CVD Prevention Guidelines Update: Clinical Impact and Current Controversies

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Overview and Introduction to Changes in the CVD Guidelines

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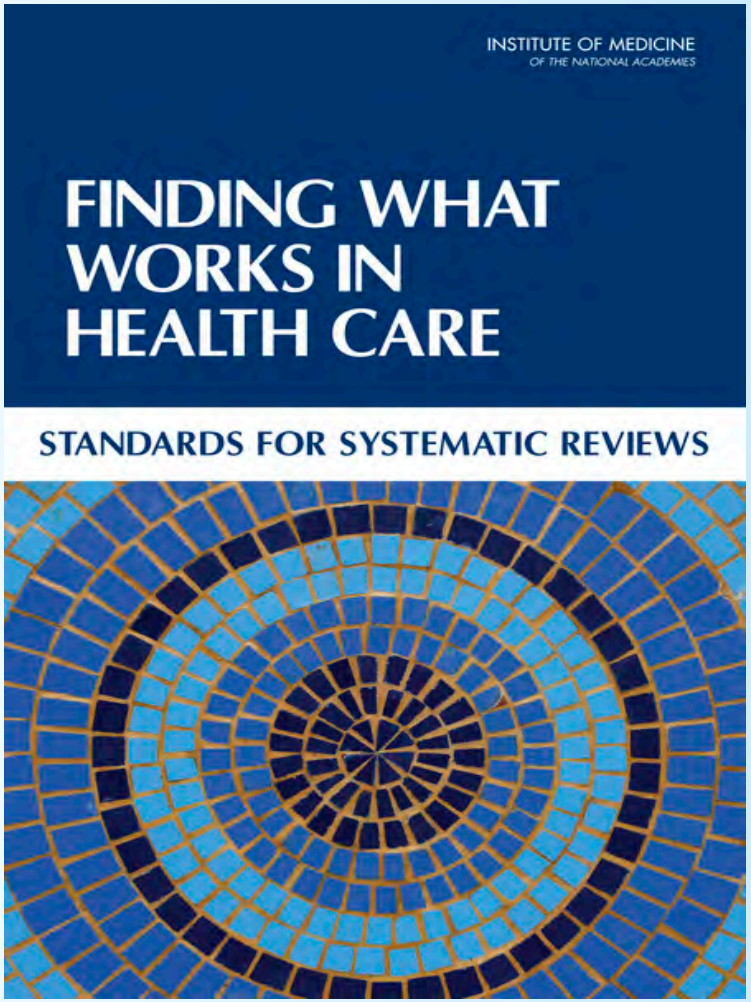
Institute of Medicine Report: Quality Chasm

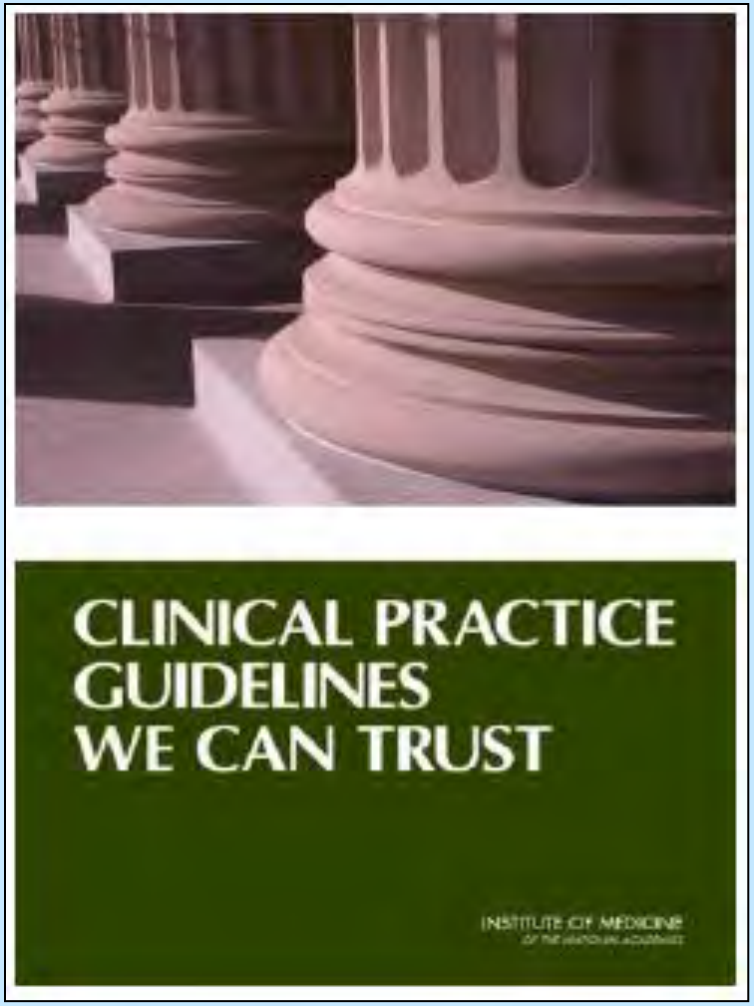
"In its **current form**, habits, and environment, American health care is **incapable** of providing the public with the **quality** health care it expects and deserves."

- **Design Rule 5:** *Current: Decision making is based on training and experience.* ***New: Decision making is based on evidence.*** Patients should receive care based on the best available scientific knowledge. Care should not vary illogically from clinician to clinician or from place to place.

Institute of Medicine, Crossing the Quality Chasm: A New Health System for the Twenty-first Century. 2001; Washington: National Academy Press.

The Landscape for Developing Clinical Practice Guidelines Has Changed





Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

Pierluigi Tricoci, MD, MHS, PhD
Joseph M. Allen, MA
Judith M. Kramer, MD, MS
Robert M. Califf, MD
Sidney C. Smith Jr, MD

Context The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care.

Objective To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence.

Data Sources and Study Selection Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division. Fifty-three guidelines on 22 topics, including a total of 7196 recommendations, were abstracted.

Data Extraction The number of recommendations and the distribution of classes of recommendation (I, II, and III) and levels of evidence (A, B, and C) were deter-

CLINICAL PRACTICE GUIDELINES are systematically developed statements to assist practitioners with decisions about appropriate health care for specific patients' circumstances.[1] Guidelines are often assumed to be the

Tricoci et al. JAMA. 2009;301:831-41.

ACC/AHA Practice Guidelines: COR and LOE

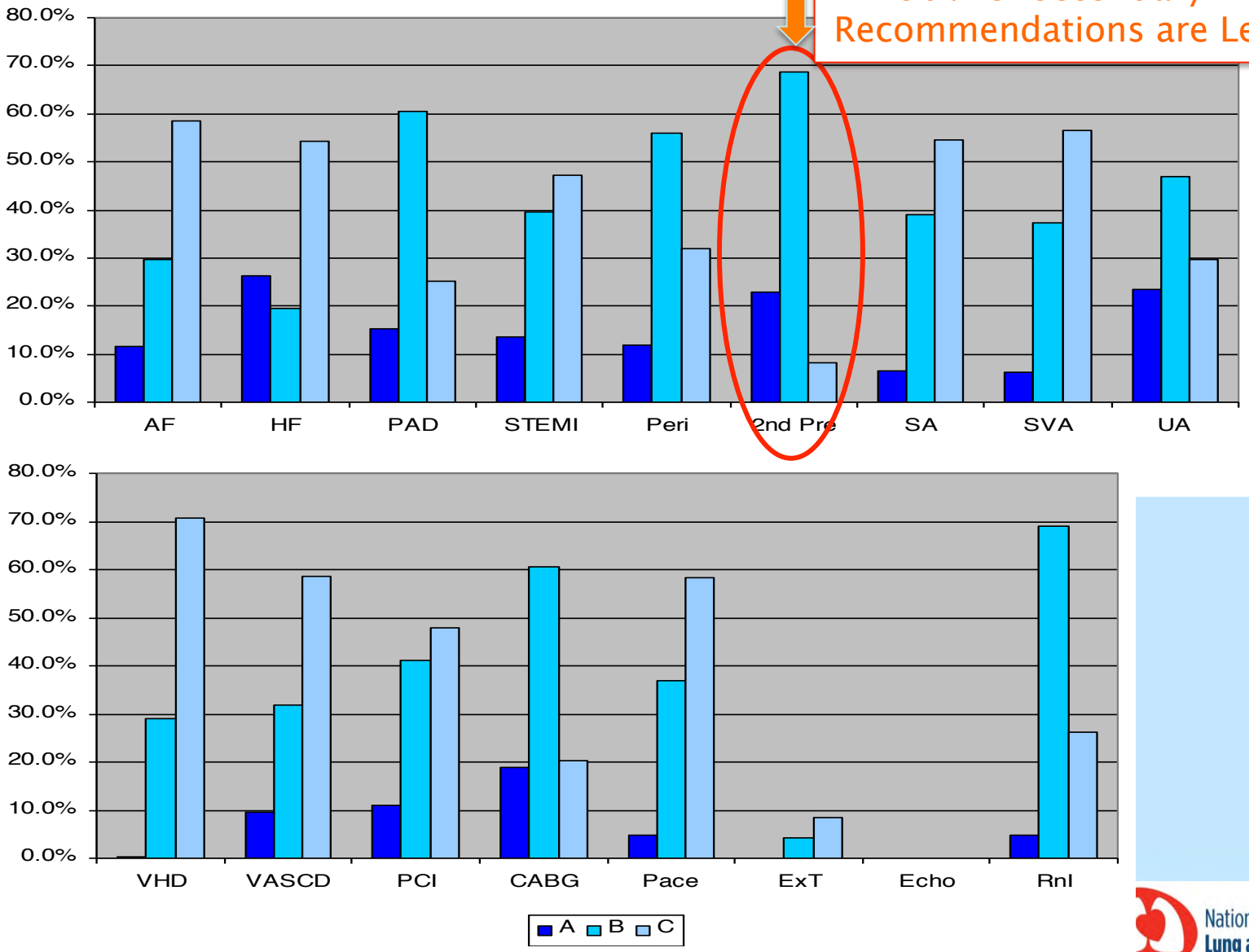
SIZE OF TREATMENT EFFECT →

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *Risk ≥ Benefit* *No additional studies needed* Procedure/Treatment should **NOT** be performed/administered **SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
LEVEL A Multiple (3-5) population risk strata evaluated* General consistency of direction and magnitude of effect	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited (2-3) population risk strata evaluated*	■ Recommendation that procedure or treatment is useful/effective ■ Limited evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Limited evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited (1-2) population risk strata evaluated*	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard-of-care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard-of-care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard-of-care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard-of-care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

