Abordaje del paciente diabético: recomendaciones 2013

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Conflictos de interés

- He recibido honorarios por conferencias, advisory board y/o investigación clínica de:
  - Astra Zeneca
  - Novartis Pharma Logistics Inc
  - Novartis Oncology
  - Novo Nordisk
  - Merck Sharp & Dohme
  - Roche
  - Glaxo SmithKline
  - Sanofi Aventis
  - Boehringer
  - Organon
  - Abbott Nutrición

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Agenda

- Algunas consideraciones de las guías de ADA/ EASD 2012
- Consenso de hipoglicemias
- Guías para el adulto mayor
- Guías canadienses 2013
- Otros aspectos interesantes

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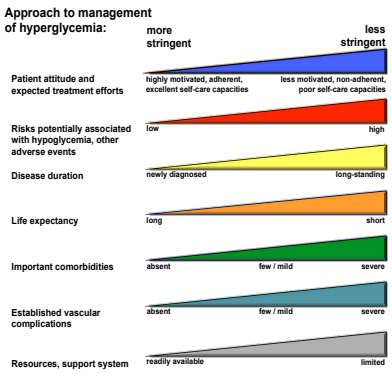

Figure 1

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Diabetes Care, *Diabetologia*. 19 April 2012 [Epub ahead of print]
(Adapted with permission from: Ismail-Beigi F, et al. *Ann Intern Med* 2011;154:554)

Caso #1

- Masculino de 60 años, con DM-2 diagnosticado hace 2 meses durante un internamiento por IAM. IMC 30 kg/m2. Tabaquista.
- Cuál sería su meta de Hba1c?
  1. <6.5%
  2. <7%
  3. <7.5%

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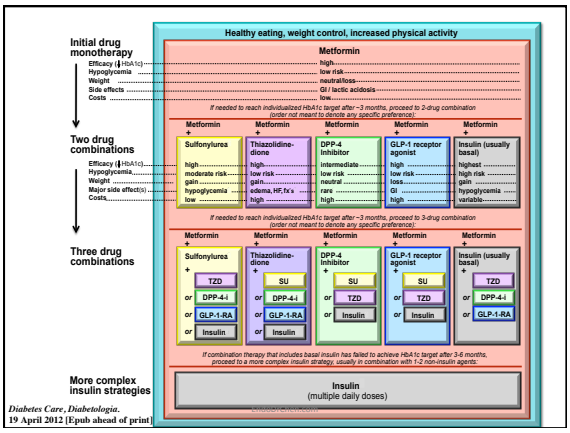
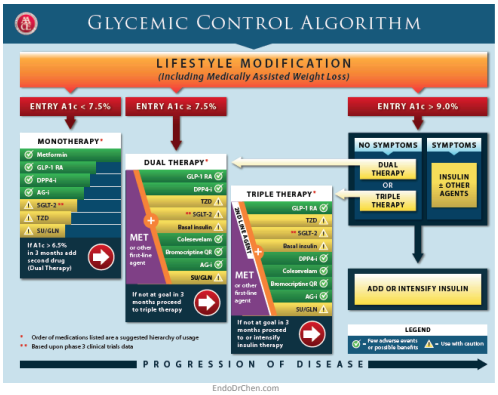
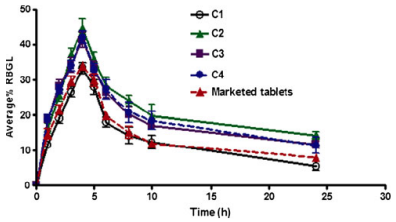


Diabetes Care, *Diabetologia*.
19 April 2012 [Epub ahead of print]



Efecto hipoglicemiante



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Mohamed EA. AAPS PharmSciTech. 2012:13:1013

News Alerts > Medscape Medical News

No Cancer Risk With Insulin Glargine, Says EMA

Lisa Nainggolan | Disclosures

May 31, 2013

5 comments Print Email

Editors' Recommendations

Insulin Glargine Does Not Boost Cancer Risk

New Studies 'Close the Loop' on Cancer/Insulin Link

Drug & Reference Information

Hyperosmolar Hyperglycemic State

Diabetes Mellitus and Pregnancy

Diabetic Lumbosacral Plexopathy

The European Medicines Agency (EMA) has concluded that insulin-glargine–containing medicines (*Lantus*, *Optisulin*, Sanofi) for diabetes do not show an increased risk of cancer, so the balance of the medicine's benefits and risks remains unchanged.

