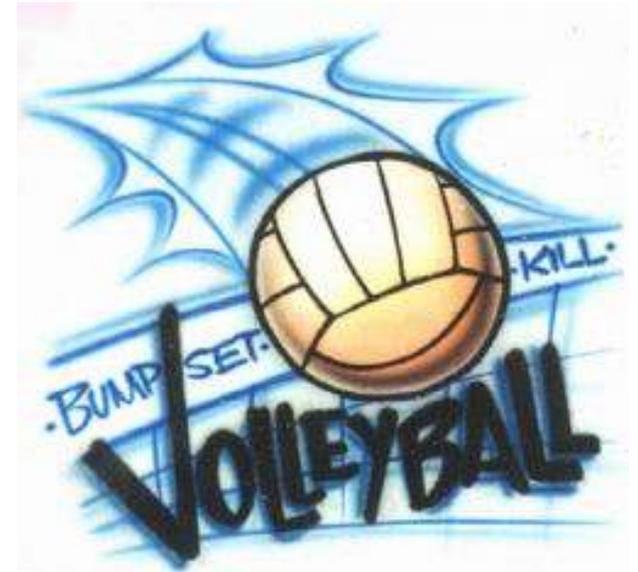


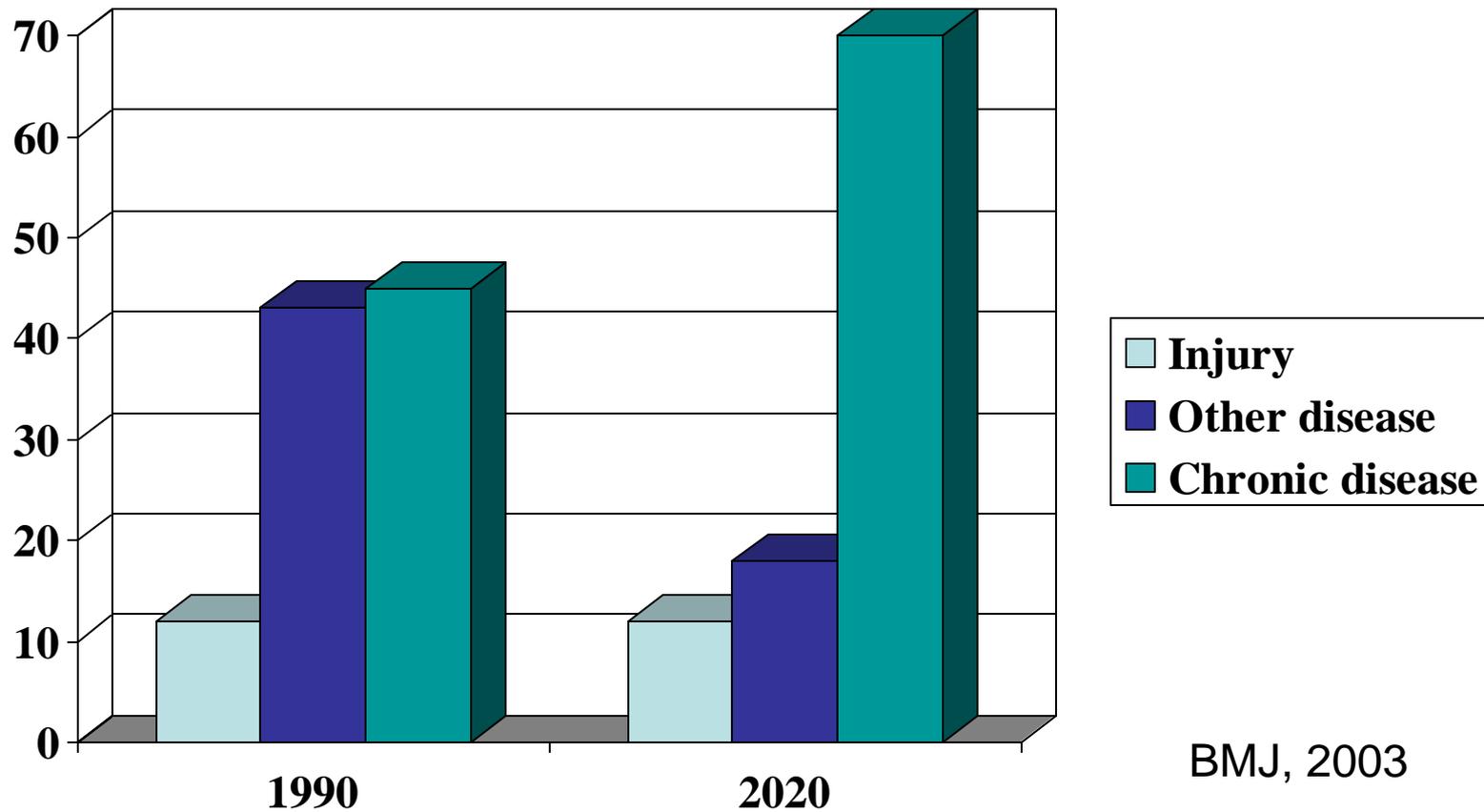
**DIABETES FOR THE PRIMARY
CARE PROVIDER...WHAT WE CAN
DO AS PCP'S...PART I**

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SEPTEMBER 22, 2005**

This product was developed by the Providence St. Peter Family Medicine Residency Program in Olympia, WA with support from the Robert Wood Johnson Foundation © in Princeton, NJ.



What you will be seeing in practice



So who is better? FP's or Endo

- Specialist
 - <10%
 - Give better foot care
 - More likely to use insulin
 - Use newer and more expensive meds
 - Outcomes are better when in an organized program
- Generalist
 - >90%
 - More likely to have other health issues addressed
 - Less likely than non-DM (ie mammograms)
 - Less likely to work in a Chronic Care Program

Only 9% of patients are at goal for HBA1c, BP, Lipids, ASA, and Screening