Level of Evidence in Current Guidelines

> 90 % of Secondary Prevention Recommendations are Level A or B



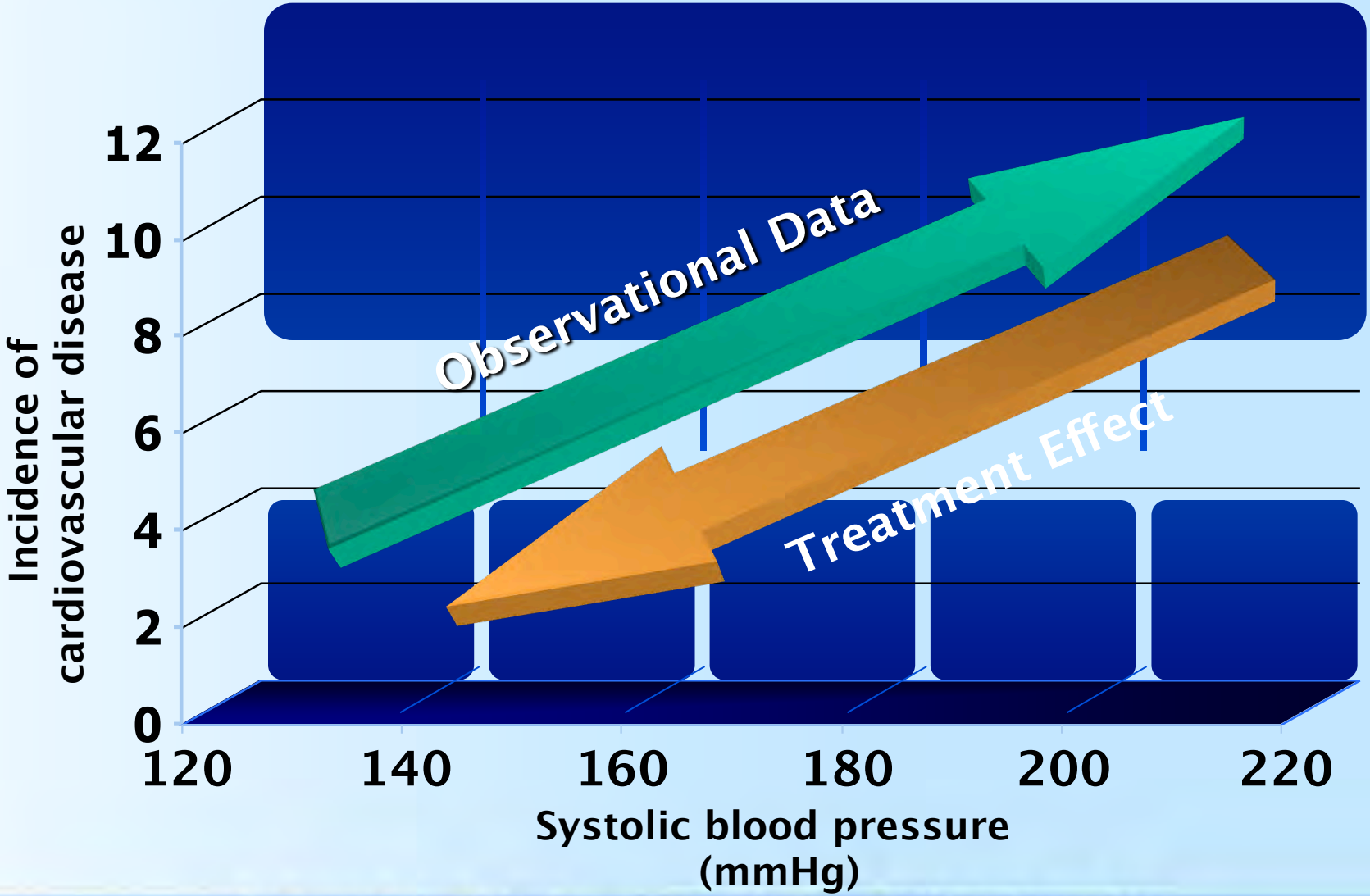
Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines; Tricoci et al.;*JAMA*.2009; 301: 831–841.

National Heart Lung and Blood Institute

Patient Groups Where RCT Guideline Evidence Is Frequently Lacking

- Women
- Elderly
- Racial/Ethnic Groups
- Multiple Co-Morbidities
- Procedure Related (Imaging, VHD, CHD)

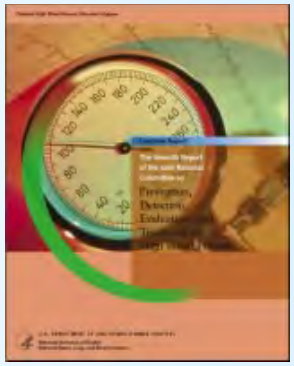
Does Hypertension Treatment Effect in RCTs Mirror Observational Data?



Development of Clinical Practice Guidelines Was a Key Role for NHLBI in Those Years

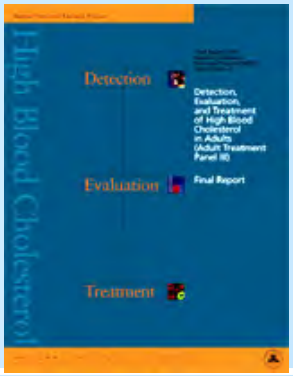
Joint National Committee on Prevention, Detection, Evaluation, & Treatment of High Blood Pressure (JNC)

- JNC 7: 2003
- JNC 6: 1997
- JNC 5: 1992
- JNC 4: 1988
- JNC 3: 1984
- JNC 2: 1980
- JNC 1: 1976



Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP, Adult Treatment Panel)

- ATP III Update: 2004
- ATP III: 2002
- ATP II: 1993
- ATP I: 1988



Clinical Guidelines on the Identification, Evaluation, & Treatment of Overweight and Obesity in Adults

- Obesity 1: 1998

Adult CVD Prevention Guidelines
Expert Panels and Work Groups

BP Panel
Evidence Review on BP Tx
3 CQs

Cholesterol Panel
Evidence Review on Cholesterol Tx
3 CQs

Obesity Panel
Evidence Review on Obesity
5 CQs (2 SRs)

Lifestyle WG
Evidence Review on Diet & Physical Activity
3 CQs (1 SR)

Risk Assessment WG
Evidence Review & Risk Prediction Model
2 CQs + model (1 SR)

Total of 16 CQs

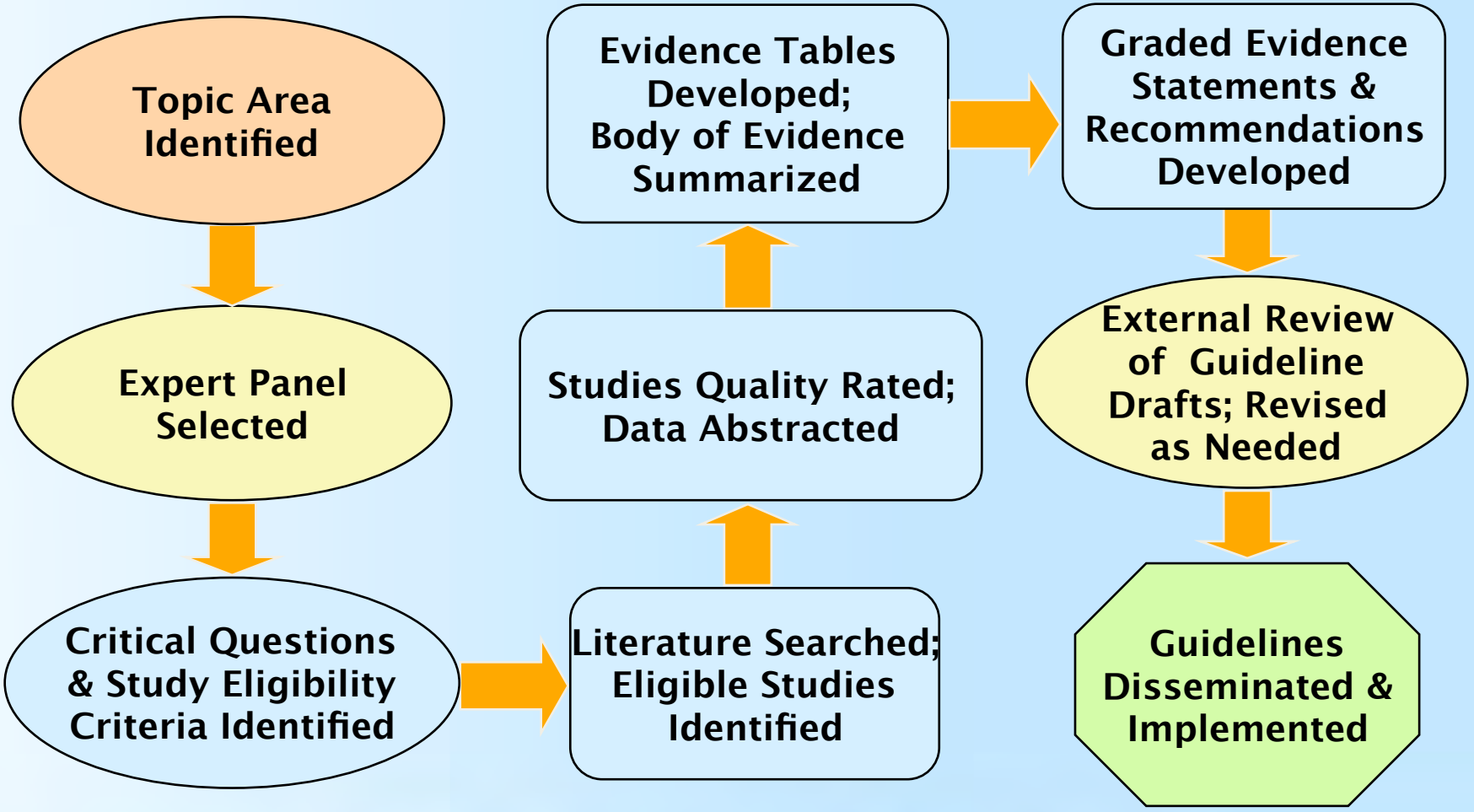
5 draft reports released for public comment and later integr