Concern arose after the publication of 4 registry studies some years ago, which highlighted a potential link between insulin-glargine products, which are long-acting, and malignancies, particularly breast cancer. However, in July 2009, the EMA's Committee for Medicinal Products for Human Use (CHMP) concluded that some limitations in the way these studies were conducted meant a link between insulin glargine and cancer could not be confirmed or excluded from the results.

The CHMP therefore requested that Sanofi provide further data; the company subsequently carried out further studies and submitted the results to the CHMP for review.

The new data include results from 2 cohort studies. The first collected information from around 175,000 patients in northern Europe treated with insulin glargine, human insulin, or combined insulin, while the other obtained data from approximately 140,000 patients

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Diagnóstico diabetes gestacional

Perform a 75-g OGTT, with plasma glucose measurement fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with overt diabetes.
The OGTT should be performed in the morning after an overnight fast of at least 8 h.
The diagnosis of GDM is made when any of the following plasma glucose values are exceeded:

- Fasting: ≥92 mg/dL (5.1 mmol/L)
- 1 h: ≥180 mg/dL (10.0 mmol/L)
- 2 h: ≥153 mg/dL (8.5 mmol/L)

American Diabetes Association. Diabetes Care. 2013;36:S11

Hipertensión

- Metas de tratamiento:
  - PAS <140 mm Hg
  - PAD <80 mm Hg
  - Metas menores pueden ser consideradas (<130) para algunos individuos, por ejemplo, más jóvenes, si se puede alcanzar sin mucha carga de tratamiento
- Administre uno o más medicamentos HS
- Para mujeres embarazadas, meta PAS 110-129 y PAD 65-79 mm Hg

American Diabetes Association. Diabetes Care. 2013;36:S11

Lípidos

- Si no se alcanzan las metas con las dosis máximas de estatinas toleradas, se puede considerar como opción terapéutica una meta de reducción de LDL 30-40%
- La terapia combinada no ha mostrado proveer beneficios adicionales comparado a monoterapia con estatinas y usualmente no está recomendado

American Diabetes Association. Diabetes Care. 2013;36:S11

Otras morbilidades

- Hipoacusia
- Apnea obstructiva de sueño
- Hígado graso
- Hipogonadismo
- Enfermedad periodontal
- Cáncer
- Fractura
- Deterioro cognitivo
- depresión

American Diabetes Association. Diabetes Care. 2013;36:S11

ENFERMEDAD PERIODONTAL

J Clin Periodontol 2013; 40 (Suppl. 14): S106–S112 doi: 10.1111/jcpe.12077

Journal of Clinical Periodontology

Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases

Iain L. C. Chapple[1], Robert Genco[2] and on behalf of working group 2 of the joint EFP/AAP workshop*

[1]Periodontal Research Group & MRC Centre for Immune Regulation, University of Birmingham School of Dentistry, Birmingham, UK; [2]University at Buffalo, Oral Biology and Microbiology and Immunology, Buffalo, NY, USA

Enfemerdad periodontal

- Es la condición inflamatorio crónica más frecuente en el mundo
- 50% de los adultos tienen periodontitis
- 60% de los mayores de 65 años
- Periodontitis severa afecta 10-15% de la población
- Iniciado por bacterias, la reacción inflamatoria sistémica viene de la invasión

EndoDrChen.com Chapple ILC. J Clin Periodontol. 2013;40:S106

Periodontitis

- Asociación entre periodontitis y control glicémico e incluso con casos nuevos de DM
- Tratamiento de la enfermedad periodontal puede reducir hba1c en 0.36% en promedio
  - Se desconoce si esto se mantiene a largo plazo
- Tratamiento consiste en debridación mecánica y cuidados ambulatorios. No se recomiendan antibióticos.

