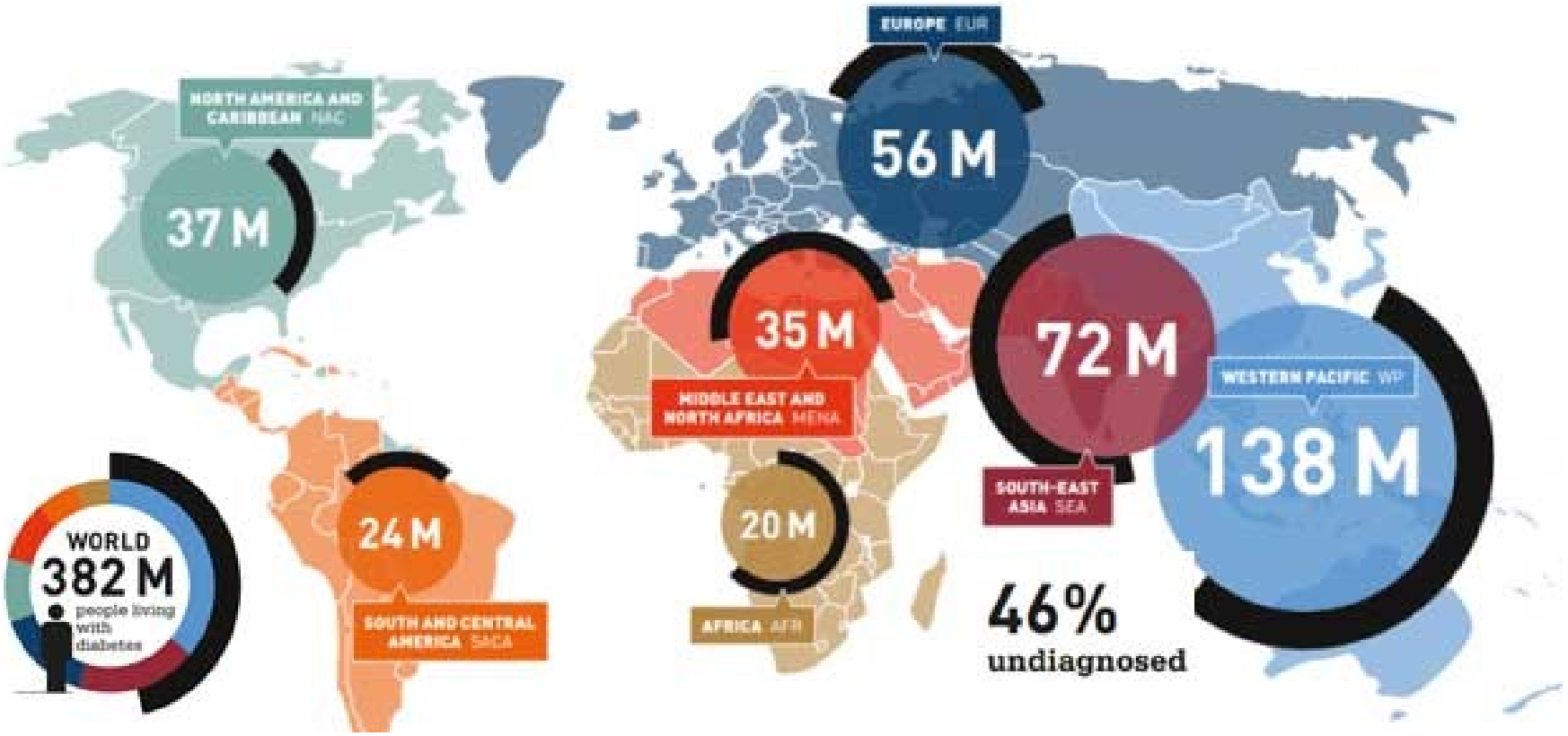
PREVENÇÃO E MANEJO DAS COMPLICAÇÕES CRÔNICAS DO DIABETES

PROF. CRISTINA NEUMANN

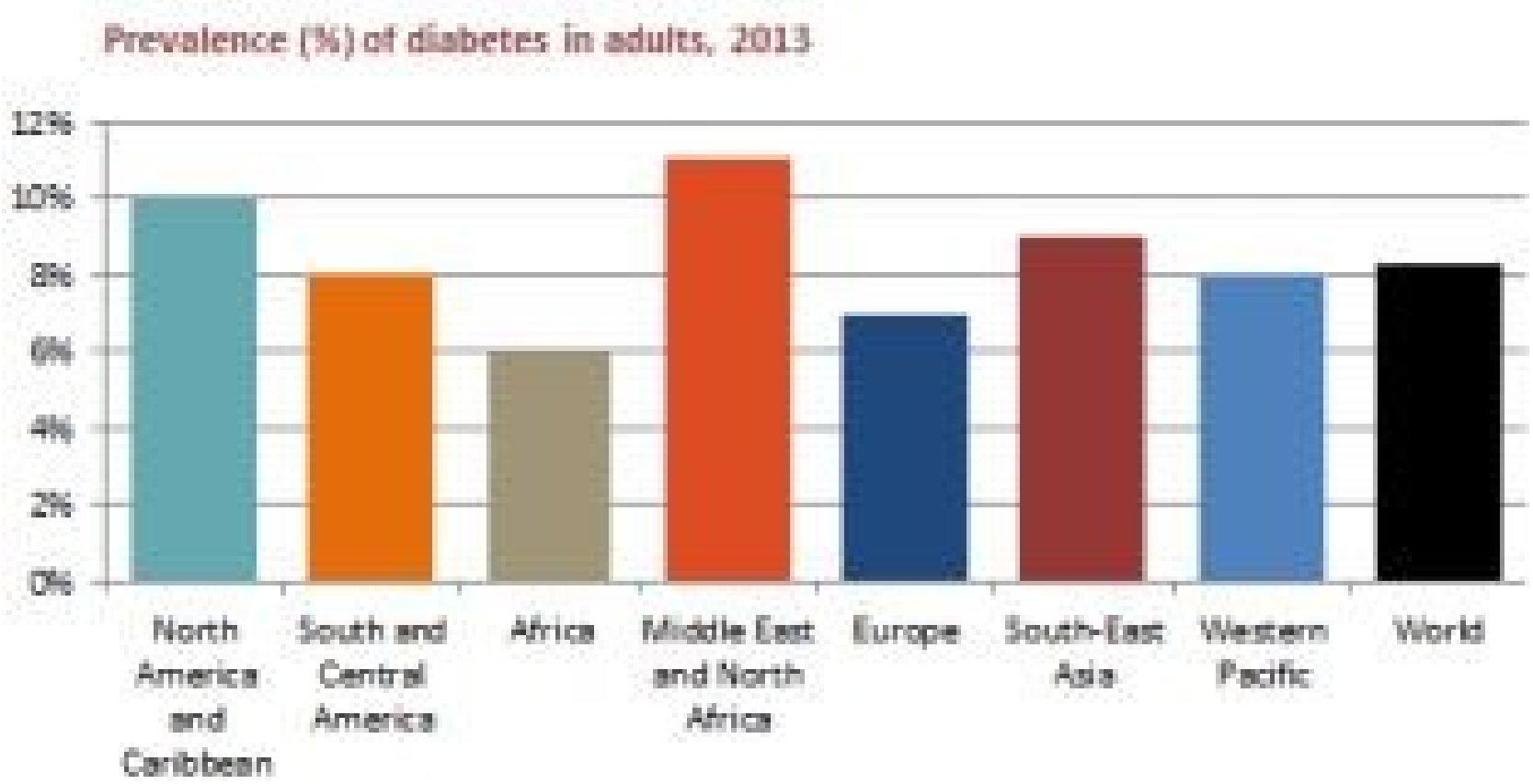
UFRGS

Pessoas com diabetes no mundo



IDF Diabetes Atlas Sixth Edition, International Diabetes Federation 2013

Prevalência de diabetes em adultos



IDF Diabetes Atlas Sixth Edition, International Diabetes Federation 2013

Top 10 countries for number of people with diabetes (20-79 years), 2013

Country/territory	Number
China	98.4 million
India	65.1 million
United States of America	24.4 million
Brazil	11.9 million
Russian Federation	10.9 million
Mexico	8.7 million
Indonesia	8.5 million
Germany	7.6 million
Egypt	7.5 million
Japan	7.2 million

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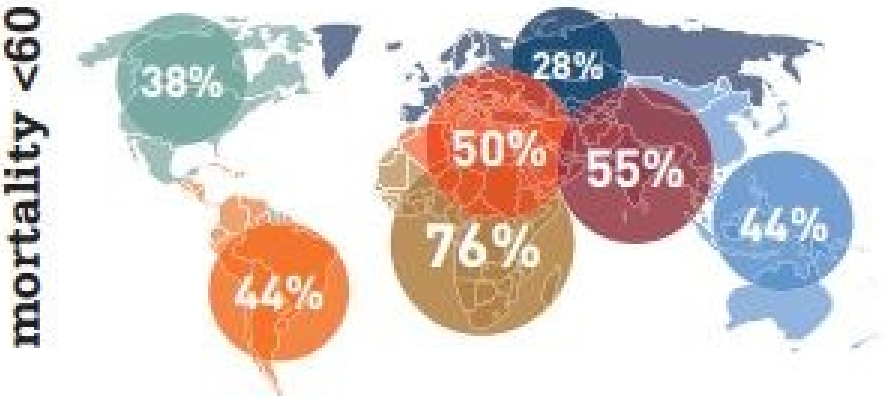
Gastos X Mortalidade por diabetes

Health expenditure (USD) due to diabetes (20-79 years), 2013



Proportion of deaths due to diabetes in people under 60 years of age, 2013

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Complicações Crônicas

- Macrovasculares
  - Aterosclerose acelerada
  - Principal causa de morbimortalilade no DM
- Microvasculares
  - Diretamente relacionadas à presença de DM
  - Nefropatia
  - Retinopatia
  - Neuropatia

Mecanismo de lesão induzida pela hiperglicemia

- Ativação da via do poliol
- Ativação da proteina quinase C
- Formação de produtos glicosilados (AGE)
- Aumento do Stress oxidativo

Fatores de risco para o surgimento de Complicações Crônicas

- Duração do DM
- Fumo
- **Hipertensão arterial**
- **Dislipidemia**
- **Obesidade**
- **Hiperglicemia**
- **Resistência à insulina**
- **Inflamação branda crônica**
- **Disfunção endotelial**

Síndrome Plurimetabólica

Principais complicações do diabetes

Risco de cegueira: 30 x
Amputações em Mis: 40 x
IAM: 2-5 x
AVC: 2-3 x

IDF Diabetes Atlas Sixth Edition, International Diabetes Federation 2013

O caso do Raul...

- Raul é um homem de 60 anos com uma história de 10 anos de diabete tipo 2 e história de pressão elevada que consulta pela primeira vez no PSF.
- Nega dor torácica ou dispnéia aos esforços. Nega história de IAM ou AVC. Faz uso de metformina 850mg/dia somente. Não é tabagista. Não tem historia familiar de doença cardiovascular nem de DM.
- A=1,70cm, P=108kg, CA=106cm, PA=155x80mmHg, Ausculta cardíaca e pulmonar normais, bons pulsos periféricos, sem sopros carotídeos ou abdominais, sensibilidade normal em ambos pés.
- Hemoglobina glicada de 7,5 %

Como manejar o risco cardiovascular deste paciente?