Implementation WG
Implementability Guidance (GLIA)
Implementation Science Review

How the Process Has Evolved

- Strictly evidence-based
- Focus only on randomized controlled trials assessing important health outcomes (no use of intermediate/surrogate measures)
- Every included study is rated for quality by two independent reviewers using standardized tools
- Evidence statements graded for quality using prespecified criteria
- Separate grading for recommendations by committee including cardiovascular specialists and primary care
- Independent methodology team to ensure objectivity of the review
- Initial set of recommendations focused on 3 key questions

Systematic Review and Guideline Development Process



Critical Questions and I/E Criteria

- Critical Question (CQ) in PICO format
  - **P**opulation
  - **I**ntervention/Exposure
  - **C**ontrol/Comparator
  - **O**utcomes
- Study Inclusion/Exclusion criteria for each CQ:
  - Types of studies (e.g., RCTs, epidemiology, systematic reviews)
  - Subgroups (e.g., elderly, diabetes, gender, race/ethnicity)
  - Specific outcomes (e.g., CVD mortality, MI, stroke, HF)

Evidence Quality Grading and Recommendation Strength

Evidence Quality for Each ES

- High
  - Well-designed and conducted RCTs
- Moderate
  - RCTs with minor limitations
  - Well-conducted observational studies
- Low
  - RCTs with major limitations
  - Observational studies with major limitations

Strength of Each Recommendation

- A – Strong
- B – Moderate
- C – Weak
- D – Against
- E – Expert Opinion
- N – No Recommendation

Refocusing the Agenda on Cardiovascular Guidelines:
An Announcement From the National Heart, Lung, and Blood Institute

Gary H. Gibbons, Susan B. Shurin, George A. Mensah and Michael S. Lauer

Gibbons et al. Circulation. **2013;128:1713-1715; originally published online June 19, 2013**

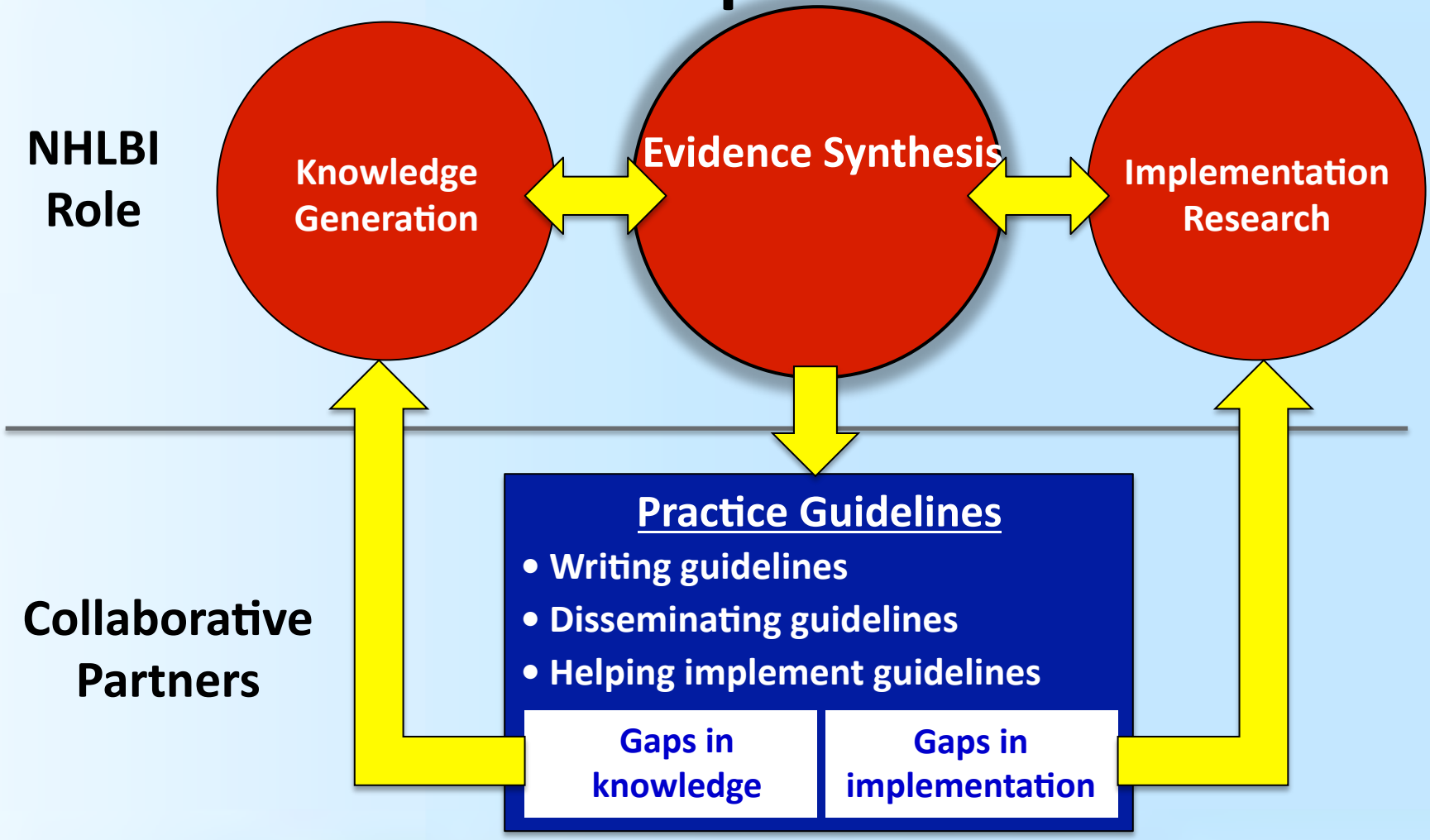
NHLBI/AHA/ACC Commentary: Next Steps in Developing Clinical Practice Guidelines for Prevention

Gary H. Gibbons, John Gordon Harold, Mariell Jessup,
Rose Marie Robertson, William J. Oetgen

Gibbons et al. Circulation. **2013;128:1716-7; originally published online October 8, 2013**

Both documents also published in JACC:
Gibbons et al. J Am Coll Cardiol. 2013 Oct 8;62:1396-8;
Gibbons et al. J Am Coll Cardiol. 2013 Oct 8;62:1399-40.

NHLBI Role in Research Evidence for Guideline Development



NHLBI and ACC/AHA Recommendation Mapping Table

NHLBI Strength of Recommendations Certainty of Benefit/Risk/Harm		ACC/AHA Classification of Recommendations Size of Treatment Effect	
A	**Strong recommendation** There is high certainty that the net benefit is substantial. Benefits are much greater than risks/harms.	I	**Benefit >>>Risk** Procedure/Treatment **SHOULD** be performed/administered
B	**Moderate recommendation** There is reasonable certainty that the net benefit is moderate to substantial or there is high certainty that the net benefit is moderate. Benefits are greater than risks/harms.	IIa	**Benefit >>Risk** Additional Studies with focused objectives needed **IT IS REASONABLE** to perform procedure/administer treatment
C	**Weak recommendation** There is at least moderate certainty that the net benefit is small. Benefits may slightly outweigh risks/harms.	IIb	**Benefit≥Risk** Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/Treatment **MAY BE CONSIDERED**
D	**Recommendation against** There is at least moderate certainty that it has no net benefit or that risks/harms outweigh benefits.	III (No Benefit or Harm)	No Benefit = Not Helpful – No Proven Treatment Harm = Excess Cost w/o Benefit or Harmful – Harmful to Patients
E	**Expert opinion** Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, or conflicting evidence, but the panel thought it was important to provide clinical guidance and make a recommendation. Further research is recommended.		Expert Opinion expressed as COR I, IIa, IIb or III with LOE B or C.
N	**No recommendation for or against** Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, or conflicting evidence, and the panel thought no recommendation should be made. Further research is recommended.	N/A	Discussed in Text

New Guidelines for CVD Prevention

- **I - Published / Endorsed by ACC/AHA & Others**
  - Risk Assessment
  - Lifestyle
  - Blood Cholesterol
  - Obesity
- **II - Published as Committee Report**
  - Hypertension

2013 ACC/AHA Lifestyle Management and ACC/AHA/TOS Obesity/Overweight Guidelines to Reduce Cardiovascular Risk

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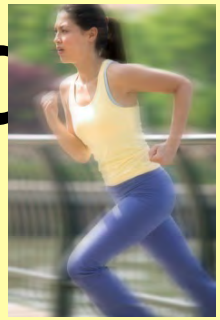
Aurora, Colorado

2013 ACC/AHA Lifestyle Guidelines to Reduce Cardiovascular Risk

Eckel et al. *JACC* 2014;63(25 Pt B):2960-84
Eckel et al. *Circulation* 2014;129(25 Suppl 2):S76-99

Charge of Lifestyle Workgroup

Lifestyle
Lifestyle
Reco  n  ons:

Evidence Review on Diet and Physical Activity (in the absence of weight loss) to be integrated with the recommendations of the Blood Cholesterol and

Lifestyle Workgroup Critical

Lifestyle Workgroup Critical

CQ1	patterns and/or macronutrient composition on CVD risk factors, when compared to no treatment or to other types of interventions?
CQ2	Among adults, what is the effect of dietary intake of sodium and potassium on CVD risk factors and outcomes, when compared to no treatment or to other types of interventions?
CQ3	Among adults, what is the effect of physical activity on blood pressure and lipids when compared to no treatment, or to other types of interventions?

