    Diabetes:

        During a mean of 17+ years, 1173 cases of DM-2 were diagnosed between ages 25 and 45. (Young adulthood). After adjustment for age, presence or absence of family history of diabetes, BP, physical activity, and glucose levels, adolescent BMI was predictive of incident diabetes, with a significantly increased risk observed in those who at age 17 had the three highest BMI deciles (22.8. 24.1 and 27.6) Hazard ratio of the highest 3 deciles vs the lowest decile was 2.76. The risk of diabetes increased by 9.8% for each 1 BMI unit.

    CHD:

During 17 years of and 327 cases of angiographic-proven CHD occurred.

The risk of CHD increased by 12% for each 1 BMI unit increase in BMI inadolescence.

4. Trajectory of BMI:

The mean annual increase in BMI was 0.3 BMI units between age 17 and age 30, and 0.2 BMI units thereafter.

Only BMI in adulthood was significantly associated with risk of diabetes.

In contrast, both BMI in adolescence and adulthood were significantly and independently associated with risk for CHD. Adolescent BMI remained a risk factor for CHD that was independent of adult BMI.

(This may be confusing. If an adolescent who had a high BMI gradually lost weight when he became an adult and his BMI reached lower levels, his risk of DM-2 would become much less. If an adolescent who had a low BMI gained weight in adulthood, his risk of DM-2 would became high. For CHD, even if an adolescent with a high BMI lost weight and reached a low BMI in adulthood, his risk for CHD would remain higher. Ed.)

DISCUSSION

1. This large-scale, long-term follow-up study strongly suggests that elevated BMI in adolescence has distinct relationships with DM-2 and CHD in young adulthood.

2. Diabetes is influenced mainly by recent BMI in adulthood and weight gain whereas, for CHD, both elevated BMI in adolescence and recent BMI in adulthood are independent risk factors. The natural history of CHD (in contrast with that of diabetes) is probably the consequence of gradual increasing atherosclerosis during adolescence and early adulthood that leads to clinically important disease in midlife.

3. It is noteworthy that these conclusions were deduced with BMI values that are well within the range of normal. Adolescent BMI corresponding with the CDC growth charts at the percentile of 49 was already associated with increased risk of CHD.

4. These conclusions highlight the clinical importance of considering BMI history when assessing the risk of CHD vs the risk of diabetes in overweight or obese young men.

5. In terms of public health, the study supports concerns about the associations between increasing cardio-metabolic morbidity in early adulthood and the increase in BMI in adolescence The findings may suggest specific age-related considerations for the design of diabetes prevention programs are distinct from those needed for prevention of CHD.

6. Being placed in the lower deciles for BMI during adolescence may be associated with having a lower risk of CHD or DM-2 in early adulthood.

7. The exclusion of women precludes the ability to determine sex-based differences in the relation between BMI and risk of disease.

8 An elevated BMI in adolescence predicts CHD in early adulthood independently of the BMI in adulthood.The upper decile of adolescents BMI is related to seven times the risk of CHD in the lowest decile. *(This is because almost all adolescents with a high BMI retained their high BMI into adulthood. Ed.)*

   Risk is increased even in adolescents who are considered, in population surveys, to be within normal limits. Thus obesity in adolescence is probably only the tip of the iceberg that is relevant to approximately 50% of adolescent boys.

9. Remarkably, for DM-2, a significantly elevated hazard ratio was observed only in the 80th percentile of adolescent BMIs and higher (over 22.4), translating into a risk of diabetes that is nearly 3 times as high as that of those whose adolescent BMI is in the lowest decile. .

10. Adjustment for BMI in adulthood completely attenuated this effect, suggesting that BMI in adolescence has a more reversible or shorter term effect on risk of diabetes compared with the risk of CHD.

11. These results may be explained by the fact that diabetes represents a more functional patho-mechanism than CHD, which relies on anatomical changes (atherosclerosis). Even clinically established diabetes is readily reversible in response to changes in lifestyle interventions, whereas atherosclerosis is responsive to diet interventions only if the intervention takes place before the "clinical horizon" of the disease is reached.

CONCLUSION

   Higher BMI in adolescence is an independent predictor of CHD in young adulthood even when it is well within what is now defined as the normal range of BMI (23 to 25).

   Atherosclerosis begins at an early age,

   Incident diabetes was mainly due to high BMI in adulthood.

   What constitutes "normal" or "healthy" BMI in adolescence may have to be redefined.