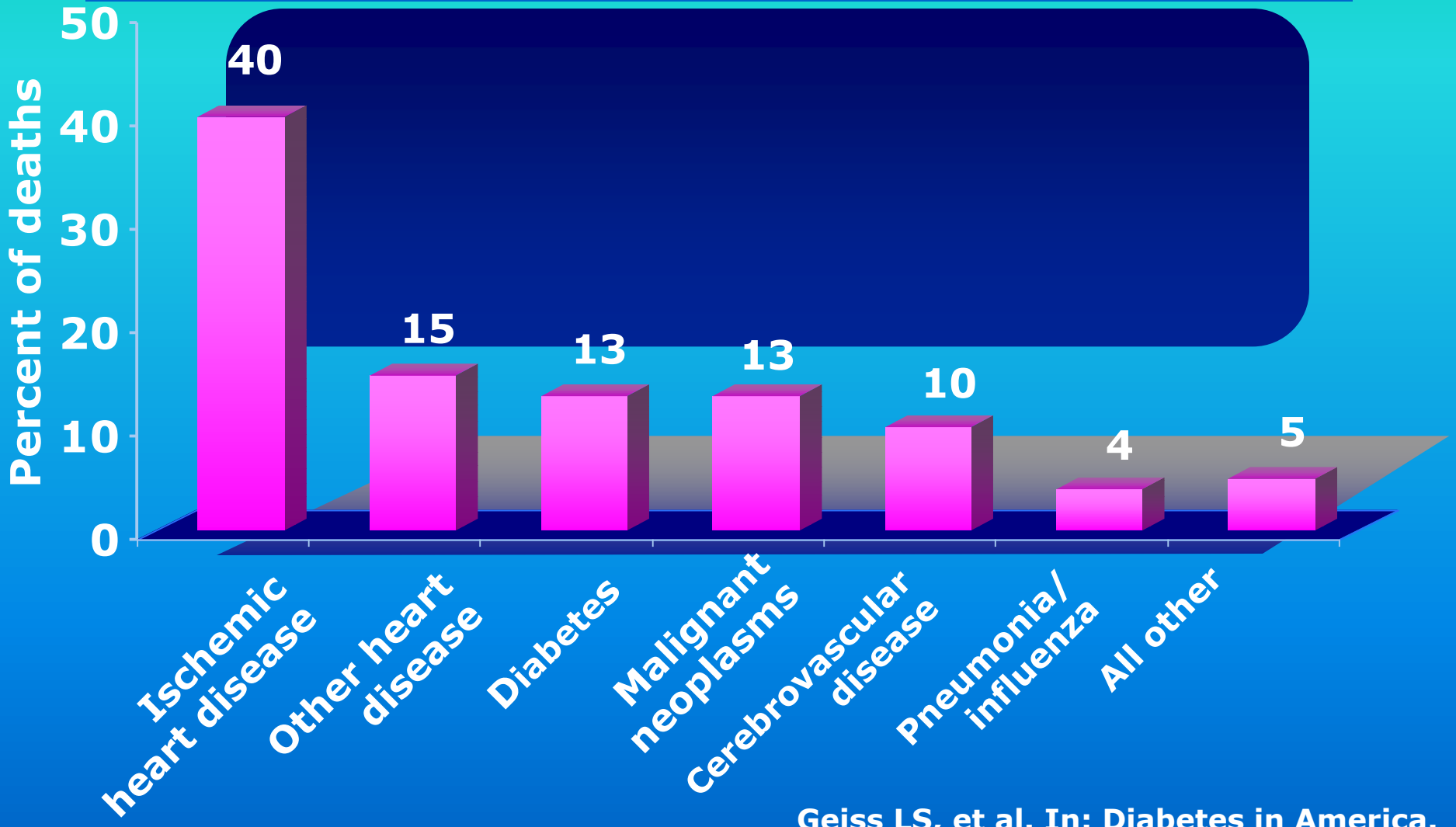
A. O risco é baixo pois é assintomático e não tem historia familiar de doença cardíaca.
B. Como tem 60 anos a hemoglobina glicada está adequada.
C. Deveria fazer eletrocardiograma de esforço e monitorização ambulatorial da pressão arterial para avaliar se deve ser tratado.
D. Deve fazer controle anual de lipídeos e albuminúria e manter a PA $\leq$ 140 mmHg
E. Deve ser aconselhado para realizar mudanças do estilo de vida (aumentar exercícios, perder de peso, reduzir o sal e aumentar do potássio da dieta, moderar a ingesta de álcool) reavaliar em 3 meses e então se necessário tratar a PA.

Cardiovascular Disease

- CVD is the major cause of morbidity, mortality for those with diabetes
  - Largest contributor to direct/indirect costs
- Common conditions coexisting with type 2 diabetes (e.g., hypertension, dyslipidemia) are clear risk factors for CVD
- Diabetes itself confers independent risk
- Benefits observed when individual cardiovascular risk factors are controlled to prevent/slow CVD in people with diabetes

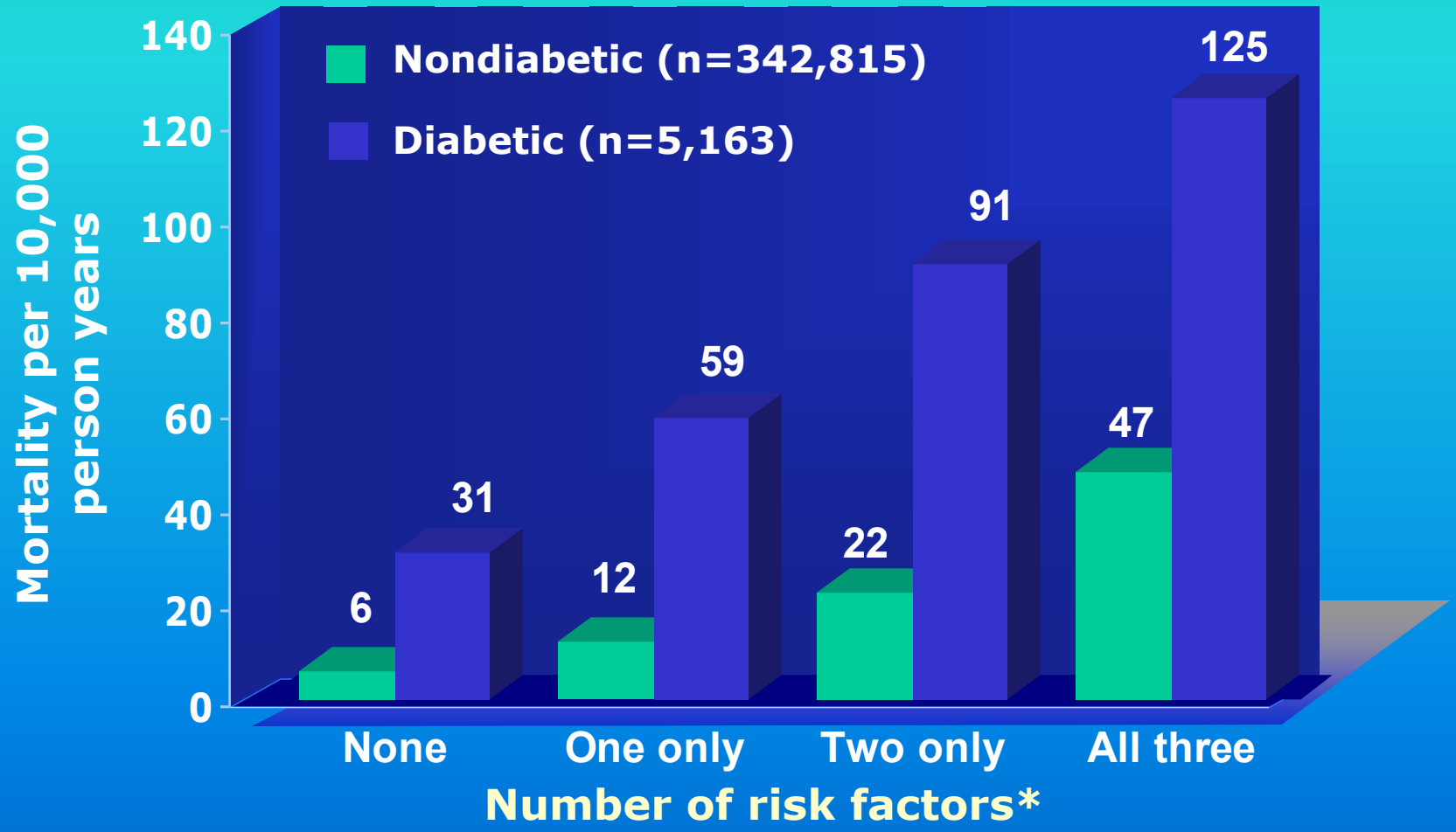
ADA. VI. Prevention, Management of ComplicatioAns. Diabetes Care 2014;37(suppl 1):

Causas de Morte em Indivíduos com Diabetes



Geiss LS, et al. In: Diabetes in America. National Institutes of Health;1995.

Impacto do Diabetes na Mortalidade Cardiovascular: MRFIT

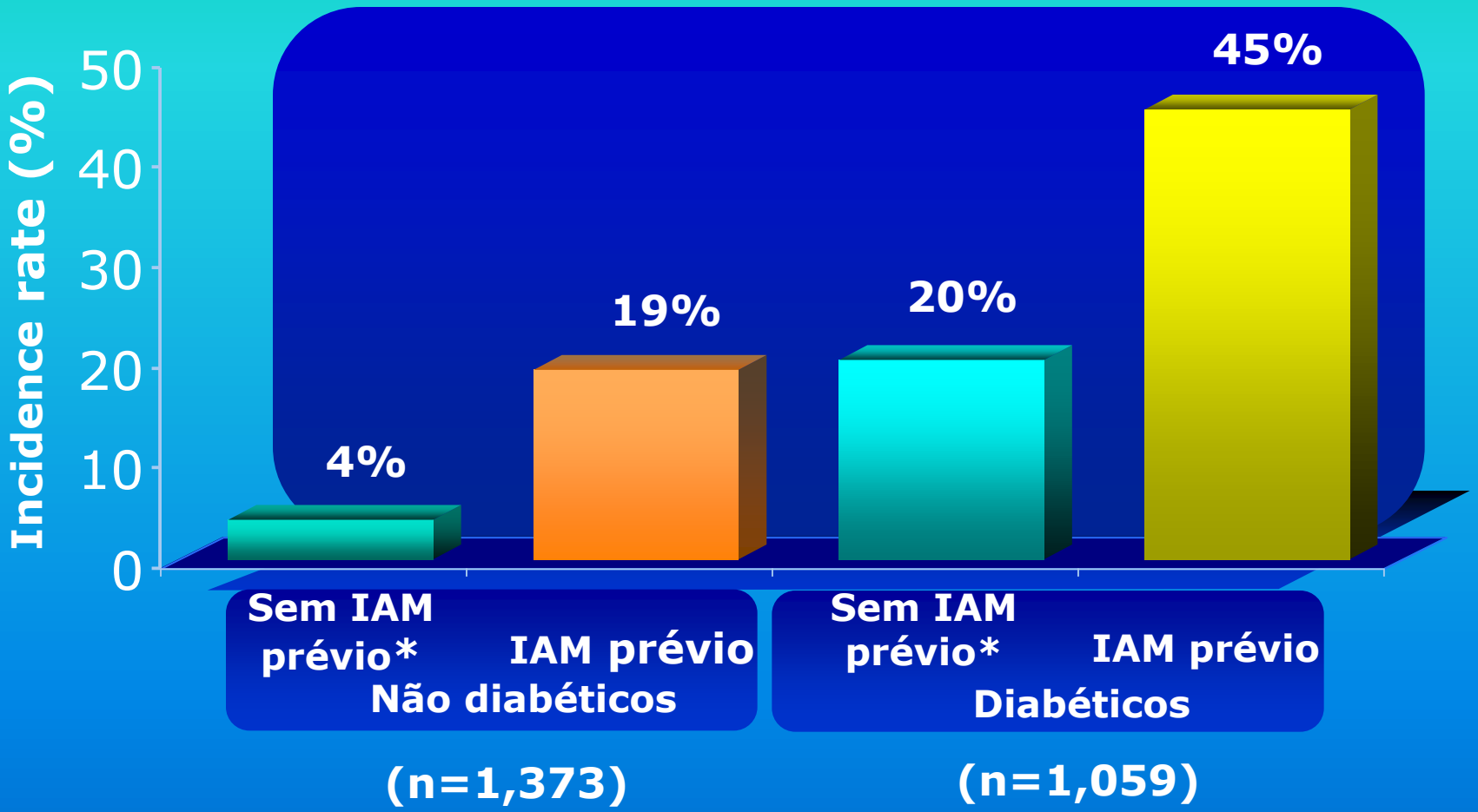


MRFIT=Multiple Risk Factor Intervention Trial

*Fatores de risco analisados: fumo, hipercolesterolemia, HAS

Stamler J, et al. Diabetes Care. 1993;16:434-444.

Incidência de IAM Fatal e Não Fatal



* Basal

Haffner SM, et al. N Eng J Med. 1998;339:229-234.