EndoDrChen.com Chapple ILC. J Clin Periodontol. 2013;40:S106

CONSENSUS REPORT

Diabetes in Older Adults

care.diabetesjournals.org DIABETES CARE 1

Diabetes Care Publish Ahead of Print, published online October 25, 2012

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DM en adultos mayores

- Prevalencia 22-33%
- 1/3 no diagnosticados
- No es lo mismo el diabético que llega a la tercera edad al que inicia en la tercera edad
- Mayor prevalencia de complicaciones
- Tamizar si el tratamiento va a proveer beneficios
- No hay ensayos clínicos específicos para esta población

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Patient characteristics/ health status	Rationale	Reasonable A1C goal (A lower goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden)	Fasting or preprandial glucose (mg/dL)	Bedtime glucose (mg/dL)	Blood pressure (mmHg)	Lipids
Healthy (Few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5%	90–130	90–150	<140/80	Statin unless contraindicated or not tolerated
Complex/intermediate (Multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild to moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90–150	100–180	<140/80	Statin unless contraindicated or not tolerated
Very complex/poor health (Long-term care or end-stage chronic illnesses** or moderate to severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%†	100–180	110–200	<150/90	Consider likelihood of benefit with statin (secondary prevention moreso than primary)

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CALCULADORA RIESGO DE MORTALIDAD: SCORE GARGANO

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Gargano Mortality Risk Score

All-cause 2-year mortality risk score in patients with type 2 diabetes mellitus

Age (yrs)	
Antihypertensive drug (yes/no)	no
Insulin therapy (yes/no)	no
BMI (Kg/m2)	
HDL (mg/dl)	
LDL (mg/dl)	
Triglyceride (mg/dl)	
Diastolic Blood Pressure (mmHg)	
ACR (mg/mmol)	

Run

Reference:

S De Cosmo[1*], M. Gaspeti[2*], O. Lamacchia[1], A. Fontana[2], M. Masoi[1], E. Mastio[1], A. Pacilli[1], S Fiorelis[1], A. Pdrini[1], A. Bonow[1], R. Vist[1], B. Di Paolo[1], C. Menaghi[1], M. Cignarelli[1], F. Pellegrini[2,3], V. Trischitta[4,5]
Development and validation of a predicting model of all-cause mortality in patients with type 2 diabetes mellitus
Diabeter Care, May 1, 2013, doi: 10.2337/dc12-1906

http://www.operapadrepio.it/rcalc/rcalc.php

EndoDrChen.com

Caso #2

Gargano Mortality Risk Score

All-cause 2-year mortality risk score in patients with type 2 diabetes mellitus

Age (yrs)	60
Antihypertensive drug (yes/no)	yes
Insulin therapy (yes/no)	no
BMI (Kg/m2)	30
HDL (mg/dl)	34
LDL (mg/dl)	132
Triglyceride (mg/dl)	280
Diastolic Blood Pressure (mmHg)	80
ACR (mg/mmol)	20

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Gargano Mortality Risk Score

All-cause 2-year mortality risk score in patients with type 2 diabetes mellitus

Results

RISK SCORE (0.00-1.00)
0.56

RISK CLASS (LOW: 0.00-0.67; MEDIUM: 0.68-0.79; HIGH: 0.80-1.00)
LOW RISK SCORE

ANNUAL INCIDENCE RATE
1 per 100 person-year

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GUIÍAS HIPOGLICEMIA ADA/ ENDOCRINE SOCIETY 2013

Guías hipoglicemia

- Nivel de alerta <70 mg/dl
  - No implica ingesta de CHO
  - Poner más cuidado, ajustar tratamiento, evitar ejercicio hasta que esté más alto
  - Definirlo como umbral en sensor
  - Todas las definiciones de hipoglicemia (severa, asintomática, etc) basado en este valor

Seaquist ER. Diabetes Care. 2013. Online 15 abril.