Medical Outcomes Study found little advantage between Endocrine and FP's

Overall functional status at 4 yrs and mortality at 7 years was the same...but

45 year old

BMI= 33

Great-grandmother
with DMII

Loves the couch

Wants to know if he
needs to be
screened for DM



Should we screen?

- DM II is a major public health affecting 8% of the population
- There is a long asymptomatic period
- There is an available and inexpensive test
- DM II is a treatable condition
- Treatment can result in prevention/delay of complications
- Jury is out as to whether it is cost effective or not (common sense says it does make sense, but our track record for tx DM effectively isn't good)

So who and when?



...so how?

- Fasting BS (ADA)
- The IHOP challenge (WHO)...
- In 2003 an *international expert committee* issued a report revising recommendations- FBS X2

FBS = 105

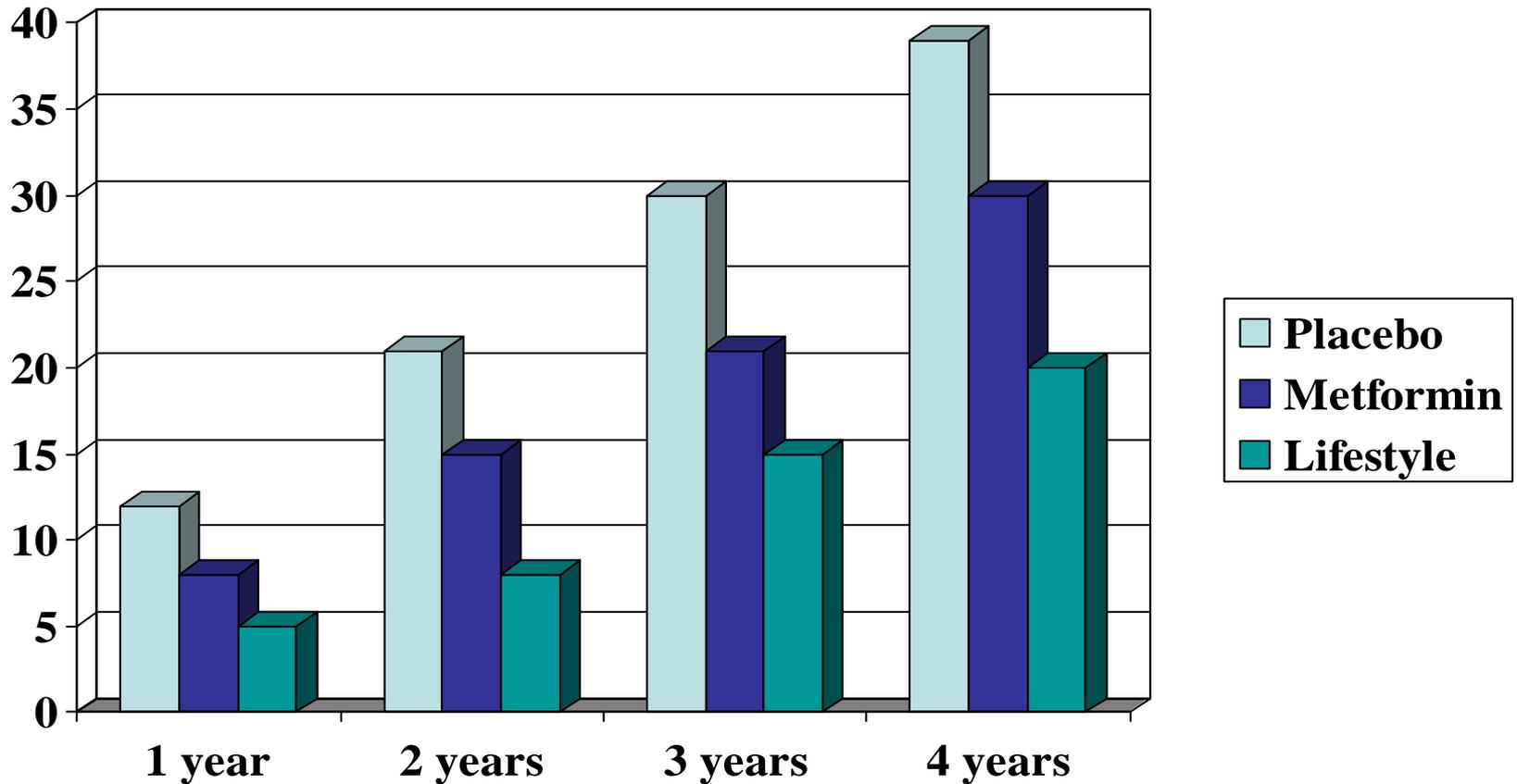
So what do you tell him?