As complicações crônicas são resultado de vários insultos que ocorrem simultâneamente

A implementação de medidas farmacológicas e não farmacológicas que visam controlar a hiperglicemia, hipertensão, dislipidemia e microalbuminúria é eficaz na redução de várias complicações no diabete tipo 2

Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes

Table 1. Treatment Goals for the Conventional-Therapy Group and the Intensive-Therapy Group.*

Variable	Conventional Therapy		Intensive Therapy	
	1993–1999	2000–2001	1993–1999	2000–2001
Systolic blood pressure (mm Hg)	<160	<135	<140	<130
Diastolic blood pressure (mm Hg)	<95	<85	<85	<80
Glycosylated hemoglobin (%)	<7.5	<6.5	<6.5	<6.5
Fasting serum total cholesterol (mg/dl)	<250	<190	<190	<175
Fasting serum triglycerides (mg/dl)	<195	<180	<150	<150
Treatment with ACE inhibitor irrespective of blood pressure	No	Yes	Yes	Yes
Aspirin therapy				
For patients with known ischemia	Yes	Yes	Yes	Yes
For patients with peripheral vascular disease	No	No	Yes	Yes
For patients without coronary heart disease or peripheral vascular disease	No	No	No	Yes

Gæde, Vedel, Larsen,et all.N Engl J Med 2003;348:383-93

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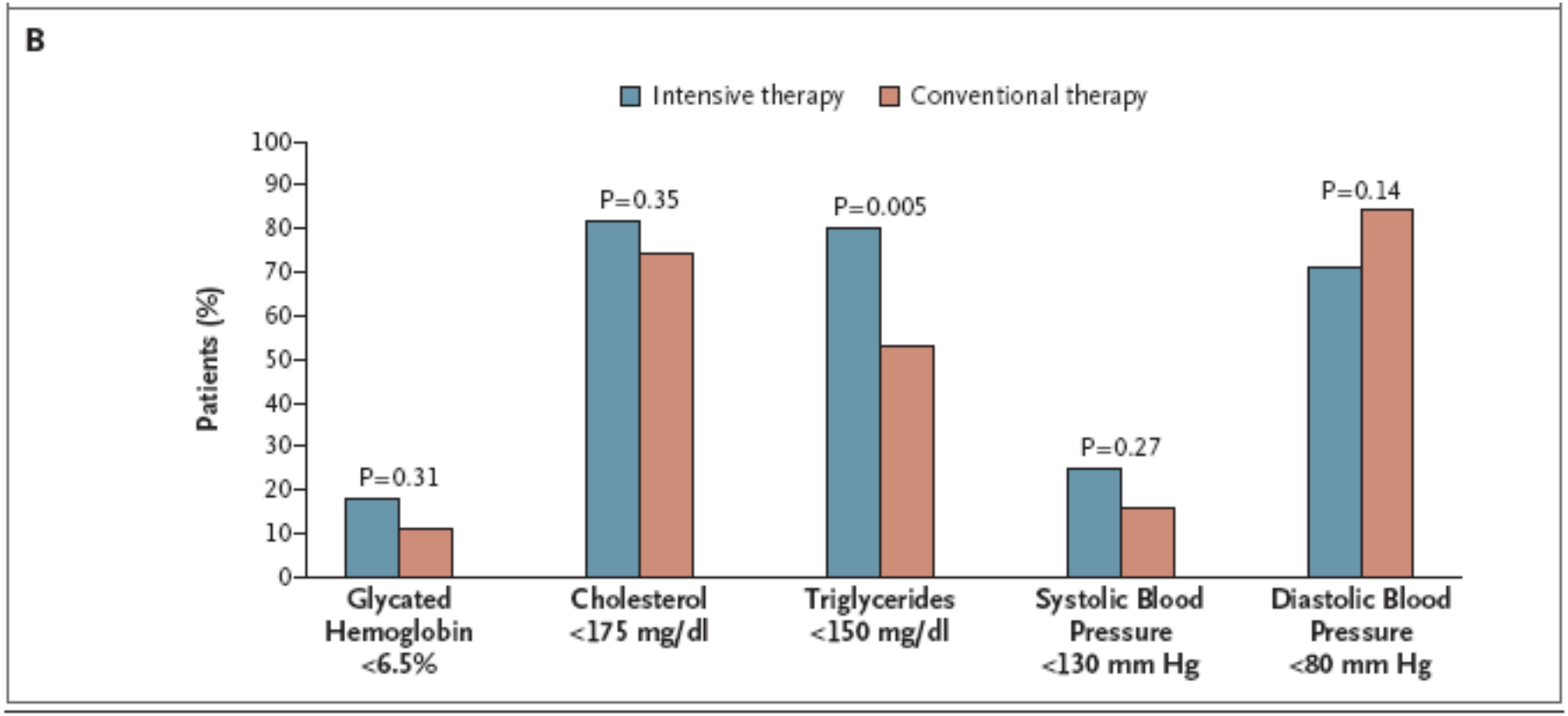
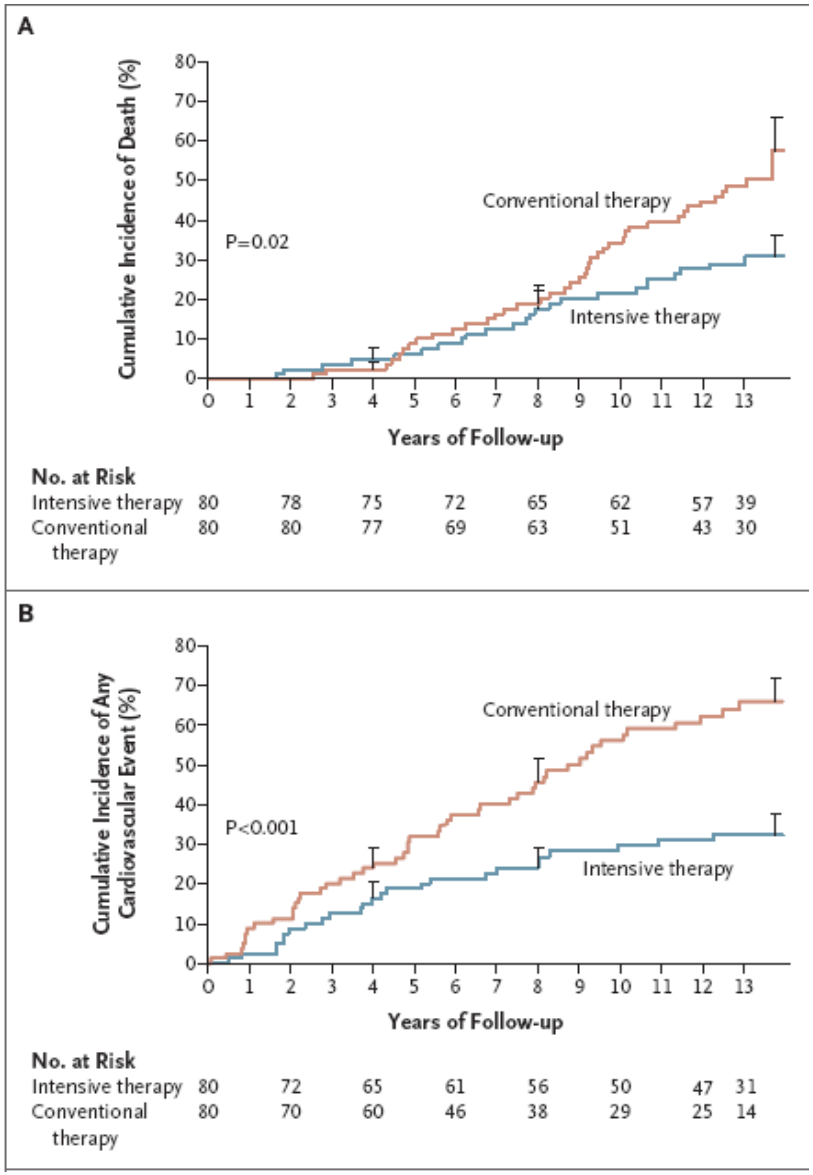
ORIGINAL ARTICLE

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Peter Gæde, M.D., D.M.Sc., Henrik Lund-Andersen, M.D., D.M.Sc., Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.

Periodo observacional após a intervenção
Seguimento 13,3 anos
Desfecho: morte por qualquer causa




A
Cumulative Incidence of Death (%)
Conventional therapy
P=0.02
Intensive therapy
Years of Follow-up
No. at Risk
Intensive therapy 80 78 75 72 65 62 57 39
Conventional therapy 80 80 77 69 63 51 43 30
B
Cumulative Incidence of Any Cardiovascular Event (%)
Conventional therapy
P<0.001
Intensive therapy
Years of Follow-up
No. at Risk
Intensive therapy 80 72 65 61 56 50 47 31
Conventional therapy 80 70 60 46 38 29 25 14
C
Intensive therapy
Conventional therapy
No. of Cardiovascular Events
Death from Cardiovascular Causes
Stroke
Myocardial Infarction
CABG
PCI
Revascularization
Amputation

Recommendations: Hypertension/Blood Pressure Control

Screening and diagnosis

- Blood pressure should be measured at every routine visit
- Patients found to have elevated blood pressure should have blood pressure confirmed on a separate day **B**

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Recommendations: Cardiovascular Disease (1)

Screening

- In asymptomatic patients, routine screening for CAD is not recommended because it does not improve outcomes as long as CVD risk factors are treated **A**

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S42

Recommendations: Hypertension/Blood Pressure Control

Goals

- People with diabetes and hypertension should be treated to a systolic blood pressure goal of <140 mmHg **B**
- Lower systolic targets, such as <130 mmHg, may be appropriate for certain individuals, such as younger patients, if it can be achieved without undue treatment burden **C**
- Patients with diabetes should be treated to a diastolic blood pressure <80 mmHg **B**

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Recommendations: Hypertension/Blood Pressure Control

Treatment (1)

- Patients with blood pressure >120/80 mmHg should be advised on lifestyle changes to reduce blood pressure **B**
- Patients with confirmed blood pressure higher than 140/80 mmHg should, in addition to lifestyle therapy, have prompt initiation and timely subsequent titration of pharmacological therapy to achieve blood pressure goals **B**

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Recommendations: Hypertension/Blood Pressure Control

Treatment (2)

- Lifestyle therapy for elevated blood pressure **B**
  - Weight loss if overweight
  - DASH-style dietary pattern including reducing sodium, increasing potassium intake
  - Moderation of alcohol intake
  - Increased physical activity

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Recommendations: Hypertension/Blood Pressure Control

Treatment (3)

- Pharmacological therapy for patients with diabetes and hypertension **C**
  - A regimen that includes either an ACE inhibitor or angiotensin II receptor blocker; if one class is not tolerated, substitute the other
- Multiple drug therapy (two or more agents at maximal doses) generally required to achieve blood pressure targets **B**
- Administer one or more antihypertensive medications at bedtime **A**

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Recommendations: Hypertension/Blood Pressure Control

Treatment (4)

- If ACE inhibitors, ARBs, or diuretics are used, serum creatinine/eGFR and potassium levels should be monitored **E**
- In pregnant patients with diabetes and chronic hypertension, blood pressure target goals of 110–129/65–79 mmHg are suggested in interest of long-term maternal health and minimizing impaired fetal growth; ACE inhibitors, ARBs, contraindicated during pregnancy **E**

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S36

ORIGINAL ARTICLE

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

N Engl J Med 2010;362:1575-85.

The ACCORD Study Group*

- ECR comparando níveis de controle da PA em pacientes com RCV elevado
  - 135-140 comparado <120
- Foi obtido PA media: 133,5 e 119,3
- Mortalidade ou eventos cardiovasculares combinados: sem diferenças
- AVC: menos
- Efeitos colaterais graves: 3,3% e 1,3%

Table 3. Primary and Secondary Outcomes.

Outcome	Intensive Therapy (N=2363)		Standard Therapy (N=2371)		Hazard Ratio (95% CI)	P Value
	no. of events	*%/yr*	*no. of events*	*%/yr*		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
Any	36	0.32	62	0.53	0.59 (0.39–0.89)	0.01
Nonfatal	34	0.30	55	0.47	0.63 (0.41–0.96)	0.03
Death						
From any cause	150	1.28	144	1.19	1.07 (0.85–1.35)	0.55
From cardiovascular cause	60	0.52	58	0.49	1.06 (0.74–1.52)	0.74
Primary outcome plus revascularization or nonfatal heart failure	521	5.10	551	5.31	0.95 (0.84–1.07)	0.40
Major coronary disease event†	253	2.31	270	2.41	0.94 (0.79–1.12)	0.50
Fatal or nonfatal heart failure	83	0.73	90	0.78	0.94 (0.70–1.26)	0.67

* The primary outcome was a composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes.

† Major coronary disease events, as defined in the protocol, included fatal coronary events, nonfatal myocardial infarction, and unstable angina.

REVIEW ARTICLE

Intensive and Standard Blood Pressure Targets in Patients With Type 2 Diabetes Mellitus

Systematic Review and Meta-analysis

Kerry McBrien, MD, MPH; Doreen M. Rabi, MD, MS; Norm Campbell, MD; Lianne Barnieh, PhD; Fiona Clement, PhD; Brenda R. Hemmelgarn, MD, PhD; Marcello Tonelli, MD, SM; Lawrence A. Leiter, MD; Scott W. Klarenbach, MD, MSc; Braden J. Manns, MD, MSc

- Metanálise de 7 ECR comparando níveis de controle da PA em pacientes DM2
  - 130/80 comparado 140-160/85-100
- Mortalidade (RR D, 0.76; 95% CI, 0.55-1.05)
- Infarto do Miocardio (RR D , 0.93; 95% CI, 0.80-1.08)
- AVC (RR, 0.65; 95% CI, 0.48-0.86)

Arch Intern Med. 2012;172(17):1296-1303.