Lifestyle Inclusion/Exclusion Criteria

≥

- With and without CVD risk factors/CVD
- Normal, overweight, obese
- Excluded weight change ±3%
- Excluded cross-sectional studies
- Used systematic reviews/meta-analyses in some cases
- Sample sizes
  - ≥
  - 500 (hard outcomes)
- Date range 1998–2009
  - Sodium extended to April 2012
  - Dietary fat and cholesterol accepted evidence back to 1990

Lifestyle Topics: Dietary Patterns

  - BP and Lipids
- DASH and DASH variations
  - BP and lipids, and in subpopulations
- High vs. Low Glycemic Diets
  - BP and Lipids

Dietary Fat, Cholesterol & Lipids

- Replacement of SFA with CHO, MUFA, or PUFA
- Replacement of CHO with MUFA or PUFA Replacement of *trans* fatty acids with CHO, MUFA, PUFA, or SFA
- Dietary Cholesterol

CHO=carbohydrate; MUFA=monounsaturated fat; PUFA=polyunsaturated fat

Lifestyle Topics: Sodium

- Sodium Reduction + DASH
- Sodium/ Other Minerals

CVD Outcomes

- Sodium Reduction – CVD events
- Sodium Intake – Stroke, CVD Risk
- Sodium Intake – Stroke, CVD Risk
- Sodium Intake – Heart Failure

Lifestyle Topics: Potassium

- Potassium intake – Stroke Risk
- Potassium intake – CHD/ CHF/ CVD mortality

Physical Activity
Physical Activity

- The *2008 Physical Activity Guidelines*
  - The *2008 Physical Activity Guidelines Advisory Committee Report* was used as the starting point for evidence review.
  - Additionally, a systematic search identified 8 meta-analyses from 2001 onwards and 5 systematic reviews rated fair to good that addressed this question and were included as the
identified 8 meta-analyses from 2001

Guidelines

Diet Pattern Recommendations for LDL-C and BP Lowering

Advise adults who would benefit from LDL-C or BP lowering to:

- Consume a dietary pattern that emphasizes
  - Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils and nuts; and limits intake of sweets, sugar-sweetened beverages, and red meat.

Strength of evidence: Strong IA

for LDL-C and BP Lowering

Advise adults who would benefit from LDL-C or BP lowering to:

calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes mellitus).

- Achieve this pattern by following plans such as the DASH dietary pattern, the USDA Food Pattern, or the AHA Diet.

Strength of evidence: Strong IA

Diet Pattern Recommendations for LDL-C Lowering

Advise adults who would benefit from LDL-C lowering to:

- Aim for a dietary pattern that achieves 5% to 6% of calories from saturated fat.
- Reduce percent of calories from saturated fat.
- Reduce percent of calories from *trans* fat.

Strength of evidence: Strong IA

- Aim for a dietary pattern that achieves 5% to 6% of calories from saturated fat.
- Reduce percent of calories from saturated fat.
- Reduce percent of calories from *trans* fat.

Strength of evidence: Strong IA

BP Lowering

Advise adults who would benefit from LDL-C or BP lowering to:

Strength of evidence – Strong I

- Consume no more than 2,400 mg of sodium/ day and that a further ↓ of sodium intake to 1,500 mg/day can result in even greater ↓ in BP.
  - Even without achieving these goals, ↓ sodium intake by at least 1,000 mg/ day ↓ BP. ***Strength – Moderate IIA***
- Combine the DASH dietary pattern with ↓

Physical Activity Guidelines: Physical Activity Guidelines:

- In general, advise adults to engage in aerobic physical activity to ↓ LDL-C and non-HDL-C
  - 3 to 4 sessions a week
  - lasting on average 40 min per session
    - involving moderate-to-vigorous intensity physical activity

Strength of evidence – Moderate IIA

What's New in Lifestyle?

-
  and structure
  - More depth, less breadth
- **More emphasis on dietary patterns**
- **More data provided to support**
  - **saturated and *trans* fat restriction**
  - **dietary salt restriction**
- Evidence to support dietary cholesterol restriction in those who could benefit from ↓ LDL–C is inadequate.

Overweight Guidelines to Reduce Cardiovascular Risk

Jensen et al. *Circulation* 2014;129(25 Suppl 2):S102-38

Critical Questions Selected

CQ1: Benefits of weight loss – Is weight loss good for you?

CQ1: Benefits of weight loss – Is weight loss good for you?

CQ2: Risks of overweight – How do you identify who is sufficiently at risk to mandate weight loss efforts?

CQ3: Diets for weight loss – What is the efficacy/effectiveness of the different dietary strategies?

CQ4: Comprehensive Lifestyle Intervention (Diet + efficacy/effectiveness of this approach in achieving and maintaining weight loss?

CQ5: Bariatric surgery – What are the benefits and risks of the various procedures?

Obesity Panel Recommendation #1

Obesity Panel Recommendation #1

Identifying patients who need to lose weight

Identifying patients who need to lose weight

- Continue to measure BMI as screening tool to identify patients at greater risk (keep current cut-points)
- Use waist circumference as additional screening tool for BMI 25-35; use NIH or WHO cut-points
- Inform patients about continuous relationships between BMI, waist circumference, and disease

Obesity Panel Recommendation

Obesity Panel Recommendation

Matching treatment benefits with risk profiles

Matching treatment benefits with risk profiles

- Inform patients with obesity-related hypertension, dyslipidemia, and hyperglycemia that lifestyle changes resulting in sustained weight loss of 3–5% produce clinically meaningful health benefits, and greater weight losses produce greater benefits.
  - Sustained weight loss of 3–5% is likely to result in clinically meaningful reductions in triglycerides, blood glucose, HbA1C, and the risk of developing type 2 diabetes.

dyslipidemia, and hyperglycemia that lifestyle changes
and the risk of developing type 2 diabetes.

improve LDL-C and HDL-C; reduce the need for

#3

loss and no superiority for any of the myriad diets reviewed.

- Prescribe a diet to achieve reduced caloric intake, as part of a

intervention.

considering the patient's preferences and health status and preferably refer to a nutrition professional for counseling.

Obesity Panel Recommendation #4

lose weight should receive a comprehensive program (diet, physical activity and behavior modification) of 6 months or longer.

- The gold standard is on-site, high-intensity (>14 sessions in 6 months) comprehensive intervention delivered in group or individual sessions by a trained interventionist and persisting for a year or more.

- Other approaches, i.e. web-based, telephonic may be used when patients can't access the gold standard, although the amount of weight loss on average may be less.

Obesity Panel Recommendation #5

Selecting Patients for Bariatric Surgical Treatment for Obesity

- Advise adults with a BMI ≥40 or ≥35 with obesity-related comorbidities who are motivated to lose weight and who have not responded to behavioral treatment ± pharmacotherapy with sufficient weight loss to achieve targeted health outcome goals that bariatric surgery is an option to improve health and offer referral to an experienced bariatric surgeon for consultation and evaluation.
- For individuals with a BMI <35, there is insufficient evidence to recommend for or against undergoing bariatric surgical procedures.
- Advise patients that choice of a specific bariatric surgical procedure may be affected by patient factors, i.e., age, severity of obesity, obesity-related comorbidities, other operative risk factors, risk of short- and long-term complications, behavioral and psychosocial factors, and patient tolerance for risk and provider factors (surgeon and facility).


Thank You!

AHA/ACC CVD Risk Assessment and Cholesterol Guidelines

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Guidelines as Easy as ABC….

Always encourage adherence to lifestyle (even if patient receives a statin)

Bring practice close to the RCT evidence:

No arbitrary fixed LDL-C or non HDL-C goals

Appropriate intensity of statins for higher ASCVD risk groups in whom statins shown to benefit:

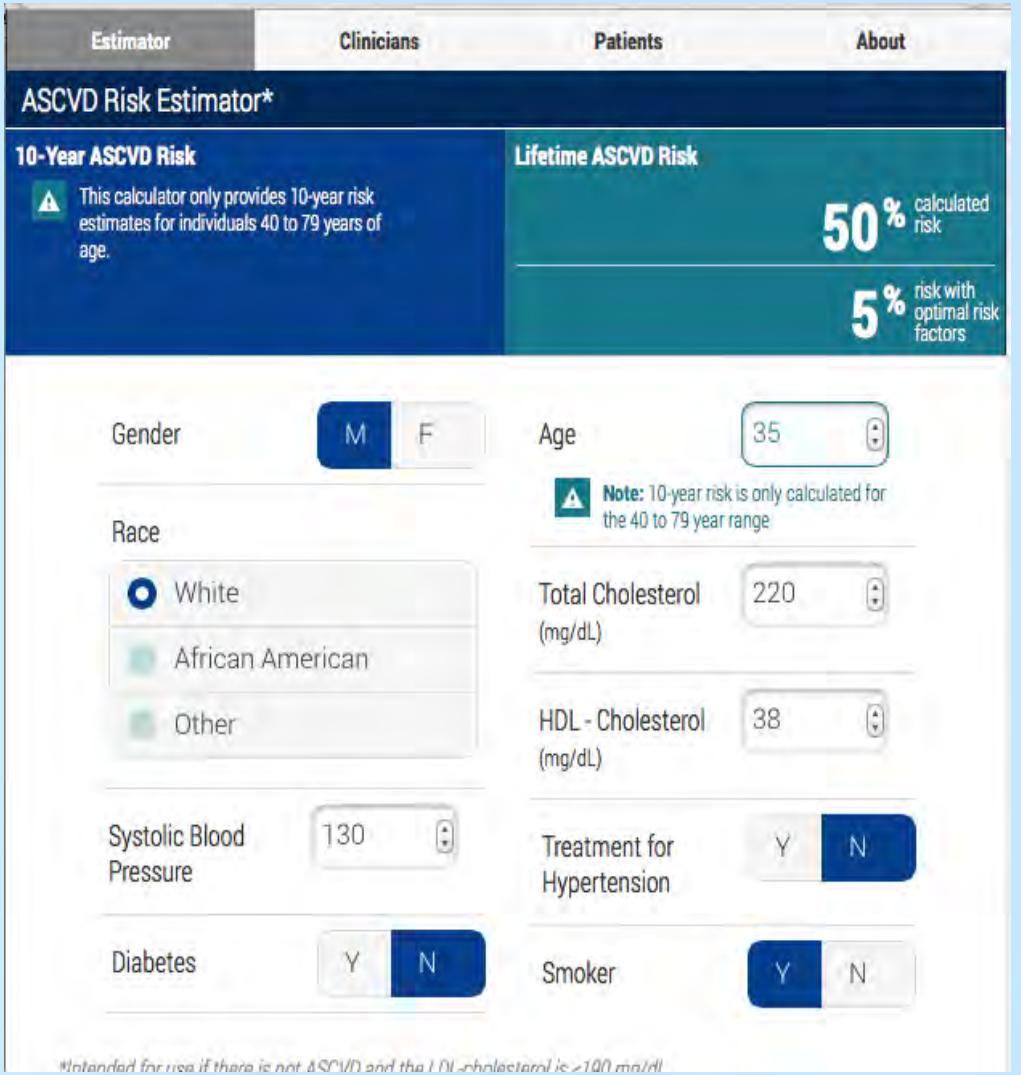
Secondary prevention, Primary LDL-C≥190 mg/dl; Diabetes 40-75 yrs

Choose Risk Estimator to estimate lifetime and 10-year risk with ASCVD risk estimator in primary prevention. It provides useful decision support. Not for those on treatment already.