NEJM April 7, 2011; 364: 1315-25 Original investigation, first author Amir Tirosh,, Brigham and Women's Hospital and Harvard Medical School, Boston Mass.

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"There Are Few Healthcare Interventions More Impactful Than Helping Smokers Quit"

4-2 SMOKING CESSATION INTERVENTIONS: A Primer for Physicians

About 1 in 5 Americans still smoke. Half of all smokers will die prematurely (*On average about 7 years compared with non-smokers. Ed.)* Most smokers want to quit. Many try on their own. Without help, success rate is low--less than 10%.

There are few, if any, healthcare interventions more impactful than helping smokers quit.

What works?

There has been steady progress in identifying effective interventions. The most effective includes both counseling and pharmacotherapy. Although brief counseling by physicians can lead to a small increase in quitting, professional smoke-cessation counselors likely produce greater success.

All counselors should follow the 5 A's:

    1) Ask abut tobacco use

    2) Advise cessation

    3) Assess willingness to quit

    4) Assist in quitting attempts

    5) Arrange follow-up

There are 3 classes of first-line drugs available to help smokers quit: 1) Nicotine replacement therapy (**NRT**), 2) Sustained-release bupropion, and 3) Varenicline (*Chantix*)

1) Nicotine replacement: Now available in several forms: gum, lozenges, patches, and nasal and oral inhalers. They deliver nicotine in various fashions. The patch delivers nicotine long-term. Gum, lozenges, and inhalers deliver a short-term "hit" and are better used to treat acute withdrawal symptoms and nicotine craving. Safety: there was concern that nicotine would worsen symptoms of vascular insufficiency. However, studies have demonstrated safety in this regard, including studies on hospitalized patients. NRT is generally avoided during pregnancy, in the presence of serious arrhythmias, and within 2 weeks of onset of unstable angina and myocardial infarction.

2) Bupropion: Sustained-release bupropion is an atypical antidepressant. Like NRT, it is proven to increase quit-rates. It is begun while patients are still smoking with a designated quit date 2 weeks off. Treatment duration is usually 7 to 12 weeks. It lowers seizure thresholds and is contraindicated in patients with seizures. Reports of development of neuro-psychiatric symptoms require patients to be monitored frequently. On average, quit rates of about 20% can be expected.

3) Varenicline: Long-term quit rates of 20% have been reported. The drug is started while the patient

continues to smoke--before the target quit date (**TQD**). A study in this issue of Archives[1] suggested one-month pre-cessation duration. It reported increased quit-rates. Duration of treatment is usually 12 weeks.

4) New approaches:

Historically only one drug was used at one time. Now combined therapy has been demonstrated to be more effective than monotherapy.

Combinations that may be more effective than monotherapy

Nicotine patch + nicotine gum, nasal spray or oral inhaler

Nicotine patch + nicotine lozenges

Nicotine oral inhaler + ad libitum bupropion

Combined varenicline + NRT is not recommended because of increased risk of adverse effects.

Nicotine: The standard dose of available patches is 21 mg/day or less. This may not be enough to prevent withdrawal symptoms in heavy smokers. Higher doses may be considered, the patch dose approximating the daily nicotine dose of the smoker. Another approach to NRT is to extend treatment beyond 14 weeks, treating nicotine addiction as a chronic disease.

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The A,B,C,Ds Of Drug Treatment For Hypertension

4-3 ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS IN HYPERTENSION

First-line antihypertension drugs are classified as A,B,C,D. Drugs classified as A include angiotensin converting enzyme inhibitors (**ACE**) and angiotensin II receptor blockers (**ARB**). B drugs are beta-blockers (**BB**); C are calcium antagonists; D are diuretics. A,B,C,D is a helpful mnemonic to use in initial treatment as well as adding a second drug when needed. It is used in UK guidelines to manage hypertension in primary care.

Beta blockers have fallen out of favor as single agents for treatment of hypertension when the BP is the only problem. This leaves A, C, and D as the main drugs to start treatment.

Patients with normal or raised plasma renin levels (eg, many young adults with essential hypertension) do better with A drugs. Those with low renin levels (patients of African descent and older patients) respond well to C and D.

This article focused on use of ACE and ARB when starting treatment.

ACE and ARB relax blood vessels and promote excretion of sodium, reduce cardiac preload and afterload, and lower BP especially in patients in whom the renin-angiotensin-aldosterone system is activated.

How do ACE and ARB compare with other antihypertensive drugs?