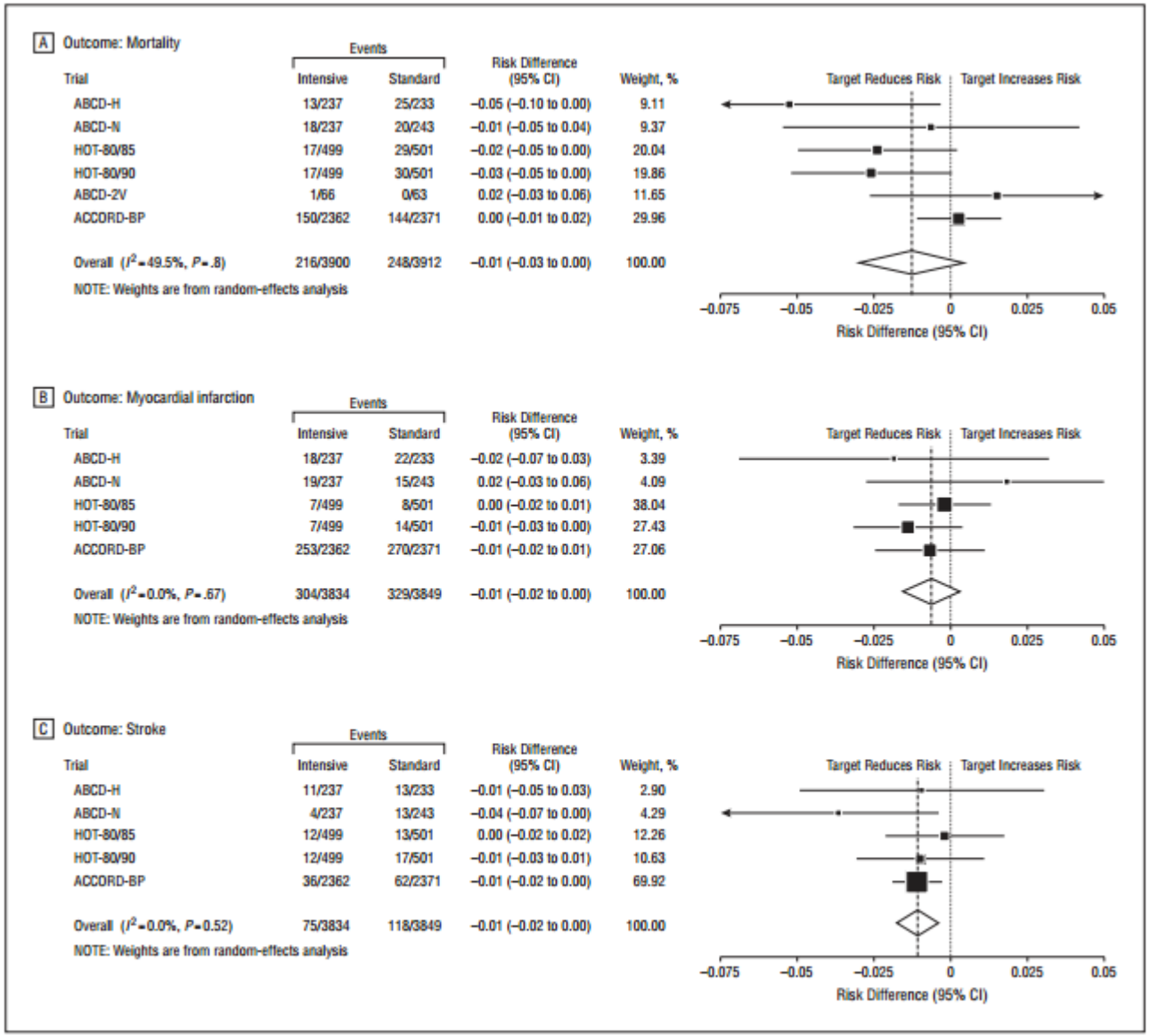


Figure 3. Absolute risk differences, showing blood pressure targets and risk difference for all-cause mortality (A), myocardial infarction (B), and stroke (C). The width of the diamond represents the 95% CI. The prediction intervals span the following ranges: −0.06 to 0.03 for A, −0.02 to 0.01 for B, and −0.02 to 0.00 for C. Abbreviations are explained in the legend to Figure 2.

O caso do Raul...

- Retorna a consulta com PA ainda elevada e traz os resultados dos lipidios:
  LDL colesterol 138 mg/dL
  HDL colesterol 35 mg/dL
  Triglicerideos 375 mg/dL
- Perdeu peso (700 gr) mas continua com a PA elevada

Qual a meta do controle do colesterol e vc avalia com que periodicidade.

A. LDL 120, repetir a cada ano
B. LDL 100 repetir a cada 2 anos
C. LDL 70 repetir a cada ano.

Vc usa estatinas para prevenção primária?

Recommendations: Dyslipidemia/Lipid Management (1)

Screening

- In most adult patients with diabetes, measure fasting lipid profile at least annually **B**
- In adults with low-risk lipid values
  - LDL cholesterol <100 mg/dL
  - HDL cholesterol >50 mg/dL
  - Triglycerides <150 mg/dL)
- Repeat lipid assessments every 2 years **E**

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S38

Recommendations: Dyslipidemia/Lipid Management (2)

Treatment recommendations and goals (1)

- To improve lipid profile in patients with diabetes, recommend lifestyle modification **A**, focusing on
  - Reduction of saturated fat, trans fat, cholesterol intake
  - Increase of n-3 fatty acids, viscous fiber, plant stanols/sterols
  - Weight loss (if indicated)
  - Increased physical activity

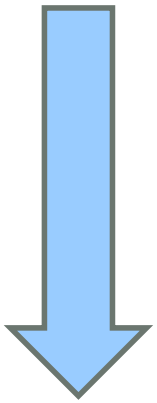
ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S38

Statins for the primary prevention of cardiovascular disease

Taylor F, Huffman MD, Macedo A, Moore THM, Burke M, Davey Smith G, Ward K, Ebrahim S

Published Online: January 20, 2014

19 trial arms: 56,934 participants
14 trials with specific conditions (raised lipids, diabetes, hypertension, microalbuminuria).



All-cause mortality (OR 0.86, 95% CI 0.79 to 0.94);
Combined fatal and non-fatal CVD (RR 0.75 (95% CI 0.70 to 0.81),
Combined fatal and non-fatal CHD events (RR 0.73 (95% CI 0.67 to 0.80)
Combined fatal and non-fatal stroke (RR 0.78, 95% CI 0.68 to 0.89).
Revascularisation rates (RR 0.62, 95% CI 0.54 to 0.72)
No evidence of any serious harm caused by statin prescription.

Efficacy of cholesterol-lowering therapy in 18 686 people with diabetes in 14 randomised trials of statins: a meta-analysis

Cholesterol Treatment Trialists' (CTT) Collaborators

- 18 686 individuals with diabetes (1466 with type 1 and 17 220 with type 2)
- mean follow-up of 4·3 years,
- 3247 major vascular events in people with diabetes.

- Reduction:
- all-cause mortality per mmol/L reduction in LDL cholesterol [RR] 0·91, 99% CI 0·82—1·01; p=0·02),
- vascular mortality (0·87, 0·76—1·00; p=0·008)
- No effect on non-vascular mortality (0·97, 0·82—1·16; p=0·7)

.

- major vascular events per mmol/L reduction in LDL cholesterol (0·79, 0·72—0·86; p<0·0001),
- myocardial infarction or coronary death (0·78, 0·69—0·87; p<0·0001),
- coronary revascularisation (0·75, 0·64—0·88; p<0·0001),
- stroke (0·79, 0·67—0·93; p=0·0002).

- whether there was a prior history of vascular disease and irrespective of other baseline characteristics.

- After 5 years, 42 (95% CI 30—55) fewer people with diabetes had major vascular events per 1000 allocated statin therapy.

The Lancet, Volume 371, Issue 9607, Pages 117 - 125, 12 January 2008

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

- A meta-analysis of 13 randomized statin trials with 91,140
- Odds ratio of 1.09 for a new diagnosis of diabetes, so that (on average) treatment of 255 patients with statins for 4 years resulted in one additional case of diabetes, while simultaneously preventing 5.4 vascular events among those 255 patients.
- Limited to those with diabetes risk factors

Sattar N et all. Lancet 2010;375:735–742

Recommendations: Dyslipidemia/Lipid Management (3)

Treatment recommendations and goals (2)

- Statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels
  - with overt CVD **A**
  - without CVD >40 years of age who have one or more other CVD risk factors **A**
- For patients at lower risk (e.g., without overt CVD, <40 years of age) **C**
  - Consider statin therapy in addition to lifestyle therapy if LDL cholesterol remains >100 mg/dL
  - In those with multiple CVD risk factors

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Recommendations: Dyslipidemia/Lipid Management (4)

Treatment recommendations and goals (3)

- In individuals without overt CVD
  - Goal is LDL cholesterol <100 mg/dL (2.6 mmol/L) **B**
- In individuals with overt CVD
  - Lower LDL cholesterol goal of <70 mg/dL (1.8 mmol/L), with a high dose of a statin, is an option **B**

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Recommendations: Dyslipidemia/Lipid Management (5)

Treatment recommendations and goals (4)

- If targets not reached on maximal tolerated statin therapy
  - Alternative therapeutic goal: reduce LDL cholesterol ~30–40% from baseline **B**
- Triglyceride levels <150 mg/dL (1.7 mmol/L), HDL cholesterol >40 mg/dL (1.0 mmol/L) in men and >50 mg/dL (1.3 mmol/L) in women, are desirable **C**
  - However, LDL cholesterol–targeted statin therapy remains the preferred strategy **A**

O caso do Raul...

- Retorna a consulta um mês depois. A PA está 135/80 (controlou com Losartana 50 mg/dia). Além disto usa Sinvastatina 40 mg/dia, e Metformim 850 mg/dia

  LDL colesterol 70 mg/dL

  HDL colesterol 37 mg/dL

  Triglicerideos 283 mg/dL

  Hemoglobina glicada 7,8%

- Está com o mesmo peso, ainda não está fazendo exercício.

O controle dos lípideos não está bom, vc associaria um fibrato?

A. Sim
B. Não
C. Depende...

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ESTABLISHED IN 1812 APRIL 29, 2010 VOL. 362 NO. 17

Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus

Table 2. Prespecified Primary and Secondary Outcomes.

Outcome	Fenofibrate (N=2765)		Placebo (N=2753)		Hazard Ratio (95% CI)	P Value
	no. of events	*rate/yr*	*no. of events*	*rate/yr*		
Primary outcome (major fatal or nonfatal cardiovascular event)	291	2.24	310	2.41	0.92 (0.79–1.08)	0.32*
Secondary outcomes						
Primary outcome plus revascularization or hospitalization for congestive heart failure	641	5.35	667	5.64	0.94 (0.85–1.05)	0.30
Major coronary disease event†	332	2.58	353	2.79	0.92 (0.79–1.07)	0.26
Nonfatal myocardial infarction	173	1.32	186	1.44	0.91 (0.74–1.12)	0.39
Stroke						
Any	51	0.38	48	0.36	1.05 (0.71–1.56)	0.80
Nonfatal	47	0.35	40	0.30	1.17 (0.76–1.78)	0.48
Death						
From any cause	203	1.47	221	1.61	0.91 (0.75–1.10)	0.33*
From cardiovascular cause	99	0.72	114	0.83	0.86 (0.66–1.12)	0.26
Fatal or nonfatal congestive heart failure	120	0.90	143	1.09	0.82 (0.65–1.05)	0.10

* P values were adjusted for interim monitoring.
† A major coronary disease event was defined as a fatal coronary event, nonfatal myocardial infarction, or unstable angina.