Discuss attention to risk factor control, lifestyle, potential for benefit as well as adverse effects, drug-drug interactions and patient preference in a clinician-patient risk discussion. This precedes statin Rx in primary prevention. *Statin Rx not automatic.*

Always Encourage Adherence to Lifestyle; Use of Lifetime Risk Estimator:

- For those 20-59 years, it provides lifetime risk estimate
- This is intended to drive discussions of greater adherence to heart-healthy lifestyle
- Part of risk discussion



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Couldn't Find Evidence for or Against Arbitrary LDL-C or non HDL-C Goals

Major difficulties:

1. Current RCT data do not indicate what the targets should be
2. Unknown magnitude of additional ASCVD risk reduction with one target compared to another
3. Unknown rate of additional adverse effects from multidrug therapy used to achieve a specific goal
4. Therefore, unknown net benefit from treat-to-target approach
5. Reverse epidemiology not valid
6. Studies of plaque burden support no LDL-C target

Statin Benefit Groups

Secondary Prevention

Diabetes – 40 to 75 yrs
LDL-C 70-189 mg/dl

LDL-C ≥ 190 mg/dL

Rx: Optimal benefit with high intensity statins lower LDL-C ≥ 50%

Use moderate intensity if age >75 or can't tolerate high intensity

Primary Prevention –
40 to 75 yrs
LDL-C 70-189 mg/dl
ASCVD Risk ≥ 7.5 %

Rx: Moderate intensity
or high intensity statin

Statin Rx not automatic, requires clinician-patient discussion

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Accuracy of Statin Assignment Using the 2013 AHA/ACC Cholesterol Guideline Versus the 2001 NCEP ATP III Guideline

Correlation With Atherosclerotic Plaque Imaging

Kevin M. Johnson, MD,* David A. Dowe, MD†

ABSTRACT

BACKGROUND Accurate assignment of statin therapy is a major public health issue.

OBJECTIVES The American Heart Association and the American College of Cardiology released a new guideline on the assessment of cardiovascular risk (GACR) to replace the 2001 National Cholesterol Education Program (NCEP) Adult Treatment Panel III recommendations. The aim of this study was to determine which method more accurately assigns statins to patients with features of coronary imaging known to have predictive value for cardiovascular events and whether more patients would be assigned to statins under the new method.

METHODS The burden of coronary atherosclerosis on computed tomography angiography was measured in several ways on the basis of a 16-segment model. Whether to assign a given patient to statin therapy was compared between the NCEP and GACR guidelines.

Current Guidelines Identify Plaque Burden More Accurately

Population: 3,076 subjects; 65.3% men mean age 55; women 59; >90% white
At time of imaging 44% not on statins

Evaluated: Guideline on Assessment Cardiac Risk (GACR)

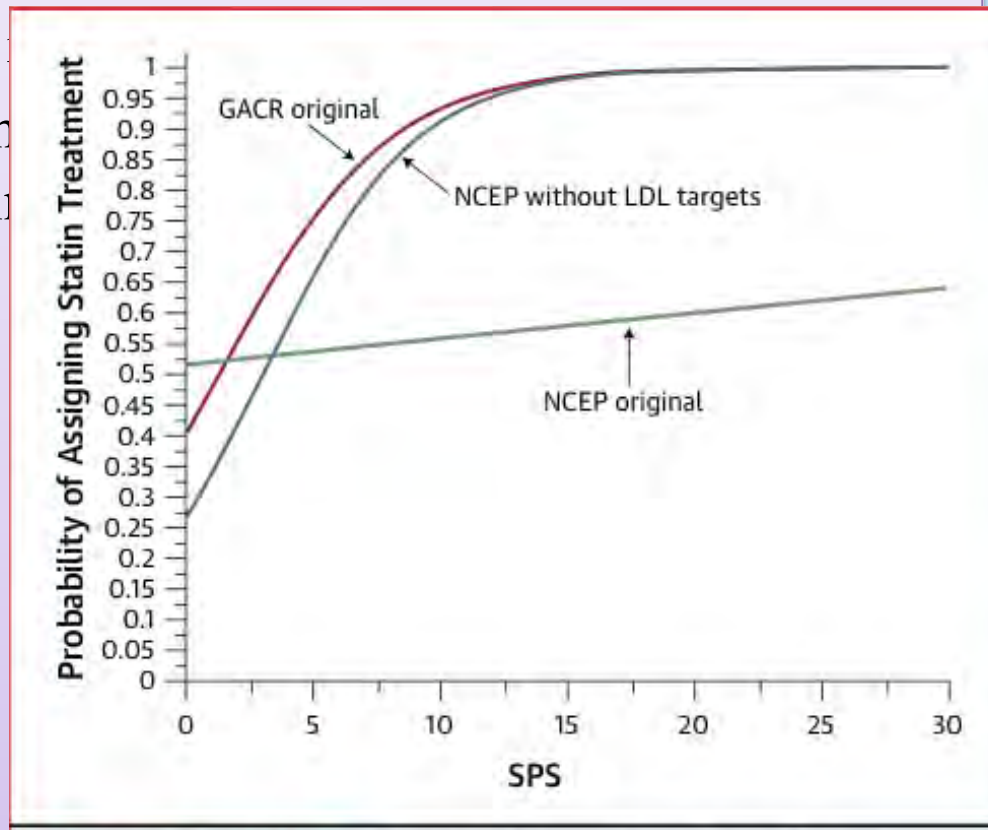
National Cholesterol Education Program ATP III (NCEP) Guideline

Probability of statin Rx rose sharply with

The GACR assigned fewer patients with

more patients with heavy plaque to stati

The correlation of serum LDL-C levels to various plaque levels is essentially zero. Targets degrade the accuracy of assignment of patients to statin therapy.



CENTRAL ILLUSTRATION Probability of Assigning Statin Therapy Versus Plaque Burden Under 2 Cardiovascular Risk Guidelines

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Appropriate intensity of statins for higher ASCVD risk groups in whom statins shown to benefit:

Secondary prevention, Primary LDL-C≥190 mg/dl; Diabetes 40-75 yrs

Choose Risk Estimator to estimate lifetime and 10 year risk with ASCVD risk estimator in primary prevention. It provides useful decision support. Not for those on treatment already.

Discuss attention to risk factor control, lifestyle, potential for benefit as well as adverse effects, drug-drug interactions and patient preference in a clinician-patient risk discussion. This precedes statin Rx in primary prevention. *Statin Rx not automatic.*

Initial Concerns Not Corroborated by REGARDS

The Claim: Pooled Cohort Equations overestimate ASCVD risk by 75-150%*

Claim based on analyses of Women's Health Study, Physician's Health Study, Women's Health Initiative Observational Study, but:

- These studies lacked active surveillance for ASCVD events (can lead to ~30% undercounting of events**)
- High prevalence of statin use in contemporary cohorts (particularly those at highest risk may cause the participants to 'underperform' in ASCVD event generation)
- Risk factor levels were self-reported in these studies
- The participants in these studies (esp. PHS) were not broadly representative of the US population

*Ridker and Cook. Lancet 2013; 382:1762-65.
**Hlatky et al. Circulation. Cardiovasc Qual Outcomes. 2014; 7:157-62.

Original Investigation

Validation of the Atherosclerotic Cardiovascular Disease Pooled Cohort Risk Equations

Paul Muntner, PhD; Lisandro D. Colantonio, MD; Mary Cushman, MD; David C. Goff Jr, MD, PhD; George Howard, DrPh; Virginia J. Howard, PhD; Brett Kissela, MD, MS; Emily B. Levitan, ScD; Donald M. Lloyd-Jones, MD, ScM; Monika M. Safford, MD

IMPORTANCE The American College of Cardiology/American Heart Ass
Pooled Cohort risk equations were developed to estimate atheroscler
disease (CVD) risk and guide statin initiation.

OBJECTIVE To assess calibration and discrimination of the Pooled Coh
contemporary US population.

DESIGN, SETTING, AND PARTICIPANTS Adults aged 45 to 79 years enrol
Geographic and Racial Differences in Stroke (REGARDS) study betwee
October 2007 and followed up through December 2010. We studied p
atherosclerotic CVD risk may trigger a discussion of statin initiation (th
atherosclerotic CVD or diabetes, low-density lipoprotein cholesterol le
189 mg/dL, and not taking statins; n = 10 997).

MAIN OUTCOMES AND MEASURES Predicted risk and observed adjudic
CVD incidence (nonfatal myocardial infarction, coronary heart disease
or fatal stroke) at 5 years because REGARDS participants have not bee
years. Additional analyses, limited to Medicare beneficiaries (n = 3333
atherosclerotic CVD events identified in Medicare claims data.