Márgenes de error

- Glucómetros
  - Variación de lecutra ± 20% si >75 mg/dl
  - Si <75 mg/dl ± 15 mg/dl
  - Implicaciones importantes para ajuste de dosis en situaciones críticas que pueden contribuir a la alta tasa de hipoglicemias en los estudios en UCI
- Sensores
  - Entre 40-80 mg/dl: exactitud 60-73%
  - No recomendado para manejo intrahospitalario

Seaquist ER. Diabetes Care. 2013. Online 15 abril.

Riesgos asociados

- 4-10% de las muertes en DM-1 están asociados a hipoglicemias
- En DM-2, los estudios cardiovasculares han mostrado la asociación de hipoglicemia severa con el riesgo subsecuente de mortalidad
- En asilos de ancianos, PROHIBIDO usar sliding scales y glibenclamida y sustituirlos por secretagogos de acción corta o agentes que no produzcan hipoglicemias

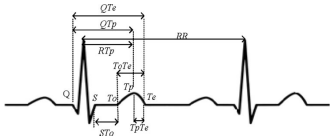
Seaquist ER. Diabetes Care. 2013. Online 15 abril.

Otros

- Se hace una serie de recomendaciones sobre monitoreo para evitar hipoglicemias
- Educación para evitar hipoglicemias
- Uso de bombas de insulina que se apagan durante un período máximo de 2 horas cuando el sensor cae por debajo de cierto umbral
- Futuras investigaciones

Seaquist ER. Diabetes Care. 2013. Online 15 abril.

Cambios ECG en hipoglicemia

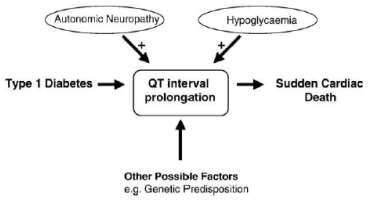


ECG parameter	Nonhypoglycemia	Hypoglycemia	*p* value
HR	1.052 ± 0.061	1.197 ± 0.128	<0.0001
QTe_c	1.040 ± 0.031	1.074 ± 0.054	<0.0001
$TpTe_c$	1.031 ± 0.032	1.074 ± 0.071	<0.0001
QTp_c	1.058 ± 0.071	1.106 ± 0.096	<0.005
$ToTe_c$	1.058 ± 0.071	1.106 ± 0.096	<0.005
RTp_c	1.044 ± 0.039	1.068 ± 0.056	<0.01
STo_c	0.994 ± 0.141	0.940 ± 0.193	<0.1

Nuryani N. Annals Biomed Eng. 2012;40:934

Sudden death in type 1 diabetes:
The mystery of the 'dead in bed' syndrome

Emily Tu [a,b], Stephen M. Twigg [b,c], Christopher Semsarian [a,b,d,*]



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Tu E. Int J Cardiol. 2008

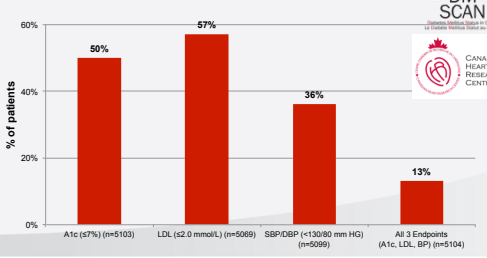
Canadian Diabetes Association
2013 Clinical Practice Guidelines