Recommendations: Dyslipidemia/Lipid Management (6)

Treatment recommendations and goals (5)

- Combination therapy has been shown not to provide additional cardiovascular benefit above statin therapy alone and is not generally recommended **A**
- Statin therapy is contraindicated in pregnancy **B**

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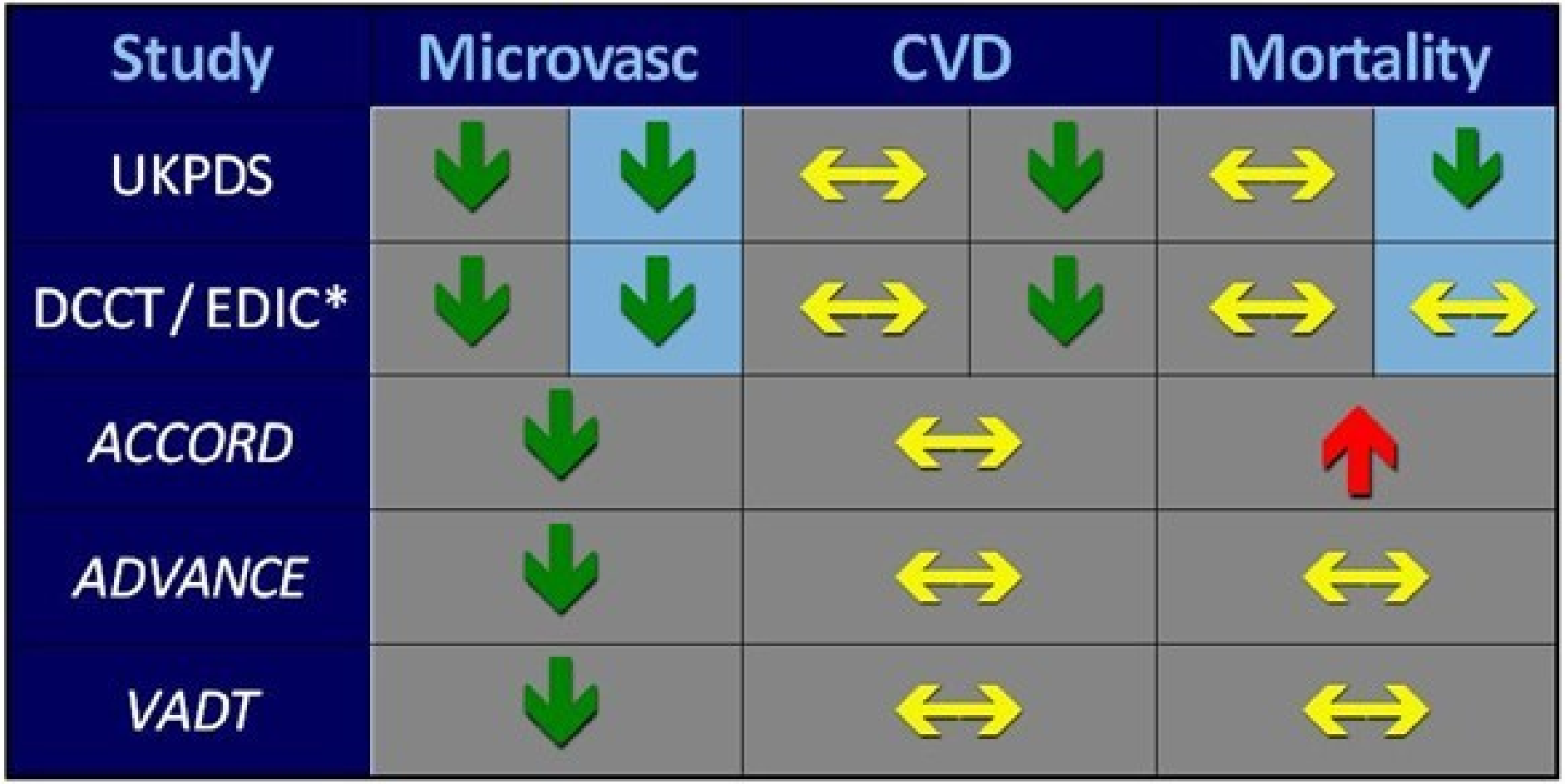
O caso do Raul...

- Na mesma consulta vc observou o controle glicêmico Hemoglobina glicada 7,8%
- Está em uso de Metformim 850 mg/dia
- Está com o mesmo peso, ainda não está fazendo exercício.

O controle glicêmico pode influenciar no manejo das complicações micro e macrovasculares? Qual é o ideal?

A. 6,5%
B. 7,0%
C. 8,0%
D. Depende...

Impact of Intensive Therapy for Diabetes: Summary of Major Clinical Trials



Kendall DM, Bergenstal RM. © International Diabetes Center 2009

UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:854.
Holman RR et al. *N Engl J Med.* 2008;359:1577. DCCT Research Group. N Engl J Med 1993;329;977.
Nathan DM et al. *N Engl J Med.* 2005;353:2643. Gerstein HC et al. *N Engl J Med.* 2008;358:2545.
Patel A et al. N Engl J Med 2008;358:2560. Duckworth W et al. N Engl J Med 2009;360:129. (erratum: Moritz T. *N Engl J Med* 2009;361:1024)

Initial Trial

Long Term Follow-up

* in T1DM

Recommendations: Glycemic Goals in Adults (1)

- Lowering A1C to below or around 7% has been shown to reduce microvascular complications and, if implemented soon after the diagnosis of diabetes, is associated with long-term reduction in macrovascular disease
- Therefore, a reasonable A1C goal for many nonpregnant adults is <7% **B**

ADA. V. Diabetes Care. Diabetes Care 2014;37(suppl 1):S23

Recommendations: A1C

- Perform the A1C test at least two times a year in patients meeting treatment goals (and have stable glycemic control) **E**
- Perform the A1C test quarterly in patients whose therapy has changed or who are not meeting glycemic goals **E**
- Use of point-of-care (POC) testing for A1C provides the opportunity for more timely treatment changes **E**

ADA. V. Diabetes Care. Diabetes Care 2014;37(suppl 1):S22–S23

Recommendations: Glycemic Goals in Adults (2)

- Providers might reasonably suggest more stringent A1C goals (such as <6.5%) for selected individual patients, if this can be achieved without significant hypoglycemia or other adverse effects of treatment
- Appropriate patients might include those with short duration of diabetes, long life expectancy, and no significant CVD **C**

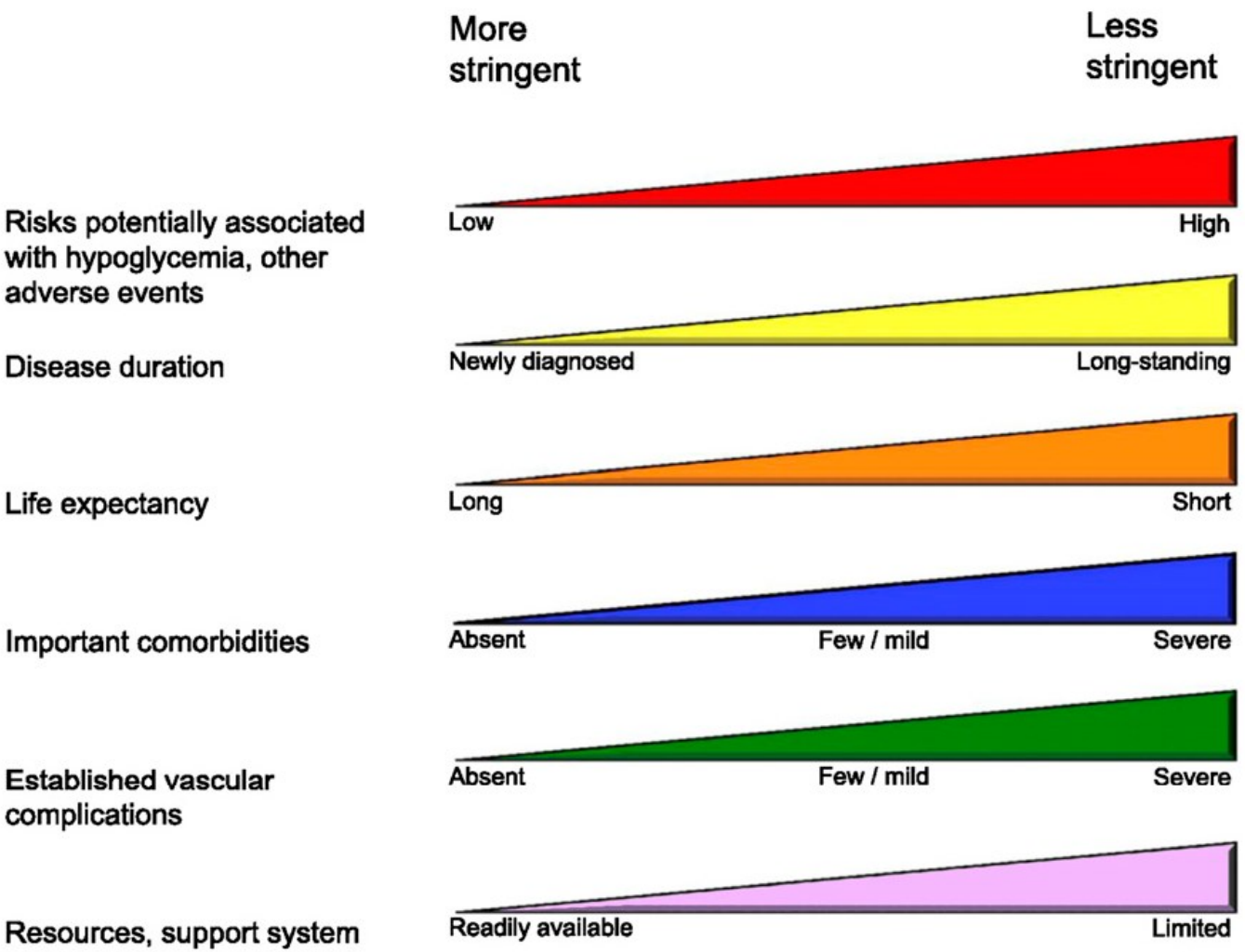
ADA. V. Diabetes Care. Diabetes Care 2014;37(suppl 1):S23

Recommendations: Glycemic Goals in Adults (3)

- Less stringent A1C goals (such as <8%) may be appropriate for patients with **B**
  - History of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions
  - Those with longstanding diabetes in whom the general goal is difficult to attain despite DSME, appropriate glucose monitoring, and effective doses of multiple glucose lowering agents including insulin

ADA. V. Diabetes Care. Diabetes Care 2014;37(suppl 1):S23

Approach to Management of Hyperglycemia



ADA. V. Diabetes Care. Diabetes Care 2014;37(suppl 1):S25. Figure 1; adapted with permission from Ismail-Beigi F, et al. Ann Intern Med 2011;154:554-559

Glycemic Recommendations for Nonpregnant Adults with Diabetes (3)

- More or less stringent glycemic goals may be appropriate for individual patients
- Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals

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

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.
†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.

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S40; Table 10

Recommendations: Antiplatelet Agents (1)

- Consider aspirin therapy (75–162 mg/day) **C**
  - As a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10-year risk >10%)
  - Includes most men >50 years of age or women >60 years of age who have at least one additional major risk factor
    - Family history of CVD
    - Hypertension
    - Smoking
    - Dyslipidemia
    - Albuminuria

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Recommendations: Antiplatelet Agents (3)

- Use aspirin therapy (75–162 mg/day)
  - Secondary prevention strategy in those with diabetes with a history of CVD **A**
- For patients with CVD and documented aspirin allergy
  - Clopidogrel (75 mg/day) should be used **B**
- Dual antiplatelet therapy is reasonable for up to a year after an acute coronary syndrome **B**

Recommendations: Antiplatelet Agents (2)

- Aspirin should not be recommended for CVD prevention for adults with diabetes at low CVD risk, since potential adverse effects from bleeding likely offset potential benefits **C**
  - Low risk: 10-year CVD risk <5%, such as in men <50 years, women <60 years with no major additional CVD risk factors
- In patients in these age groups with multiple other risk factors (10-year risk 5–10%), clinical judgment is required **E**

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Recommendations: Smoking Cessation

- Advise all patients not to smoke or use tobacco products **A**
- Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care **B**

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S41

Recommendations: Cardiovascular Disease (2)

Treatment (1)

- To reduce risk of cardiovascular events in patients with known CVD, consider
  - ACE inhibitor **C**
  - Aspirin* **A**
  - Statin therapy* **A**
- In patients with a prior MI
  - β-blockers should be continued for at least 2 years after the event **B**

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S42

O caso do Raul...

- Você o encaminhou o oftalmologista após a primeira consulta na ESF, no entanto após 1 ano de encaminhamento ele não havia sido chamado.

Qual sua conduta?