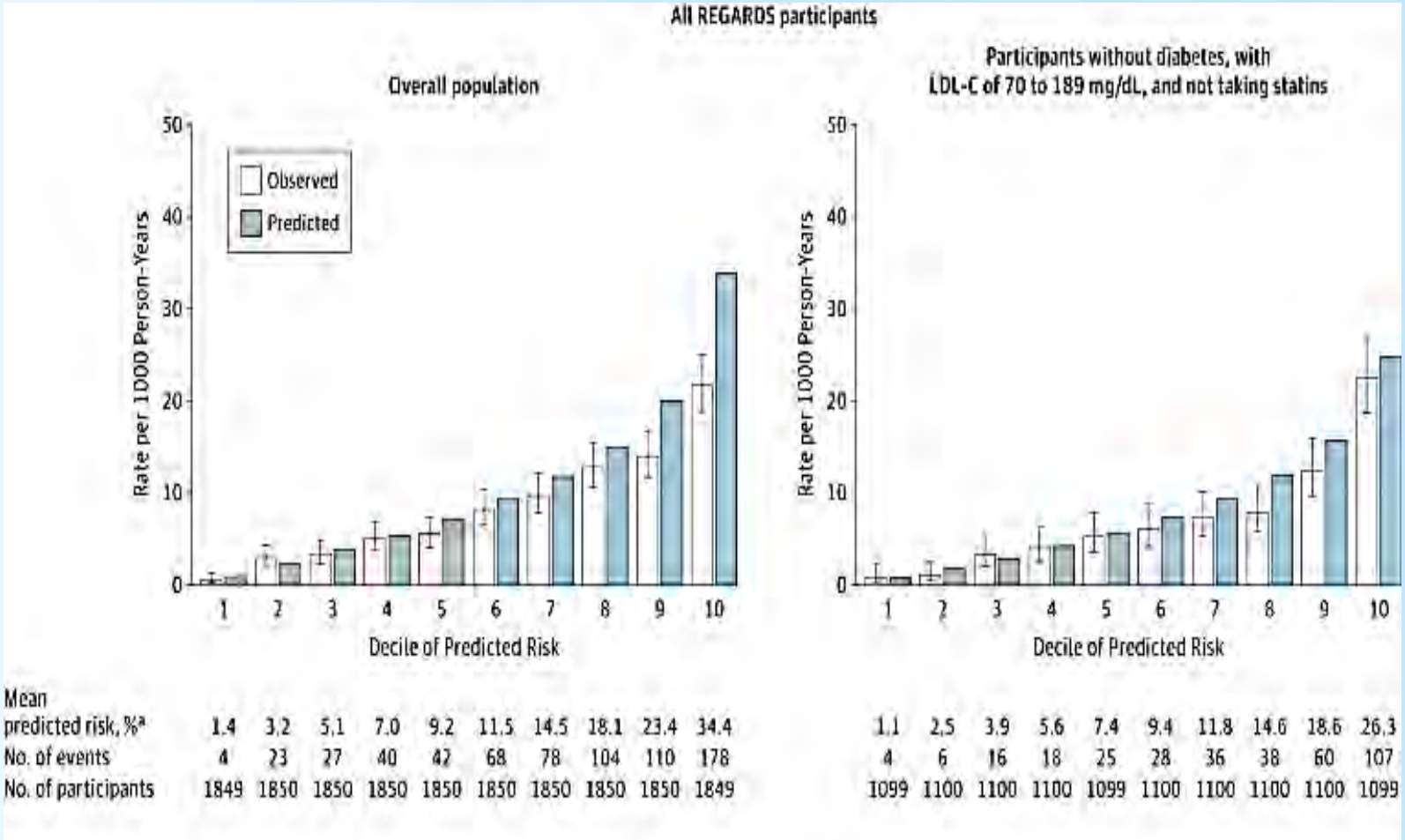
RESULTS There were 338 adjudicated events (192 CHD events, 146 str
and predicted 5-year atherosclerotic CVD incidence per 1000 person-
with a 10-year predicted atherosclerotic CVD risk of less than 5% was 1.9 (95% CI, 1.3-2.7) and
1.9, respectively, risk of 5% to less than 7.5% was 4.8 (95% CI, 3.4-6.7) and 4.8, risk of 7.5% to
less than 10% was 6.1 (95% CI, 4.4-8.6) and 6.9, and risk of 10% or greater was 12.0 (95% CI,
10.6-13.6) and 15.1 (Hosmer-Lemeshow χ^2 = 19.9, P = .01). The C index was 0.72 (95% CI,

In this cohort of US adults for whom statin initiation may be considered based on the ACC/AHA Pooled Cohort risk equations:

- observed and predicted 5-year atherosclerotic CVD risks were similar
- indicating that these risk equations were well calibrated in the population for which they were designed to be used
- demonstrated moderate to good discrimination.

Muntner et al. JAMA. 2014;311:1406-15.

Pooled Cohort Equations:
External Validation in ReGARDS Population



Mean predicted risk, %[a]	1.4	3.2	5.1	7.0	9.2	11.5	14.5	18.1	23.4	34.4
No. of events	4	23	27	40	42	68	78	104	110	178
No. of participants	1849	1850	1850	1850	1850	1850	1850	1850	1850	1849

	1.1	2.5	3.9	5.6	7.4	9.4	11.8	14.6	18.6	26.3
	4	6	16	18	25	28	36	38	60	107
	1099	1100	1100	1100	1099	1100	1100	1100	1100	1099

Muntner et al. JAMA. 2014;311:1406-15.

Pros/Cons of Risk Estimation

- All risk estimation has some error
- Mainly in the highest risk groups due to lack of event ascertainment/unknown prevention efforts
- Panel chose 7.5% cutoff based on data
  - Allows for some overestimation as benefit down to 5%
- Inclusion of stroke and having a separate equation for African-Americans are strong features of these guidelines

New Guidelines Efficiently Choose Additional Individuals to Get Statin Rx (Dallas Heart Study)

Table. Additional Statin Eligibility and ASCVD Event Rates Among Newly Statin Eligible Individuals

Outcome	Additional Statin Eligibility*	Event Rate Among Newly Statin Eligible	NNT Among Newly Statin Eligible†
Primary analysis			
ASCVD	4.8%	15.8%	14–21
CHD	4.8%	11.7%	19–29
ATPIII statin eligibility determined by optional cholesterol goals			
ASCVD	−2.8%	15.7%	14–21
CHD	−2.8%	12.4%	18–27
Restricting to individuals aged ≥40 years			
ASCVD	9.0%	15.8%	14–21
CHD	9.0%	11.6%	19–29

Paixao et al Circ Cardiovasc Qual Outcomes. 2014; pii: CIRCOUTCOMES.114.001139.

Guidelines as Easy as ABC….

Always encourage adherence to lifestyle (even if patient receives a statin)

Bring practice close to the RCT evidence:

No arbitrary fixed LDL-C or non HDL-C goals

Appropriate intensity of statins for higher ASCVD risk groups in whom statins shown to benefit:

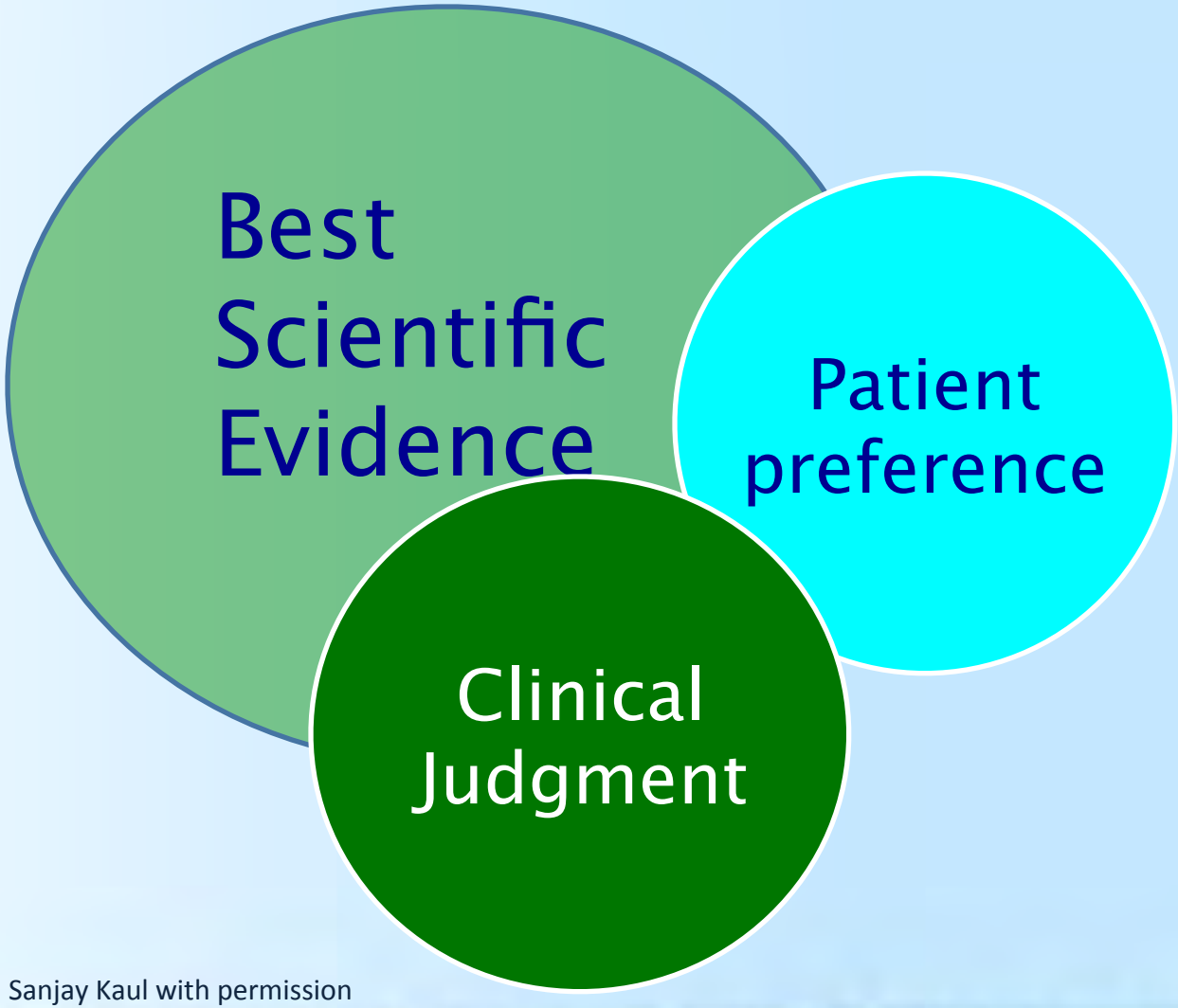
Secondary prevention, Primary LDL-C≥190 mg/dl; Diabetes 40-75 yrs

Choose Risk Estimator to estimate lifetime and 10 year risk with ASCVD risk estimator in primary prevention. It provides useful decision support. Not for those on treatment already.

Discuss attention to risk factor control, lifestyle, potential for benefit as well as adverse effects, drug-drug interactions and patient preference in a clinician-patient risk discussion. This precedes statin Rx in primary prevention.

Statin Rx not automatic.

Primary Prevention-
Risk Discussion Precedes Statin Prescription



Adapted from Dr. Sanjay Kaul with permission

Guidelines as Easy as ABC….

Evaluate additional factors that can inform the risk discussion. Factors chosen if they improve discrimination, calibration, and reclassification:

1. Family history of premature ASCVD
2. CAC score ≥ 300 or ≥75th%
3. hs-CRP ≥2.0 mg/L
4. ABI<0.9
5. May use a primary elevation of LDL-C ≥ 160 mg/dl in younger individuals to pick up those with familial hypercholesterolemia.
6. Use lifetime risk estimation in those 20-59 to enhance discussion of need for more optimal lifestyle to improve entire risk profile.

Follow-up needed to evaluate adherence to therapy, adequacy of treatment effect achieved with follow-up lipids/safety checks.