IFG

- FBS between 100 and 125
- NOT at risk for developing *microvascular* disease, but is at risk for MACROvascular disease and going on to develop DM II
- Lipids, BP, smoking, obesity.. become important issues to talk about
- 15-20% of population have IFG
- Once IFG, screen every year there after
- IS REVERSABLE (or at least DM can be delayed)



Diabetes Prevention Trial

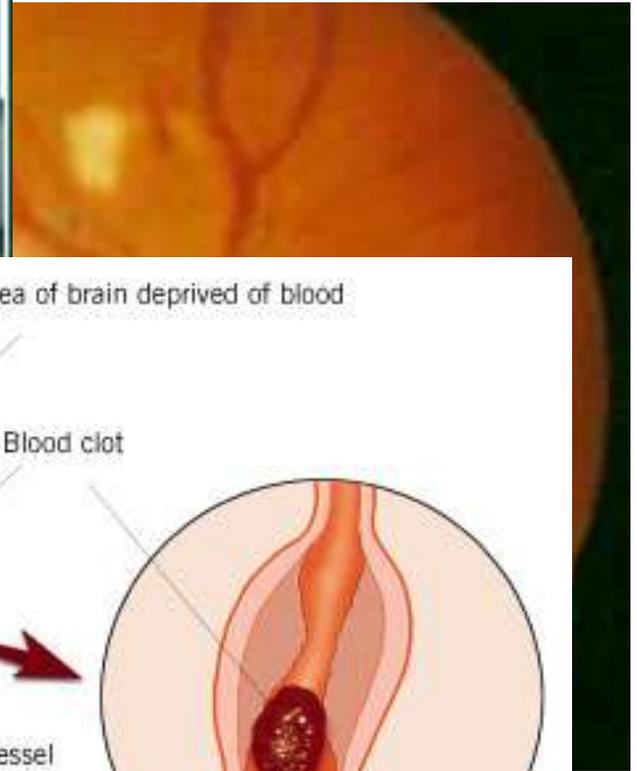


10 years later...

- 55 yo “let myself go”
 - known DMII
 - Obesity
 - still smoking
 - Hypertension
 - ...wants to “start over”
- Where is he heading?
- What do you do?



Ghost of Christmas Future...



Start small...don't go overboard

- HBA1c
- BP
- Lipids
- Weight
- Look for end organ damage (microvascular disease)
- Screen for macrovascular disease
- BS home monitoring
- DM meds
- HTN meds
- ASA
- Referrals
- Immunizations
- Screen for depression
- Smoking cessation counselling
- Diet
- Exercise

Where do you start? Let the patient guide you

He wants to talk DM Meds...