A. Faz fundoscopia com midriase para avaliar a presença de retinopatia diabética
B. Faz fundoscopia sem midriase para avaliar a presença de retinopatia diabética
C. Voce marca uma foto de retina e só encaminha para o oftalmologista se houver anormalidades, ou se o paciente tiver outras queixas oftalmológicas
D. Espera a consulta no oftalmologista

Retinopatia Diabética

- É a primeira causa de cegueira adquirida após a puberdade
- Prevalência
  - Com 20 anos de doença: 80% no diabetes Tipo 2 e 100% no Tipo 1
  - Tipo 2: 4-8% tem retinopatia ao diagnóstico
  - Proliferativa: após 15 anos 50% no Tipo1e 10% no Tipo 2

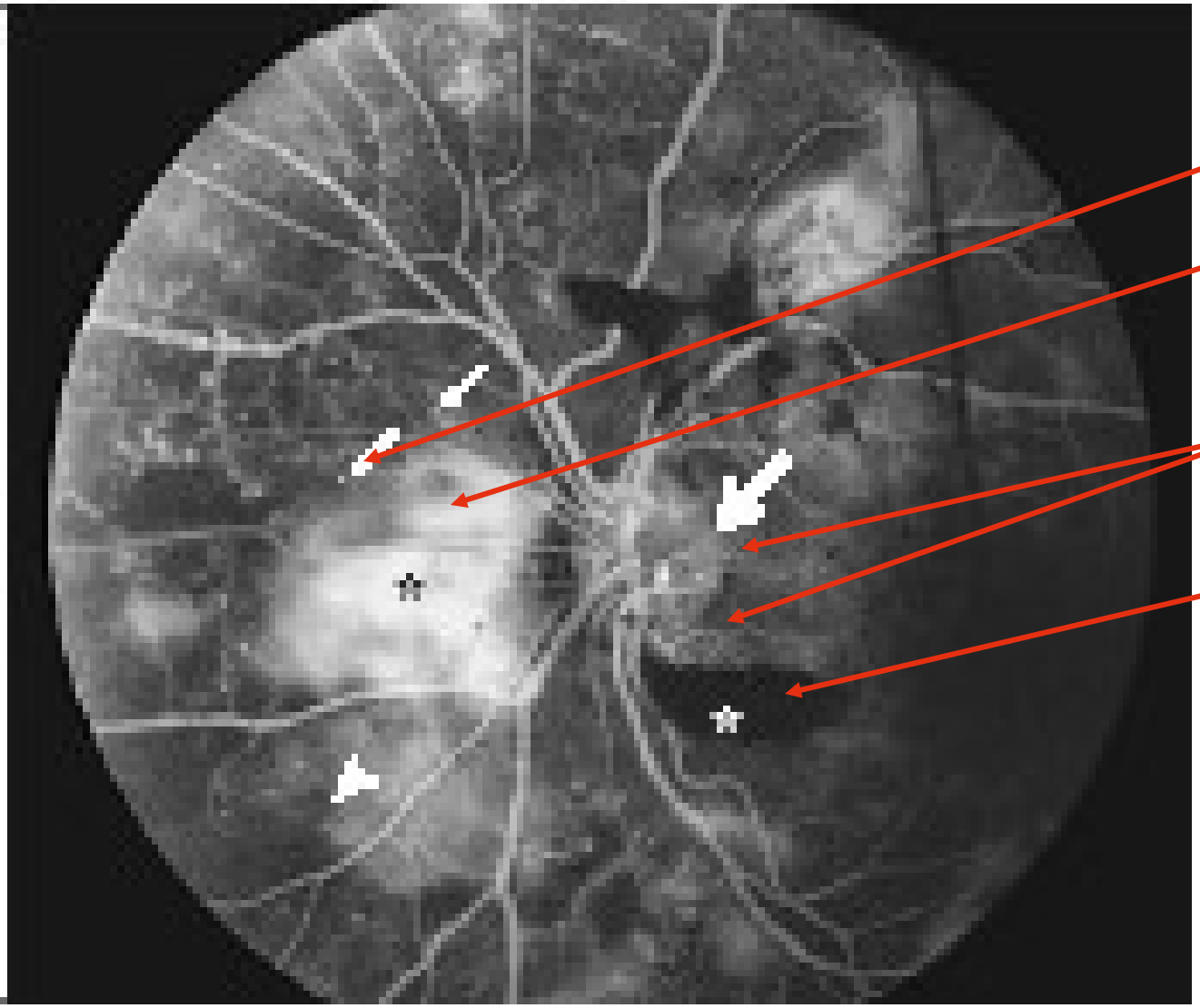
Retinopatia não proliferativa

Leve: microaneurismas, hemorragias intraretinianas, aumento da permeabilidade capilar, exsudatos duros

Moderada: Manchas algodonosas, veias em rosário anormalidades microvasculares intraretinianas

- Grave: perda de capilares, hemorragias intra-retinianas extensas, microaneurismas

Retinopatia proliferativa: neovasos na retina ou disco optico; hemorragias pré-retinianas e ou vitrea acompanhada de neovasos; proliferação fibrovascular, tração retiniana, roturas, descolamento de retina


Microaneurismas
Extravasamento da fluoresceína
Neovasos
Hemorragia Pré-retiniana

Recommendations: Retinopathy

- To reduce the risk or slow the progression of retinopathy
  - Optimize glycemic control **A**
  - Optimize blood pressure control **A**

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S44

Rastreamento

- Objetivo: diagnóstico precoce
- No diabete tipo 1: iniciar após a puberdade ou 5 anos de doença.
- No diabete tipo 2: no diagnóstico
- Periodicidade: a cada ano (ou, se normal, 2-3 anos)
- Métodos:
- Exame oftalmológico completo
- Fotografia do fundo de olho
  - sensibilidade 80%
  - especificidade 95%

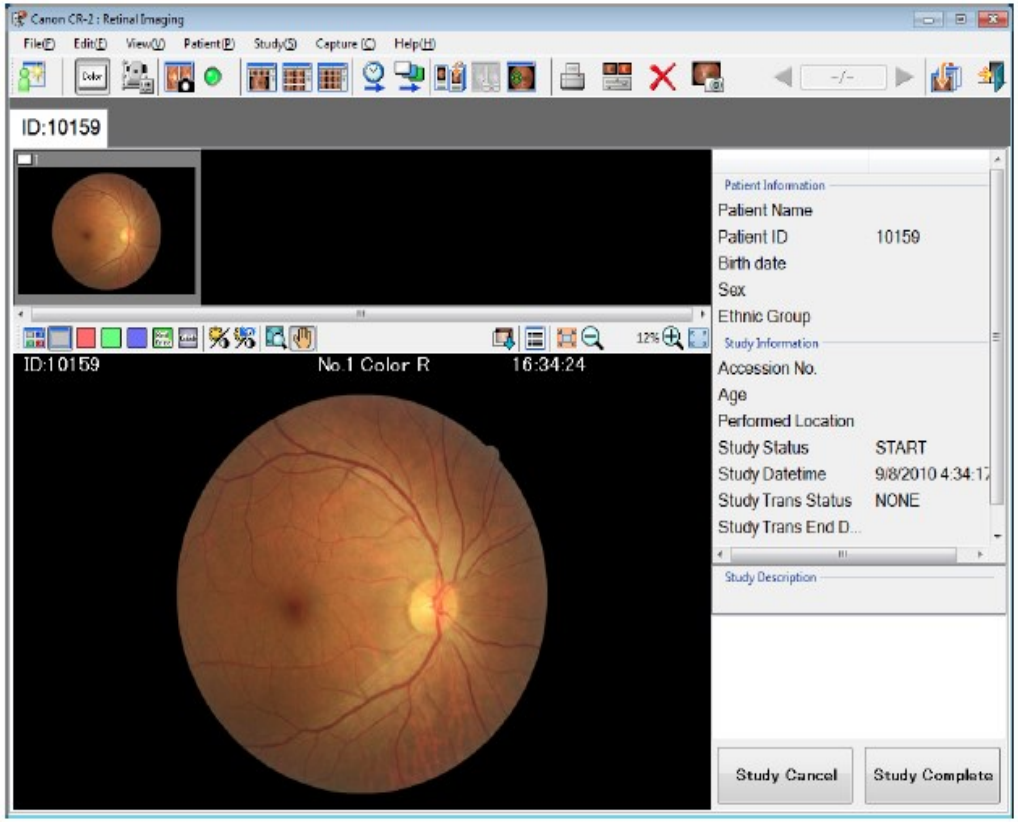
Rasteamento

- A oftalmoscopia direta é um teste usual de rastreamento, mas feita por clínicos não experientes em RD e sem midríase farmacológica tem sensibilidade de 50% para o diagnóstico de retinopatia diabética proliferativa;1
- A retinopatia digital é um exame que vem mostrando acuidade diagnóstica permitindo detecção mais eficiente e ampliação do acesso, porém sua implementação ainda é pouco difundida no Brasil;2

1 Fong DS, Alello LP, Gardner, TW, King, GL; et alli. Diabetic retinopathy. Diabetes care; 2003; 26(s1): s99-102
2 Hutchinson A, McIntosh A, Peters J, O'Keefe C, Khuntit K, Baker R, et al. Effectiveness of screening and monitoring tests for diabetic retinopathy – a systematic review. Diabetic Medicine 2000;17:495-506.

Rasteamento

- No Brasil, um estudo feito em São Paulo mostrou que o intervalo entre o diagnóstico de diabetes e a primeira avaliação oftalmológica variou 3 meses a 18 anos (média de 5,2 + 4,81anos) para diabete tipo 2, sendo, portanto muito maior que o recomendado;



Oliveira Jr. OOM; et alli Avaliação oftalmológica tardia em portadores de retinopatia diabética. Rv Assoc Méd Brasileira. 2007;53(1): 39-43

Tratamento da Retinopatia Diabética

Panfotocoagulação com Laser

Menor progressão do edema macular
(8% tratados X 20% controles)
Early Treatment Diabetic Retinopathy Study (ETDRS)

Reduz a perda visual
(6,4 % tratados X 15,9% controles)
Pacientes de risco
(11% tratados X 26% controles)
Diabetic Retinopathy Stydy (DRS)

Tratamento da Retinopatia Diabética

Controle metabólico intensivo: Reduz a progressão da retinopatia em 54%

Na gestação avaliação a cada 3 meses
Tratamento prévio a gestação

Hemorragia vítrea ou descolamento: vitrectomia

Recommendations: Retinopathy (5)

Treatment (1)

- Promptly refer patients with any level of macular edema, severe NPDR, or any PDR
  - To an ophthalmologist knowledgeable and experienced in management, treatment of diabetic retinopathy **A**
- Laser photocoagulation therapy is indicated **A**
  - To reduce risk of vision loss in patients with
    - High-risk PDR
    - Clinically significant macular edema
    - Some cases of severe NPDR

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Recommendations: Retinopathy (6)

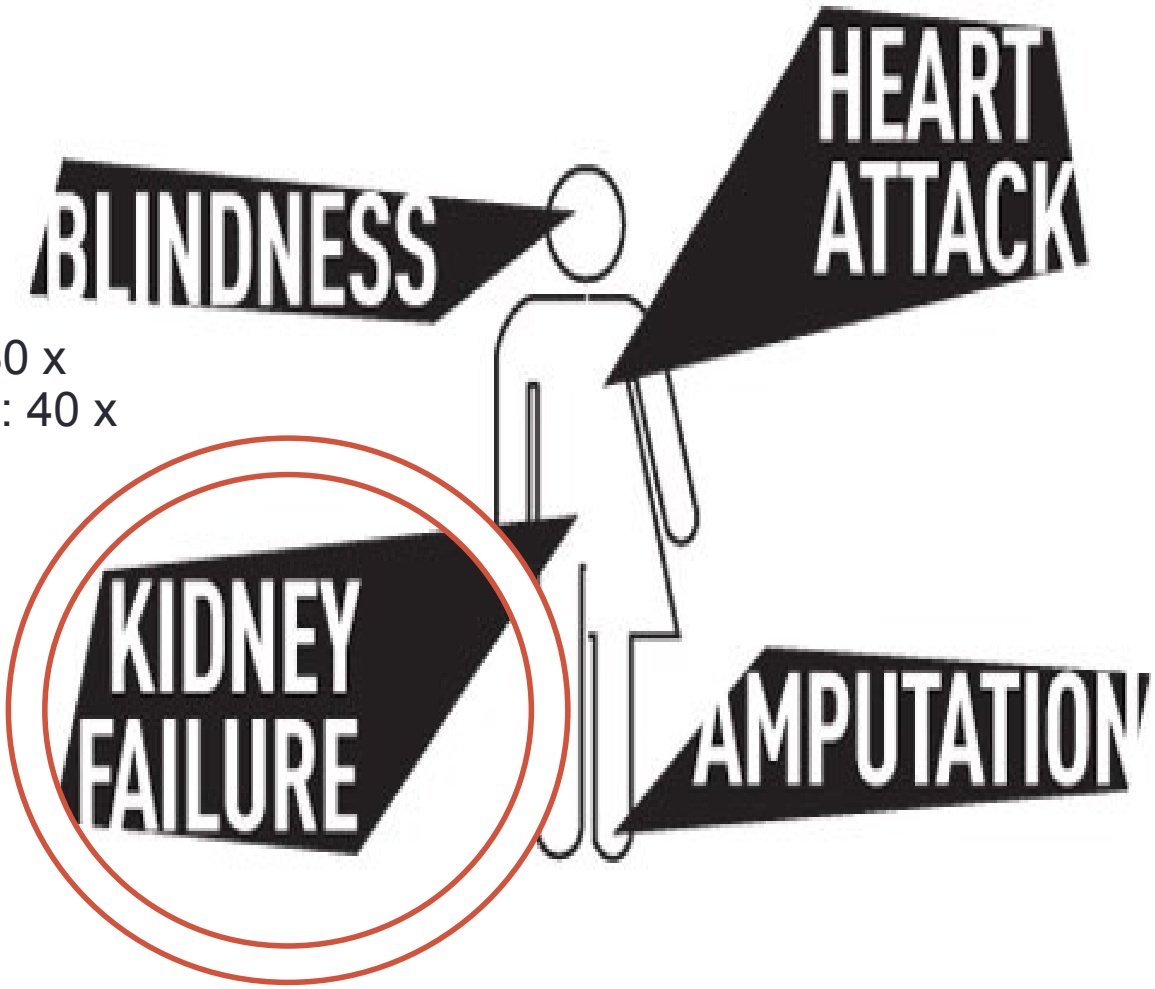
Treatment (2)

- Anti-vascular endothelial growth factor (VEGF) therapy is indicated for diabetic macular edema **A**
- Presence of retinopathy
  - Not a contraindication to aspirin therapy for cardioprotection, as this therapy does not increase the risk of retinal hemorrhage **A**

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S45

Principais complicações do diabetes

Risco de cegueira: 30 x
Amputações em Mis: 40 x
IAM: 2-5 x
AVC: 2-3 x



IDF Diabetes Atlas Sixth Edition, International Diabetes Federation 2013

O caso do Raul...