CAC= coronary artery calcium; ABI=ankle-brachial index

How Should We Manage Hypertension? 2014 - The Year of the Guidelines

George L. Bakris, MD, FAHA, FASN
Professor of Medicine
Director of the ASH Hypertension Center
The University of Chicago Medicine
Chicago, Illinois

2014 Expert Panel: Initial Question Areas Being Addressed

- (How low should you go)
- (When to initiate drug treatment)
- (How do we get there?)

2014 Expert Panel-RECOMMENDATIONS

- In the general black population initial antihypertensive treatment should include a thiazide-type diuretic or CCB

(Moderate recommendation-Grade B)

- In the general black population with diabetes initial antihypertensive treatment should include a thiazide-type diuretic or CCB

(Weak recommendation-Grade C)

- In the population 18-80 years of age with chronic kidney disease and hypertension initial (or add-on) antihypertensive treatment should include an ACE inhibitor or ARB to improve kidney outcomes

(Moderate Recommendation-Grade B)

- In the population with nondiabetic chronic kidney disease initiate pharmacological treatment at BP >140/90 mmHg and treat to <140/90 mmHg

(Expert Opinion-Grade E)

2014 Expert Panel- RECOMMENDATIONS

- In the population with diabetic chronic kidney disease initiate pharmacological treatment at BP >140/90 mmHg and treat to <140/90 mmHg

(Expert Opinion-Grade E)

- In the general, non-black population initial antihypertensive treatment should include a thiazide-type diuretic, CCB, ACEI or ARB

(Moderate recommendation-Grade B)

- In the general, non-black population with diabetes initial antihypertensive treatment should include a thiazide-type diuretic, CCB, ACEI or ARB

(Moderate recommendation-Grade B)

2014 Expert Panel-- RECOMMENDATIONS

- In the general population 60 years of age or older, initiate pharmacologic treatment to lower blood pressure at SBP >150 mmHg or DBP > 90 mmHg and treat to a goal of <150/90 mmHg

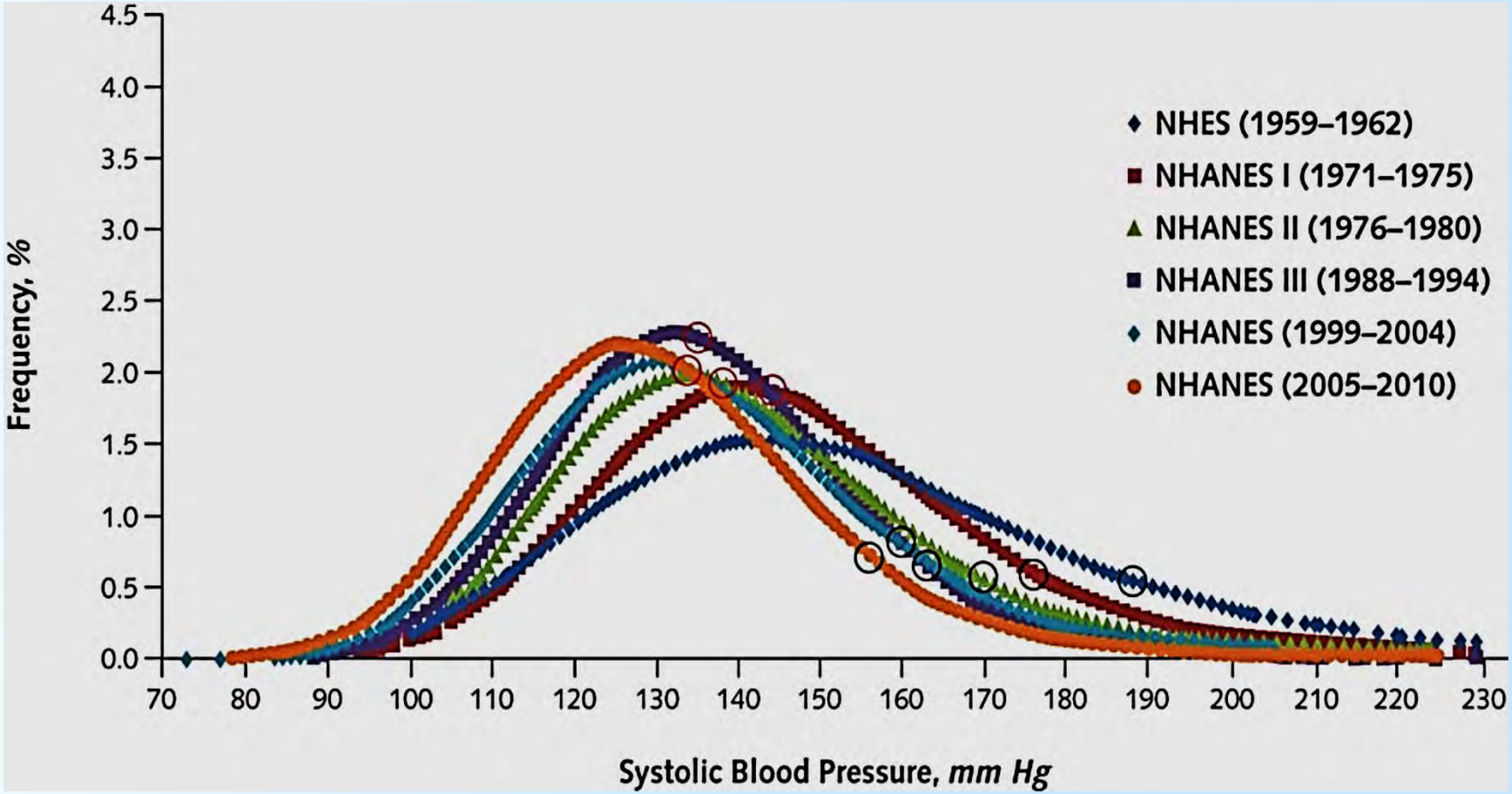
(Strong Recommendation-Grade A)

- In the general population under 60 years of age, initiate pharmacological treatment to lower BP at SBP > 140 mmHg and treat to goal < 140/90 mmHg

(Expert Opinion-Grade E)

Evidence Supporting a Systolic Blood Pressure Goal of Less Than 150mm Hg in Patients Aged 60 Years or Older:

The Minority View Systolic Blood Pressure Goal for Patients Aged 60 Years or Older



Smoothed weighted frequency distribution, median, and 90th percentile of systolic blood pressure for persons aged 60 to 74 y: United States, 1959–2010.

Reproduced from Lackland and colleagues (4). NHANES = National Health and Nutrition Examination Survey; NHES = National Health Examination Survey.

Wright et.al. Ann Intern Med. 2014;160:499-503. doi:10.7326/M13-2981

2014 Hypertension Recommendations From the Eighth Joint National Committee Panel Members Raise Concerns for Elderly Black and Female Populations

Krakoff et.al. DOI: 10.1016/j.JACC.2014.06.014

2013 BP Guideline Goals for Diabetes

<140/90 mmHg

- KDIGO/KDOQI
- NICE
- Latin Am. Consortium for Diabetes Management
- 2014 Expert Panel

<140/85 mmHg

- ESH/ESC

<140/80 mmHg

- American Diabetes Association

BP Level and Kidney Disease

- <140/90 mmHg

Blood Pressure Targets in Chronic Kidney Disease: Proteinuria as an Effect Modifier

Blood Pressure Targets in Chronic Kidney

- 3 RCTs (8 reports) with a total of 2272 participants
  - 3 RCTs (8 reports) with a total of 2272

Study

- **AASK** (African American Study of Kidney Disease and Hypertension) Trial
- **REIN-2** (Ramipril Efficacy in Nephropathy 2) trial

Upadhyay

Categories	NICE* 2011	ESH/ESC 2013	ASH / ISH 2014	AHA/ACC/CDC 2013	2014 Expert Panel
Definition of Hypertension	**≥140/90 and daytime ABPM (or home BP) ≥135/85**	**≥140/90**	**≥140/90**	**≥140/90**	Not addressed
Drug therapy/ low risk patients after non-pharm treatment	≥160/100 or day-time ABPM ≥ 150/95	≥140/90	≥140/90	≥140/90	< 60 y. ≥140/90 ≥ 60 y. ≥150/90
β-blockers - first line drug	**No**	Yes	**No**	**No**	**No**
Diuretic	Chlorthalidone - indapamide	thiazides chlorthalidone, indapamide	thiazides chlorthalidone, indapamide	thiazides	thiazides chlorthalidone, indapamide
Initial single pill combo Rx	Not mentioned	markedly elevated BP	**≥160/100**	**≥160/100**	**≥160/100**
BP targets	**< 140/90 ≥ 80 y. < 150/90**	**<140/90 ; < 80, SBP 140-150 SBP <140 in fit patients Elderly ≥ 80 y. SBP 140-150**	**<140/90 ≥ 80 y. < 150/90**	**<140/90 Lower targets may be appropriate in some patients, including the elderly**	**< 60 y. <140/90 ≥ 60 y. <150/90**
BP target in Diabetes	Not addressed	**< 140/85**	**<140/90**	**<140/90 -Consider Lower targets**	**<140 /90**

Summary

- These are guidelines, NOT edicts or “stone tablets (Moses)” or laws, so there should be license to discuss research insights and clinical data that may be useful in the future.
- Topics covered in 2014 Expert Panel report were covered in JNC 7 and the biases, if anything, made the standard tougher not easier in JNC 7.
- The major changes from JNC 7 were **higher levels for BP goal for diabetes and CKD** that weren’t defensible in JNC 7 and higher levels of BP for older people that are also questionable.
- All other international guidelines agree with the Expert Panel overall except for the older person goal.