- Increase insulin release
- Increase insulin responsiveness
- Modify intestinal absorption of carbs
- Give exogenous insulin

Drugs that increase insulin secretion

- Sulfonylureas (glyburide, glipizide)
 - Oldest class of drugs
 - Can expect a HBA1c 1-2% reduction
 - “Bridge to insulin”
 - Watch for hypoglycemia
 - Cheap
 - Effectiveness wanes over time
 - Be careful with CRI/CRF
 - 2.5mg to 10mg daily or BID

Drugs that increase insulin secretion

- Meglitinides (Starlix, Prandin)
 - TID dosing before meals
 - No renal clearance
 - Otherwise same as Sulfonylureas
 - Much more expensive
 - Not used very often



Drugs that improve insulin action

- Biguanides (Metformin)
 - Decrease liver glucose output, increase peripheral insulin sensitivity
 - Can improve lipid profile
 - Patients can loose weight (or maintain)!!! In UKPDS :
 - only group that didn't gain weight
 - Obese patients were less likely to die (*decreased risk of aggregate diabetes related endpoint and all-cause mortality*)
 - BID (500 or 850) with meals, 2550mg max
 - Be careful with RI
 - Getting cheaper
 - No hypoglycemia (but...)

Drugs that improve insulin action

- Thiazolidinediones (rosiglitazone- *Avandia*, and pioglitazone- *Actos*)
 - Act by increasing glucose utilization and decreasing glucose production
 - Mechanism not well understood
 - Best when used in combination, but be careful with insulin
 - Not as good monotherapy agents
 - Associated with weight gain
 - Expensive
 - Fluid retention- can make CHF worse

Drugs that modify the intestinal absorption

- The alpha-glucosidase inhibitors (Acarbose and Miglitol) and lipase inhibitors
 - Work best to lower PP BS, and HA1c reduction proportional to weight loss
 - May help lipid profile
 - Likely to cause flatulence (73%) and diarrhea
 - 16-20% of patients were still taking med after 1 year with a further 50% of those who stopped in year 2
 - Can expect a HBA1c reduction of 0.5 to 1%
 - 50 to 100mg with 1st bite of each meal

Insulin therapy

- Usually after combination orals are no longer effective
- Studies suggest we probably don't start soon enough (patient/provider *fear* of insulin)
- Think of insulin earlier in the young adult who may have presented with wt loss or in DKA (late type I or type 3)
- Dosing based on FBS and weight (markers for insulin resistance)

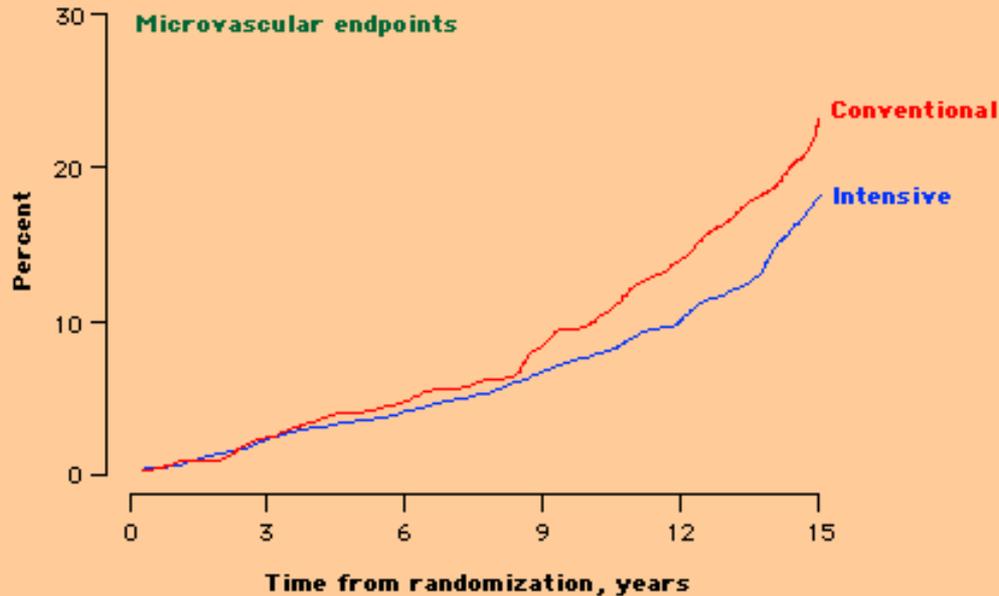
Insulin therapy

Initial Insulin Dose in Patients with Type 2 Diabetes According to Fasting Blood Glucose (FBG) and Degree of Obesity†

FBG, mg/dL	FBG, mmol/L	Percent ideal body weight					
		100	120	140	160	180	200
108	6	6	9	12	15	18	21
144	8	10	15	20	25	30	35
180	10	14	21	28	35	42	49
216	12	18	27	36	45	54	63
≥252	≥14	22	33	44	55	66	77

†Adapted from Holman, RR, Turner, RC, Diabetic Med 1985; 2:45.