- A pesquisa de proteinúria urinária mostrou microalbuminúria de 38 mcg/gr creatinina. Ele ficou assustado pois tem um amigo que faz diálise. Pergunta a você se isto acontecerá com ele.

O que voce responde?

A. É pouco provável pois a maioria das pessoas com diabete tem proteinúria e não há significado para isto.
B. Sim, mas pode demorar até 10 anos para precisar de dialise e pode ser feito um transplante renal antes.
C. É um risco, mas o tratamento da pressão, o ajuste da dieta e o cuidado do controle glicêmico podem modificar o curso desta doença. E nem todos as pessoas com proteinúria e diabete tipo 2 evoluem para insuficiência renal.
D. O maior perigo é o senhor ter um infarto.

Evolução da Microalbuminúria

Tipo 1

90 % dos microalbuminúricos progridem
A presença de HAS acelera a perda de função renal
A retinopatia é quase sempre presente
A nefropatia ocorre em 30% dos pacientes após 15 anos de DM

Tipo 2

20-40% dos microalbuminúricos progridem
20% desenvolvem Insuficiência Renal em 20 anos
Presença de microalbuminuria: DCV 30-40 x
A nefropatia ocorre em 20% dos pacientes após 15 anos de DM

Anos de doença	Curso Clínico da nefropatia
0	Rins aumentados, hiperfunção
2	espessamento da MBG, aumento da matriz mesangial
10- 15	microalbuminúria (20-200 mcg/min ou 30-300 mg/24 horas)
10- 20	proteinúria intermitente e persistente
>15	perda da função renal (em média 17 anos)
20	período urêmico

Manejo da Nefropatia

- **Controle Glicêmico**
  - Hb A1C menor que 7: -50% nefropatia em tipo 1
  - Hb A1C menor que 7: -25% nefropatia em tipo2
- **Controle da Pressão Arterial (meta 120/80)**
  - Reduz em 29% o surgimento da microalbuminúria
- **Dieta Hipoprotéica**
  - 0,8 gr/kg/dia- reduz a taxa de queda da filtração glomerular
  - Preferência por carne de peixe e frango

Recommendations: Nephropathy (1)

- Assess urine albumin excretion annually **B**
  - In type 1 diabetic patients with diabetes duration of ≥5 years
  - In all type 2 diabetic patients at diagnosis

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Recommendations: Nephropathy (2)

Treatment (1)

- ACE inhibitor, ARB not recommended in diabetic patients with normal blood pressure, albumin excretion <30 mg/24 h for primary prevention of diabetic kidney disease **B**
- Nonpregnant patient with modestly elevated (30–299 mg/day) **C** or higher levels (>300 mg/day) **A** of urinary albumin excretion
  - Use either ACE inhibitors or ARBs (not both)

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Recommendations: Nephropathy (3)

Treatment (2)

- For people with diabetes and diabetic kidney disease (albuminuria >30 mg/24 h), reducing dietary protein below usual intake not recommended **A**
  - When ACE inhibitors, ARBs, or diuretics are used, monitor serum creatinine, potassium levels for increased creatinine or changes in potassium **E**

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Recommendations: Nephropathy (4)

Treatment (3)

- Reasonable to continue monitoring urine albumin excretion to assess both response to therapy and disease progression **E**
- When eGFR is <60 mL/min/1.73 m2, evaluate and manage potential complications of CKD **E**
- Consider referral to a physician experienced in care of kidney disease **B**
  - Uncertainty about etiology; difficult management issues; advanced kidney disease

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Definitions of Abnormalities in Albumin Excretion

Category	Spot collection (µg/mg creatinine)
Normal	<30
Increased urinary albumin excretion*	≥30

ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S44; Table 11

Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min per 1.73 m^2 body surface area)
1	Kidney damage* with normal or increased GFR	≥90
2	Kidney damage* with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Kidney failure	<15 or dialysis

Management of CKD in Diabetes (1)

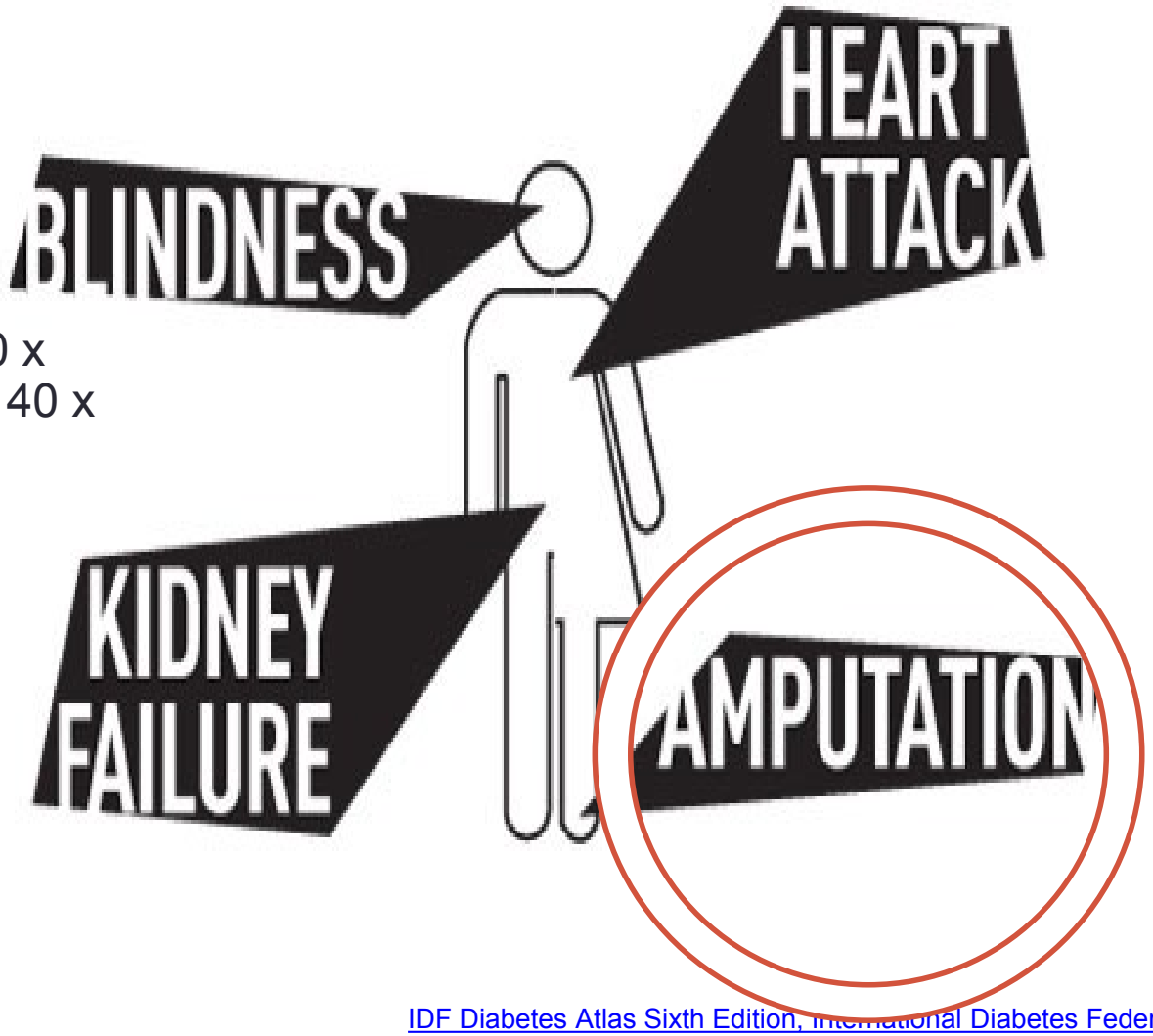
GFR	Recommended
All patients	Yearly measurement of creatinine, urinary albumin excretion, potassium
45-60	Referral to a nephrologist if possibility for nondiabetic kidney disease exists
	Consider dose adjustment of medications
	Monitor eGFR every 6 months
	Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly
	Assure vitamin D sufficiency
	Consider bone density testing
	Referral for dietary counselling

Management of CKD in Diabetes (2)

GFR	Recommended
30-44	Monitor eGFR every 3 months
	Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin weight every 3–6 months
	Consider need for dose adjustment of medications
<30	Referral to a nephrologist

Principais complicações do diabetes

Risco de cegueira: 30 x
Amputações em Mis: 40 x
IAM: 2-5 x
AVC: 2-3 x



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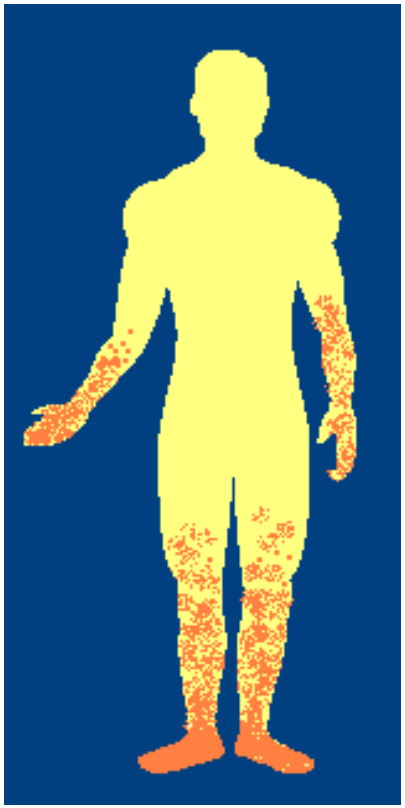
Neuropatia: aspectos clínicos



Polineuropatia Somática

Dor

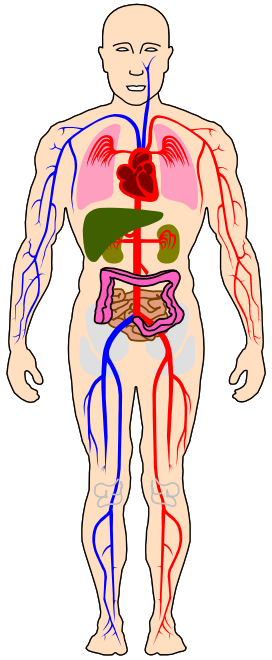
Perda de Sensibilidade

Úlceras

Fraqueza Motora

Neuropatia Autonômica

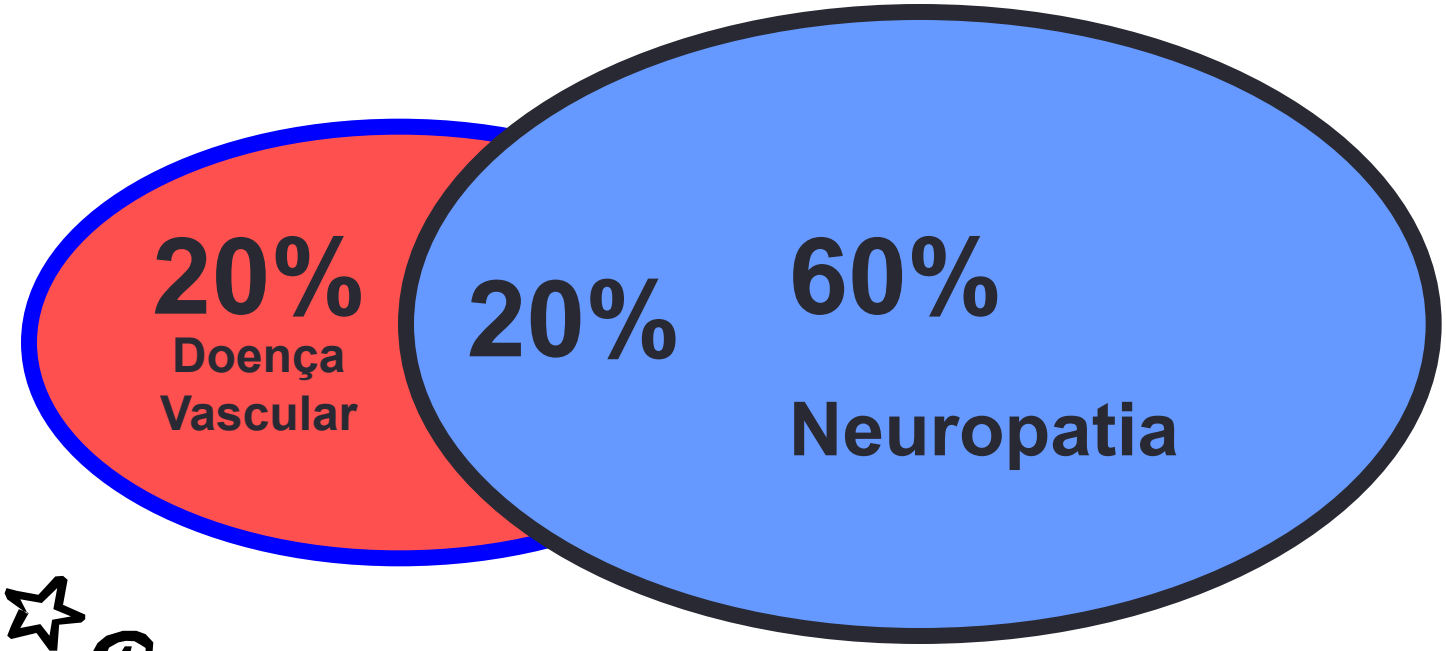
Sintomas: Cardiovasculares, Intestinais, Genito-urinários, Distúrbios de sudorese Distúrbios microcirculatórios