The Essentials

guidelines.diabetes.ca | 1-800-BANTING (226-8464) | diabetes.ca

Canadian Diabetes Association

Guideline Targets Achieved



DM SCAN

Canadian Heart Research Centre

Leiter LA et al. Can J Diabetes 2013; in press

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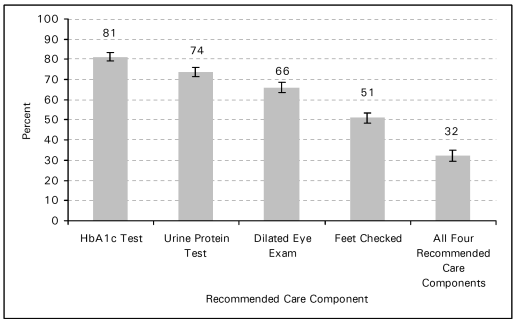
Canadian Diabetes Association

Care gap still exists for screening



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Canadian Institute of Health Information – Diabetes Care Gap 2009

2013

Targets Checklist

- ✓ **A1C ≤ 7.0%** for **MOST** people with diabetes
- ✓ **A1C ≤ 6.5%** for **SOME** people with T2DM
- ✓ **A1C 7.1-8.5%** in people with specific features

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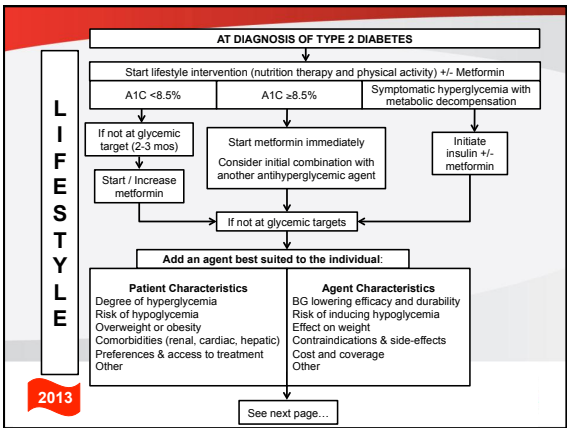

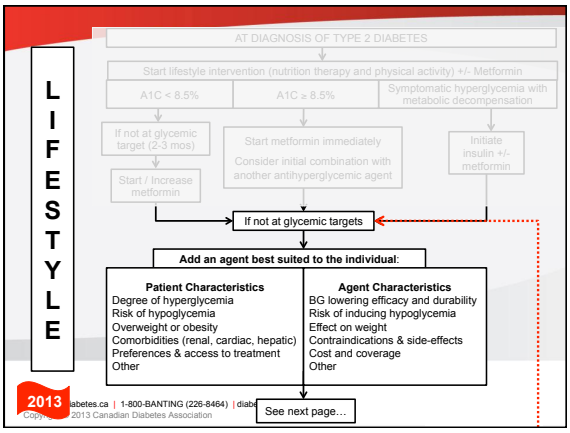

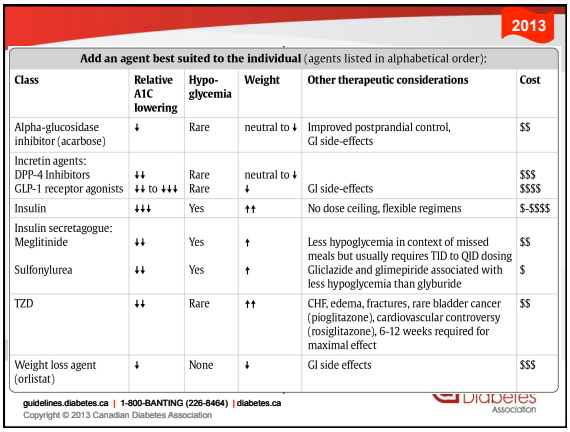

2013

Add an agent best suited to the individual (agents listed in alphabetical order):