A drugs are more effective as first line therapy in younger white patients (< age 55). C and D are preferred in older patients and Africans in whom low renin hypertension is more common. D are more effective in preventing heart failure in patents with hypertension. This supports the use of D in older patients with hypertension who are at greater risk for heart failure.

If initiating treatment with a C or D drug, and a second drug is needed, add an A drug.[1]

If treatment was started with an A drug, add a C or D drug.

If 3 drugs are needed, use A, C, and D .

B drugs are no longer preferred as first line therapy because in head-to-head comparisons they (notably atenolol) performed less well than A, C, or D in preventing cardiovascular events at doses that cause similar effects on BP. B drugs should be reserved for patients for whom there is a separate indication in addition to hypertension.

ARB are useful when ACE causes disturbing cough. ARB are also effective alternatives to ACE for heart failure and diabetic nephropathy.

1 *I believe many primary care clinicians would add a C or D drug instead of an A drug. ACE require more follow-up and cause more adverse effects. ARB are more expensive. In any case, the effect of drugs is easily gauged by the BP response, which is easily determined after a week or two. Ed/*

How well do ACE and ARB work?

ACE and C and D drugs, in doses that have similar BP lowering effects reduce cardiovascular (**CVD**) risks in patients with hypertension to a similar extent.

An ALLHAT randomized trial compared ACE with amlodipine (a C drug) and chlorthalidone (a D drug). There were no significant differences in CVD endpoints or all cause mortality. Other evidence supports the view that ACE reduce CVD events commensurate with their effect on BP. Regression of left ventricular hypertrophy is greater during use of ACE or ARB than with other drugs.

Other indications for ACE include treatment of HF and ventricular dysfunction after a myocardial infarction. And in slowing renal dysfunction in patients with diabetes and other forms of nephropathy.

In general, ARB have similar effects for these indications, but are more costly. ACE have a more robust evidence base than ARB for hypertension. ACE reduce CVD morbidity and mortality (including stroke) compared with placebo in treatment of hypertension. But for ethical and historical reasons, placebo controlled outcomes are not available for ARBs.

Management of hypertension often requires adding a second drug (either a C or D). BB are less effective in combination with an ACE.

Use of more than one drug is especially important in patients with high CVD risk for whom a target systolic of 130 is recommended (eg, concomitant diabetes complications, impaired renal function, and symptomatic atherosclerotic disease). A target of 140 is otherwise appropriate and is realistic if adherence is good.

Response to ACE and ARB depends on renin activity, which is strongly influenced by volume status. This underlies the importance of salt restriction and explains why adding diuretics to A drugs is highly effective.

A conservative estimate stated that for every 100 patients with hypertension treated over 10 years, 2 CVD events would be avoided. In real life, attention to other risk factors will reduce the number needed to treat (**NNT**) to benefit one patient. Poor compliance will increase the NNT.

Combination treatment with ACE and ARB

Differences in the pharmacology of the 2 drugs led to the hypothesis that the combination would confer additional benefit over increasing the dose of either one. A more recent large randomized trial (2008) in patients at high risk of CVD events compared telmisartan (ARB) combined with ramipril (ACE) with both used separately. The 3 groups experienced the same reduction in CVD events, but the combined drugs produced more symptoms of hypotension and greater decline in renal function and need for dialysis. Another large trial reported more adverse events with the combination with no survival benefit compared with monotherapy. The evidence undermines combined use. Unless future data to the contrary emerges, the combination should not be used in clinical practice.

How safe are A drugs? (Adverse effects)

First dose hypotension: In a few people, BP can fall too much after the first dose. It is better to take the first dose just before going to bed. Take care when going to the bathroom.

This is probably more common with short acting ACE (captopril) which produce high peak plasma concentrations than long acting (ramipril; lisinopril).

Dry cough: The most common symptom in long term use (up to 30% in those using ACE in some studies, but much lower in others). About 4% stopped ramipril due to cough. It was also reported in 1% of ARB users (telmisartan). Switching to another ACE or to a ARB may reduce frequency of cough. Cough is twice as common in women. It may take several weeks to resolve. The cause of cough in not known. It may be due to accumulation of kinins, which stimulates afferent nerve fibers. Management is individualized. The cough may be mild and well tolerated. ARB may be a good substitute if the BP response to the ACE was satisfactory.