Lantus	2 hrs	no peak	24 hrs
Ultralente	4 hrs	10-20 hrs	12-20 hrs
NPH/Lente	2 hrs	6-10 hrs	18-24 hrs
Regular	30 mins	2-4 hrs	5-8 hrs
Novalog, Humalog	5-15 mins	45-75 mins	2-4 hrs



Intensive glycaemic control prevents microvascular disease in patients with type 2 diabetes Kaplan-Meier plots of aggregate endpoints of microvascular disease in patients with type 2 diabetes mellitus in the United Kingdom Prospective Diabetes Study who were randomly assigned to receive either intensive therapy with a sulfonylurea or insulin or to conventional treatment with diet; drugs were added if the patients had hyperglycaemic symptoms or fasting blood glucose concentrations greater than 270 mg/dL (15 mmol/L). Intensive therapy was associated with a 25 percent reduction ($P = 0.01$) in the development of microvascular disease, which was defined as renal failure, death from renal failure, retinal photocoagulation, or vitreous hemorrhage. (Data from UK Prospective Diabetes Study, *Lancet* 1998; 352:837.)

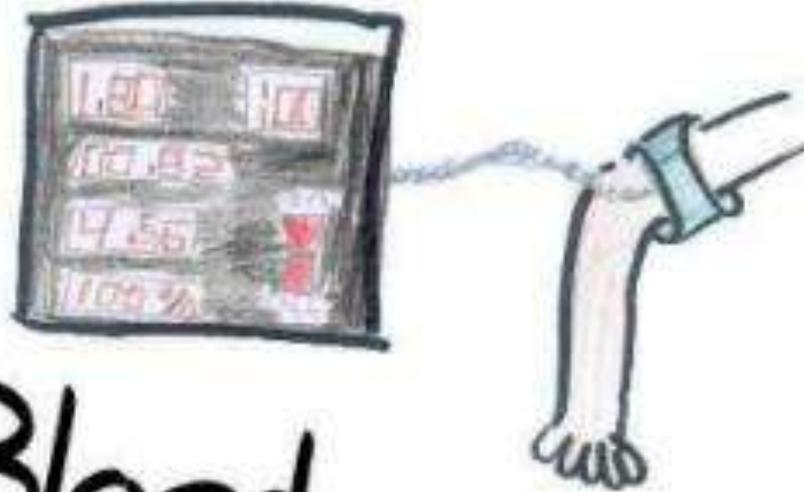
- Patients gain weight
- Issues with adherence
- Problems with hypoglycemia

- **Look for the motivated patient**

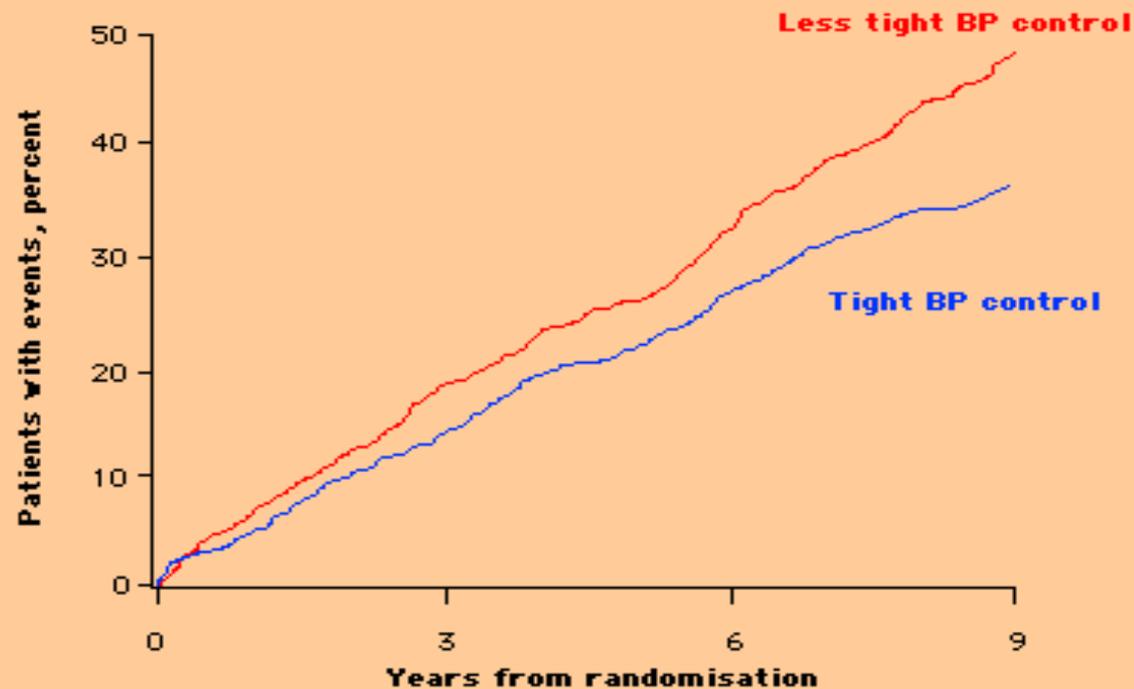
Benefits of lowering BS?