Class	Relative A1C lowering	Hypo-glycemia	Weight	Other therapeutic considerations	Cost
Alpha-glucosidase inhibitor (acarbose)	↓	Rare	neutral to ↓	Improved postprandial control, GI side-effects	$$
Incretin agents: DPP-4 Inhibitors GLP-1 receptor agonists	 ↓↓ ↓↓ to ↓↓↓	 Rare Rare	 neutral to ↓ ↓	 GI side-effects	 $$$ $$$$
Insulin	↓↓↓	Yes	↑↑	No dose ceiling, flexible regimens	$-$$$$
Insulin secretagogue: Meglitinide Sulfonylurea	 ↓↓ ↓↓	 Yes Yes	 ↑ ↑	 Less hypoglycemia in context of missed meals but usually requires TID to QID dosing Gliclazide and glimepiride associated with less hypoglycemia than glyburide	 $$ $
TZD	↓↓	Rare	↑↑	CHF, edema, fractures, rare bladder cancer (pioglitazone), cardiovascular controversy (rosiglitazone), 6-12 weeks required for maximal effect	$$
Weight loss agent (orlistat)	↓	None	↓	GI side effects	$$$

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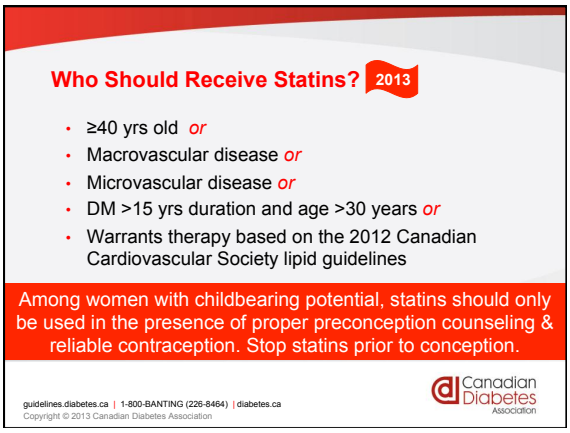

2013

If Triglycerides > 10.0 mmol/L …

- Use a **FIBRATE** to reduce the risk of pancreatitis
- Optimize glycemic control
- Implement lifestyle interventions
  - Weight loss
  - Optimal dietary strategies
  - Reduce alcohol

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2013

Who Should Receive ACEi or ARB Therapy?

- ≥55 years of age *or*
- Macrovascular disease *or*
- Microvascular disease

At doses that have shown vascular protection (ramipril 10 mg daily, perindopril 8 mg daily, telmisartan 80 mg daily)

Among women with childbearing potential, ACEi or ARB should only be used in the presence of proper preconception counseling & reliable contraception. Stop ACEi or ARB either prior to conception or immediately upon detection of pregnancy

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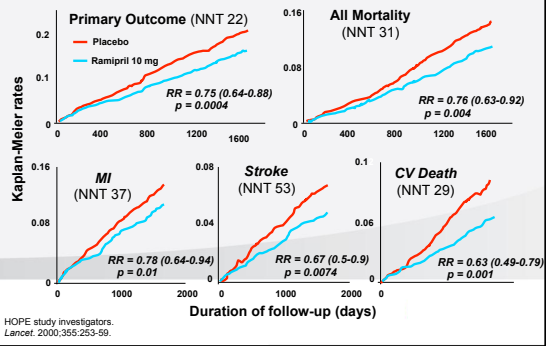
Micro-HOPE (ACEi): CV Benefits



HOPE study investigators.
Lancet. 2000;355:253-59.

ASA for 1º Prevention in Diabetes

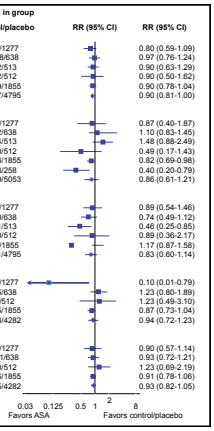
Meta analysis of 6 studies (n = 10,117)

No overall benefit for:
- Major CV events
- MI
- Stroke
- CV mortality
- All-cause mortality

JPAD = Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes
POPADAD = Prevention of Progression of Arterial Disease and Diabetes
PPP = Primary Prevention Project
ETDRS = Early Treatment Diabetic Retinopathy Study
PHS = Physicians' Health Study
WHS = Women's Health Study

De Beradis G, et al. BMJ 2009; 339:b4531.