Renal failure: In patients with significant bilateral renal artery stenosis, ACE and ARB may lead to renal failure. Glomerular filtration in such patients critically depends on selective angiotensin II-mediated vasoconstriction of the efferent (rather the afferent) arteriole. When the action of angiotensin II is blocked, glomerular pressure and filtration decline. Monitoring serum creatinine levels over 2 weeks may be indicated. The process is reversible provided the drug is stopped promptly. Renal failure can also occur among patients taking A drugs if they have salt and volume depleting or are currently taking loop diuretics or NSAID drugs. ACE and ARB protect renal function and are not contraindicated simply because of rising creatinine concentrations. When they are used in patients with severe renal impairment (creatinine clearance < 30 mL/min), the UK recommends lower starting doses and careful monitoring creatinine and electrolytes (potassium).

Hyperkalemia: Is a potential hazard, especially in patients with renal impairment. Diabetic nephropathy is a special risk. Those taking NSAIDs, diuretics, and potassium sparing drugs are particularly at risk. Electrolytes and creatinine should be monitored regularly in these patients.

Urticaria and angioedema: Is possible due to accumulation of kinins. It is not common but can be serious, even life-threatening. It is less common with ARB.

Fetal injury: Both ACE and ARB are contraindicated in pregnancy. Fetal defects may occur. Use other drugs for fertile women.

What are the precautions when starting ACE or ARB?

Before starting, review the patient's drug history. Check for hypovolemia, renal dysfunction, and electrolyte imbalance. Has the patient been taking NSAIDs, potassium sparing diuretics, or potassium supplements? If so, either stop taking these drugs, or monitor carefully for potassium levels and creatinine.

Has the patient recently had diarrhea, nausea and vomiting? (Volume depletion) If so, delay treatment until symptoms subside to avoid first dose hypotension.

Has the patient a history of angioedema? (Bradykinin is implicated in hereditary angioedema.)

Start treatment using a low dose with advice about first dose hypotension.

How cost-effective are ACE and ARB?

The joint committee (US) in 2004 recommended thiazide diuretics as initial treatment of hypertensions for most patients because they are more affordable and have similar efficacy.

The cost of ACE has come down since then. Lisinopril is now generic (*Available at some pharmacies for $4 for a month's supply, Ed*)

Drugs that inhibit the renin-angiotensin system (ACE and ARB) are likely to be the most cost effective drugs in patients under age 55..

ARBs are more expensive than ACE at present and are best reserved for patients who cannot tolerate ACE because of cough.

How are ACE and ARB taken and monitored?

After the first dose, ACE are usually taken in the morning. Ramipril at bedtime is an alternative. It has similar effects on daytime BP. Nighttime control of BP may be important because nighttime BP is more strongly correlated with CVD risk than mean daytime BP.

Several weeks after starting the drugs, check creatinine and electrolytes. (This is important, but often neglected.)

Increase the dose gradually over several months if target BP is not reached. Alternatively add a C or D drug.2[1]

Home BP monitoring is helpful in monitoring individual patients who are motivated, but not too introspective.[2]

Once the target BP is reached, follow with periodic check up visits to remind the patient about lifestyle changes, check on adherence, and symptoms of end organ damage.

1 *In general, I believe that increasing the dose of one drug will cause more adverse effects than adding a second drug. Ed.*

2 *Home BP monitoring is essential to good BP control. Ed.*

"Nothing About Me Without Me".

4-4 SUPPORTING PATIENTS TO MAKE THE BEST DECISIONS: Must be a Core Component of What if Means to be a Health Professional

"Imagine an intervention to improve patient care that systematic reviews have shown to be effective, does not seem to have any serious unwanted effectors, has been a central component of health policy for more than a decade, is popular with patients, and which in principle is embraced by most clinicians."

Such an intervention does exist.

It is shared decision making. This is a process in which patients are encouraged to participate in selecting appropriate treatment or management options on the basis of the best available evidence.

For many years, policy makers in the UK have advocated a stronger role for patients A defining mantra has become a central part of the current health reform: "Nothing about me without me".

In December 2010, a group of 58 international health leaders published the Salzburg statement on shared decision making, calling for a strong commitment to what they called "co-production of health".

The evidence in favor of shared decision making is reasonably strong, particularly when compared with that supporting most initiatives aimed at changing behavior. A systematic review, including the results of 55 randomized controlled trials conducted over the past 25 years, showed that patients involved in shared decision making are better informed than those who are not involved, and are less likely to be undecided about the best course of action at the end of the consultation. They are also more likely than the doctor to defer or decline surgical intervention, with no measurable adverse impact on health outcomes or satisfaction. Patients also seem more likely to adhere to treatment regimens and less likely to sue the doctor.