Polineuropatia diabética

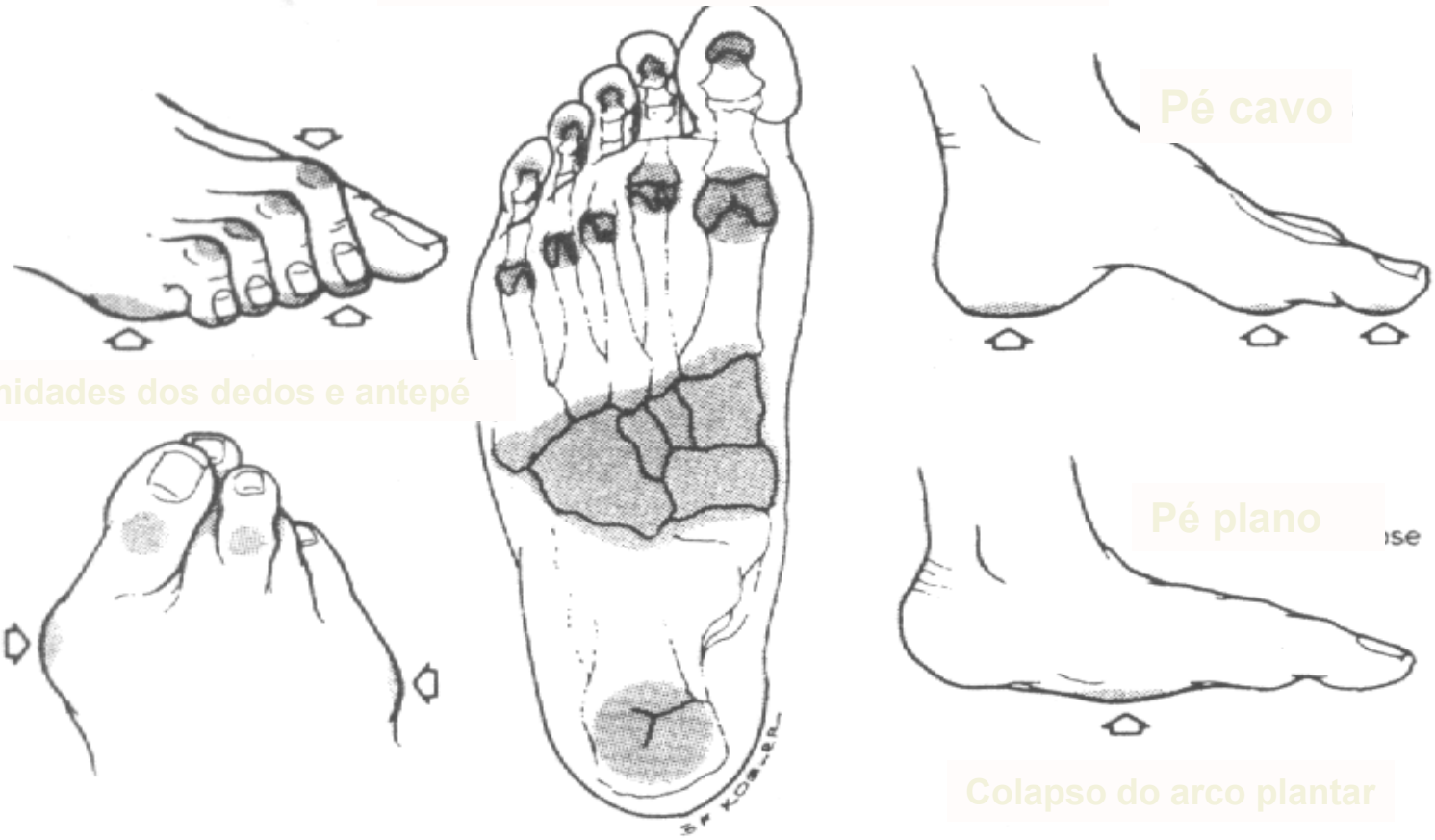
- 15% dos pacientes desenvolverão úlceras nos pés
  - 50% deverão recorrer nos primeiros 2 anos.
- 20% dos indivíduos com úlceras sofrerão amputações
- 85% das amputações são precedidas de úlceras
- Custo direto de cada amputação: $27 000
- O manejo adequado pode curar as lesões e prevenir as amputações em até 50%.

Principais componentes

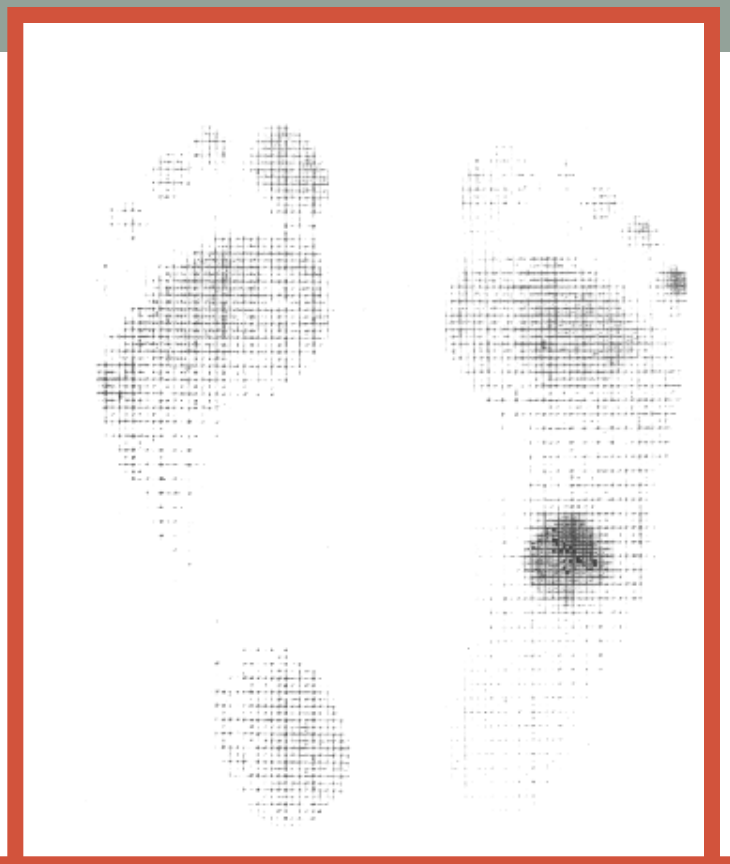


Trauma

Alteração da Bio-mecânica do pé



Pé de Charcot



Pé Neuropático Características clínicas

- Hipotrofia de músculos dorsais
- Acentuação do arco plantar
- Proeminência dos metatarsos
- Vasodilatação dorsal
- Dedos em martelo/ em garra
- Calosidades
- Pele seca - rachaduras
- Pé quente, rosáceo
- Alterações articulares (Charcot)

Pé Isquêmico características clínicas

- Pele fina e brilhante
- Cianose
- Unhas atrofiadas
- Ausência de pêlos
- Rubor postural
- Palidez à elevação
- Pé frio
- Ausência/diminuição de pulsos
- Enchimento capilar > 15 segundos
- Claudicação intermitente

Manejo da Neuropatia Dolorosa

- Controle Glicêmico (sintomas agudos)
- Analgésicos e antinflamatórios não esteróides
- Antidepressivos triciclicos (amitriptilina, imipramina, nortriptilina)
- Fenotiazidas (clorpromazina e levomepromazina)
- Carbamazepina, difenilhidantoína, clonazepam (para dores paroxisticas)
- Gabapentina
- Capsaicina tópica

Recommendations: Neuropathy Screening, Treatment (1)

- All patients should be screened for distal symmetric polyneuropathy (DPN) **B**
  - At diagnosis of type 2 diabetes and 5 years after diagnosis of type 1 diabetes
  - At least annually thereafter using simple clinical tests
- Electrophysiological testing rarely needed
  - Except in situations where clinical features are atypical **E**

Recommendations: Foot Care (1)

- For all patients with diabetes, perform an annual comprehensive foot examination to identify risk factors predictive of ulcers and amputations **B**
  - Inspection
  - Assessment of foot pulses
  - Test for loss of protective sensation: 10-g monofilament plus testing any one of
    - Vibration using 128-Hz tuning fork
    - Pinprick sensation
    - Ankle reflexes
    - Vibration perception threshold

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Recommendations: Foot Care (2)

Upper panel

- To perform the 10-g monofilament test, place the device perpendicular to the skin, with pressure applied until the monofilament buckles
- Hold in place for 1 second and then release

Lower panel

- The monofilament test should be performed at the highlighted sites while the patient's eyes are closed

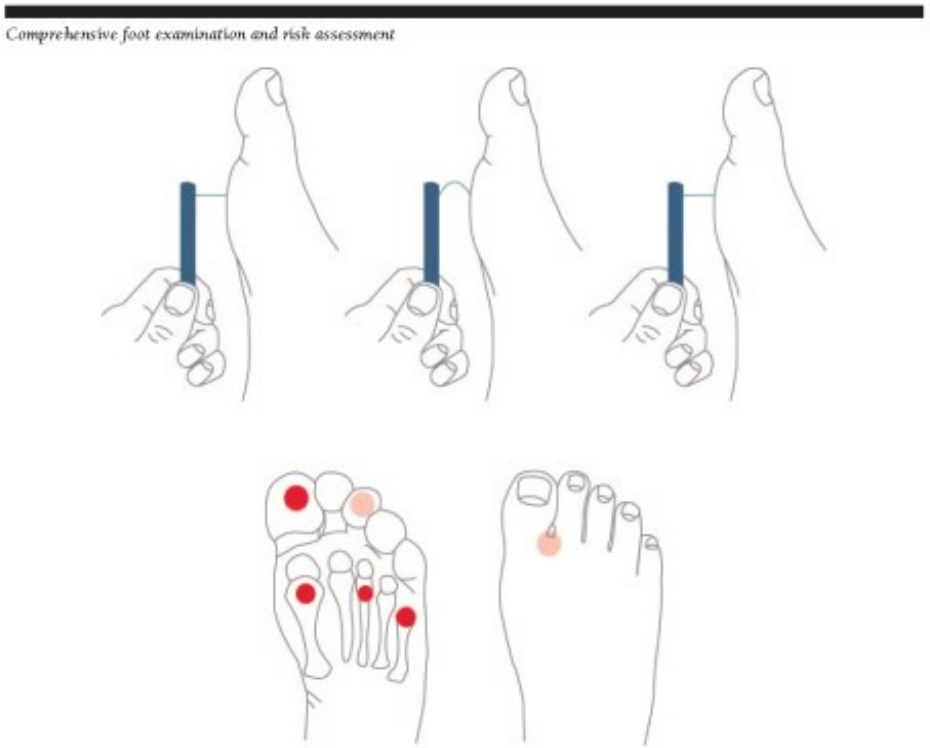

Figure 2—Upper panel: *For performance of the 10-g monofilament test, the device is placed perpendicular to the skin, with pressure applied until the monofilament buckles. It should be held in place for ~1 s and then released.* Lower panel: *The monofilament test should be performed at the highlighted sites while the patient's eyes are closed.*

Recommendations: Foot Care (3)

- Provide general foot self-care education **B**
- Use multidisciplinary approach
  - Individuals with foot ulcers, high-risk feet; especially prior ulcer or amputation **B**
- Refer patients to foot care specialists for ongoing preventive care, life-long surveillance **C**
  - Smokers
  - Loss of protective sensation or structural abnormalities
  - History of prior lower-extremity complications

Recommendations: Foot Care (4)

- Initial screening for peripheral arterial disease (PAD) **C**
  - Include a history for claudication, assessment of pedal pulses
  - Consider obtaining an ankle-brachial index (ABI); many patients with PAD are asymptomatic
- Refer patients with significant claudication or a positive ABI for further vascular assessment **C**
  - Consider exercise, medications, surgical options

Obrigado!