	No. of events/No. in group: ASA	Control/placebo	RR (95% CI)
Major CV events			
JPAD	68/1262	86/1277	0.80 (0.59-1.09)
POPADAD	105/638	108/638	0.97 (0.76-1.24)
WHS	58/514	62/513	0.90 (0.63-1.29)
PPP	20/519	22/512	0.90 (0.50-1.62)
ETDRS	350/1856	379/1855	0.90 (0.78-1.04)
Total	601/4789	657/4795	0.90 (0.81-1.00)
Myocardial infarction			
JPAD	28/1262	14/1277	0.87 (0.40-1.87)
POPADAD	90/638	82/638	1.10 (0.83-1.45)
WHS	36/514	24/513	1.48 (0.88-2.49)
PPP	5/519	10/512	0.49 (0.17-1.43)
ETDRS	241/1856	283/1855	0.82 (0.69-0.98)
PHS	11/275	26/258	0.40 (0.20-0.79)
Total	395/5064	439/5053	0.86 (0.61-1.21)
Stroke			
JPAD	12/1262	32/1277	0.89 (0.54-1.46)
POPADAD	37/638	50/638	0.74 (0.49-1.12)
WHS	15/514	31/513	0.46 (0.25-0.85)
PPP	9/519	10/512	0.89 (0.36-2.17)
ETDRS	92/1856	78/1855	1.17 (0.87-1.58)
Total	181/4789	201/4795	0.83 (0.60-1.14)
Death from CV causes			
JPAD	1/1262	10/1277	0.10 (0.01-0.79)
POPADAD	43/638	35/638	1.23 (0.80-1.89)
PPP	10/519	8/512	1.23 (0.49-3.10)
ETDRS	244/1856	275/1855	0.87 (0.73-1.04)
Total	298/4275	328/4282	0.94 (0.72-1.23)
All-cause mortality			
JPAD	34/1262	38/1277	0.90 (0.57-1.14)
POPADAD	94/638	101/638	0.93 (0.72-1.21)
PPP	25/519	20/512	1.23 (0.69-2.19)
ETDRS	340/1856	366/1855	0.91 (0.78-1.06)
Total	493/4275	525/4282	0.93 (0.82-1.05)



Does This Patient Require Vascular Protective Medications?

STEP 1: Does the patient have end organ damage?

☐ Macrovascular disease
- Cardiac ischemia (silent or overt)
- Peripheral arterial disease
- Cerebrovascular/Carotid disease

YES → STATIN* + ACEi or ARB# + ASA (Clopidrogrel if ASA-intolerant)

OR

☐ Microvascular disease
- Retinopathy
- Nephropathy (ACR ≥ 2.0)
- Neuropathy

YES → STATIN* + ACEi or ARB#

NO

STEP 2: What is the patient's age?

☐ ≥ 55 years — YES → STATIN* + ACEi or ARB#

OR

☐ 40-54 years — YES → STATIN*

NO

STEP 3: Does the patient…

☐ Have diabetes > 15 years AND age > 30 years

☐ Warrant statin therapy based on the 2012 Canadian Cardiovascular Society Lipid Guidelines

YES → STATIN*

Conclusiones

- Metas de Hba1c puede ser que no sea tan fácil de establecer
- Nuevas metas de control de HTA y lípidos
- Algunas diferencias entre guías de ADA y canadienses
- Papel relevante de hipoglicemias
- Ponerle atención a periodontitis
- Scores de mortalidad como herramienta adicional para estratificación de riesgo

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Preguntas…

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