Given the evidence base and the sustaining support from policy makers, it is surprising that shared decision making is not yet a standard feature of clinical practice. Clinicians are often poor at eliciting the patient's agenda. One in three patients in primary care, and one in two patients in the hospital would have liked greater involvement in decisions about their care. There is clearly a gap between aspiration and reality. Why? The evidence cited in favor of shared decision making relates primarily to the effectiveness of a specific set of tools called decision aids. Clinicians find them difficult to use within the constraints of a routine consultation. And there is currently little evidence that they improve clinical outcomes for patients. Some clinicians are not convinced that the overall benefit to patients outweighs the effort required to change their established routine.

The explanation is probably more fundamental. Shared decision making is a concrete manifestation of a more substantial social process, a re-conceptualization of the roles and responsibilities of patients and health professionals This is challenging territory. Although clinicians are traditionally seen as the

dominant player in the consultation, the interaction is increasingly being framed as a meeting between two experts. The clinician brings an understanding of the effectiveness, benefits, and harms of specific actions. The patient brings an understanding of preferences and attitudes to illness and risk.

Shared decision making is deeply countercultural. It challenges the belief that professionals know what is best for the patient and that patients are not able to understand complex information and are not emotionally ready to make decisions. It also challenges the view of patients that the doctor is usually making the best decisions, an assumption that research increasingly shows is not accurate. It challenges the way in which the health system operates to deliver established patterns of practice, rather than being designed to encourage a different dynamic between patients and professionals.

Promoting shared decision making is increasingly seen as something that is needed to keep pace with changing social expectations.

The challenge for practitioners is to change attitudes and introduce new skills. Time and difficulty in access of high quality evidence are barriers.

Most fundamentally, the ability to share decisions must be seen as a core component of what it means to be a health professional.

The Goal Focuses On Quality Of Life And Symptom Management.
4-6 GLYCEMIC CONTROL IN FRAIL OLDER PATIENTS WITH DIABETES

More than 40% of adults with diabetes are older than 65. Many are frail with functional disabilities that limit their ability to live independently. Many live in nursing homes. Many are community-dwellers depending on others for care.

Large randomized trials examining the effects of glycemic control exclude elders. This has led to uncertainty regarding their appropriate level of glycemic control. Different guidelines recommend different targets. Guidelines generally agree on a target HbA1c of less than 7% for most adults. For frail older patients (**FOP**), The American Geriatric Society recommends a target less than 8%; the V.A. recommends 8% to 9%; the ADA recommends "less stringent glycemic control", not specifying the goals.

The appropriate glycemic target differs between FOPs and otherwise healthy younger patients.

The goal for younger patients is appropriately focused on decreasing devastating vascular compilations such as stroke and retinopathy. These complications are often the result of decades of poor glycemic control, suggesting that approximately 8 years of tight control is necessary before decreases in

vascular outcomes occur. However, most frail patients over age 65 with diabetes have competing risks for mortality that limit life expectancy to less than 8 years and make vascular outcomes less important. (The median life expectancy of nursing home residents is fewer than 2.5 years.) Most nursing home patients are unlikely to benefit from tight control.

In FOPs, tight control often leads to substantial burdens (dietary restrictions, insulin injections, finger sticks, polypharmacy, and hypoglycemia). Each of these complications leads to further complications. The goal of care for FOPs focuses on quality of life and symptom management. Many of the interventions required for tight control are not consistent with these goals. Tight glycemic control imposes immediate substantial burdens with little chance of benefit.

Moderate glycemic control, however, may provide important benefits (decreased symptomatic hyperglycemia, improved cognition, and possibly decreased incontinence). The level of glycemic control necessary to obtain these benefits appears to be substantially higher than the level required to minimize vascular risk in otherwise healthy younger patients.

Diabetes is associated with numerous geriatric syndromes common in FOPs (functional decline, falls, depression, and incontinence). The most appropriate glycemic target for FOPs depends on 2 factors: the degree of frailty and the outcomes that are most important for the patient. Older patients with diabetes span a broad spectrum in terms of their frailty and life expectancy. For healthy older persons with an extended life expectancy a glycemic target similar to that of younger patients may be most appropriate. For FOPs a less aggressive target would be more appropriate. Frailty and life expectancy can guide the initial determination of the most appropriate glycemic range for a given patient.

By considering an individual older patient's frailty, life expectancy, and the special outcomes most important to the individual, clinicians can provide patient-centered care that appropriately balances the burdens and benefits of glycemic control.

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