CVD Prevention Guidelines Update: Clinical Impact and Current Controversies

Diabetes Guidelines

Jay S. Skyler, MD, MACP
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University of Miami Miller School of Medicine
Deputy Director for Clinical & Academic Programs
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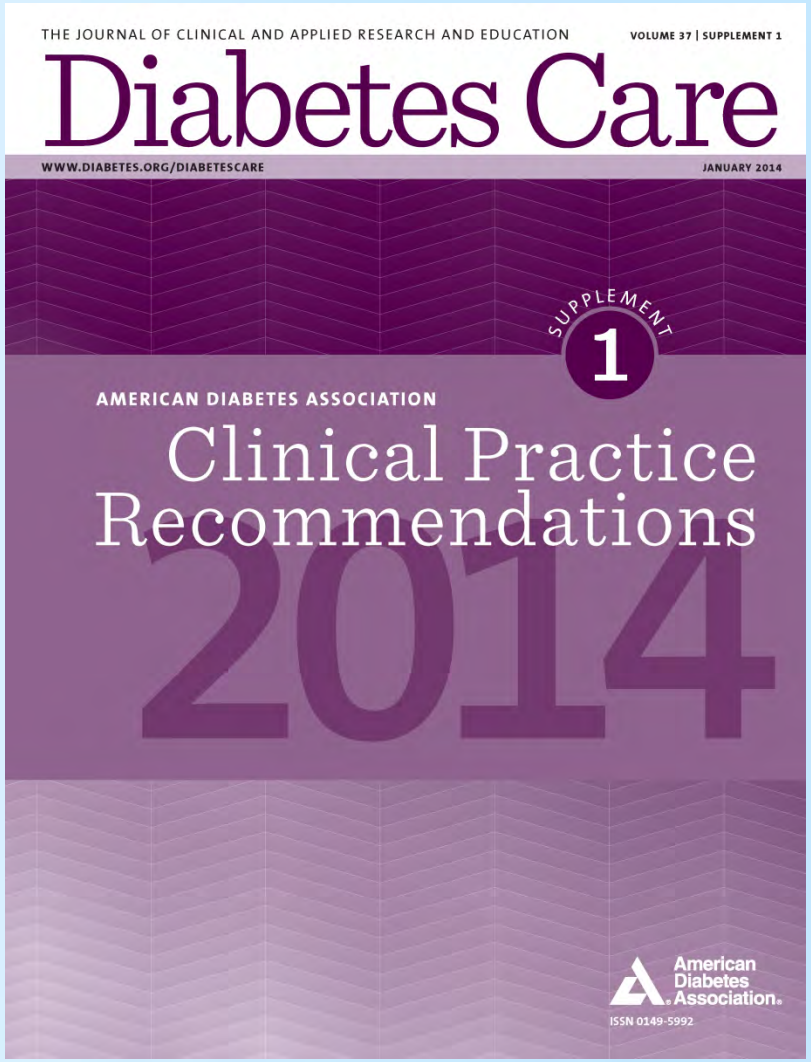
Standards of Medical Care in Diabetes—2014



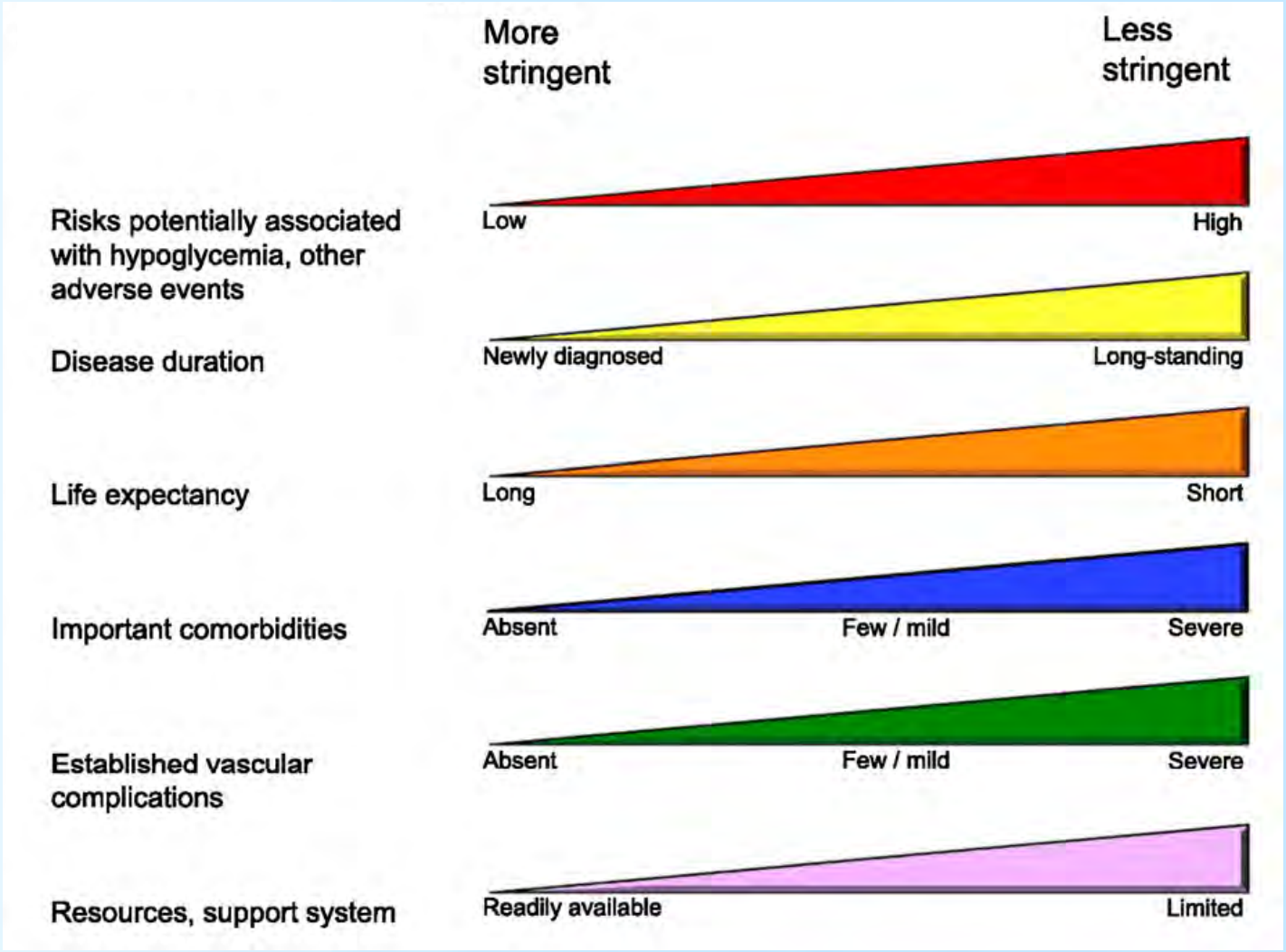
Glycemic Recommendations for Nonpregnant Adults with Diabetes

A1C	<7.0%*
Preprandial capillary plasma glucose	70–130 mg/dL* (3.9–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (<10.0 mmol/L)

*Goals should be individualized based on these values.
†Postprandial glucose measurements should be made 1–2 h after the beginning of the meal; generally peak levels in patients with diabetes.

Diabetes Care. 2014;37 Suppl 1:S14-80.

Approach to Management of Hyperglycemia



Diabetes Care. 2014;37 Suppl 1:S14-80.

Recommendations: Glycemic, Blood Pressure, Lipid Control in Adults

A1C	<7.0%*
Blood pressure	<140/80 mmHg†
Lipids: LDL cholesterol	<100 mg/dL (<2.6 mmol/L)‡ Statin therapy for those with history of MI or age >40+ or other risk factors

*Goals should be individualized based on these values.
†Based on patient characteristics and response to therapy, lower SBP targets may be appropriate.
‡In individuals with overt CVD, a lower LDL cholesterol goal of <70 mg/dL (1.8 mmol/L), using a high dose of a statin, is an option.

Diabetes Care. 2014;37 Suppl 1:S14-80.

FDA Diabetes Approvals 2014

Once Weekly GLP-1s

- Albiglutide
- Dulaglutide

SGLT2s

- Dapagliflozin
- Empagliflozin

Insulin

- Human Insulin Inhalation Powder

CONSENSUS REPORT

Diabetes in Older Adults

M. Sue Kirkman, MD[1]
Vanessa Jones Briscoe, PHD, NP, CDE[2]
Nathaniel Clark, MD, MS, RD[3]
Hermes Florez, MD, MPH, PHD[4]
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Jeffrey B. Halter, MD[6]
Elbert S. Huang, MD, MPH[7]
Mary T. Korytkowski, MD[8]
Medha N. Munshi, MD[9]
Peggy Soule Odegard, BS, PHARMD, CDE[10]
Richard E. Pratley, MD[11]
Carrie S. Swift, MS, RD, BC-ADM, CDE[12]

Diabetes Care 2012; 35:2650-64.
J Am Geriatr Soc 2012; 60:2342-56.

A1c Goals in Older Adults

Patient Characteristics/ Health Status	Rationale	Reasonable A1c Goal*
Healthy (few coexisting illnesses; intact cognitive & functional status)	Longer remaining life expectancy	<7.5%
Complex/intermediate (multiple coexisting illnesses or 2+ ADL impairments or some cognitive impairment)	Intermediate remaining life expectancy, high Rx burden, hypoglycemia vulnerability, fall risk	<8.0%
Very complex/poor health (long-term care or end-stage chronic illness or significant cognitive impairment)	Limited remaining life expectancy makes benefit uncertain	<8.5%

*Lower goal may be set if achievable without hypoglycemia or undue Rx burden

As They Were: A1c Targets in T1DM for Children & Adolescents

ADA Standards of Care			
	Plasma blood glucose goal range (mg/dL)		A1c
Age group (years)	Before meals	Bedtime/ overnight	
Toddlers and pre-schoolers (0 to 6)	100-180	110-200	< 8.5%
School age (6 to 12)	90-180	100-180	< 8%
Adolescents / young adults (13 to 19)	90-130	90-150	< 7.5%

Type 1 Diabetes Through the Life Span: A Position Statement of the American Diabetes Association

Diabetes Care 2014;37:2034–2054 | DOI: 10.2337/dc14-1140

As They Are: Harmonized A1c Targets

"In light of the above evidence, the ADA will harmonize its glycemic goals with those of ISPAD (as well as the Pediatric Endocrine Society and the International Diabetes Federation) by using a single A1C goal of <7.5% across all pediatric age groups."

- Type 1 Diabetes Through the Life Span: A Position Statement of the American Diabetes Assn

A1c Recommendations for Non Pregnant People with Diabetes*	
Youth (<18 years)	<7.5%
Adults	<7.0%
Older adults	
Healthy**	<7.5%
Complex/intermediate	<8.0%
Very complex/poor health	<8.5%

*Targets must be individualized based on a patient's circumstances.

**No comorbidities, long life expectancy

Type 1 Diabetes Mellitus and Cardiovascular Disease: A Scientific Statement From the American Heart Association and American Diabetes Association

DOI: 10.2337/dc14-1720