- Risk reduction from micro-vascular complications (DCCT and UKPDS)
 - Nephropathy (50% RR A1c 12 to 8)
 - Retinopathy (linear reduction with A1c)
 - Neuropathy
 - NNT (per UKPDS) was 19.6 patients to prevent one diabetes related endpoint at 10 years (with intensive therapy and average A1c of 7)
 - Benefits are independent of method, and UKPS summary “no firm conclusions regarding the optimal choice of therapy can be made at this time”
- Macro-vascular complications? probably negligible benefits

Next...BP=154/87...and he wants
to *go there*



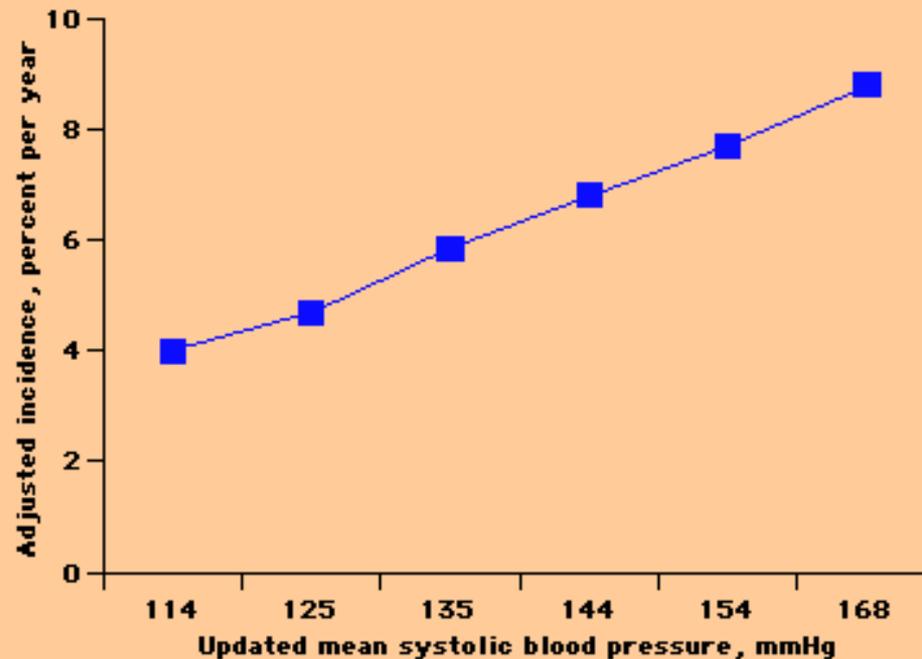
Blood
Pressure
Cuff



Number of patients at risk:

Less tight control	390	321	247	106
Tight control	758	640	494	235

Tight blood pressure control in type 2 diabetes Kaplan-Meier plot of the proportion of patients with type 2 diabetes with a clinical endpoint, fatal or nonfatal, according to the degree of blood pressure (BP) control in the UKPDS. The mean BP in the two groups was 144/82 and 154/87 mmHg, respectively. At eight to nine years, patients in the tight BP control group had a 24 percent reduction in diabetes-related endpoints, including microvascular disease (37 versus 49 percent, $P = 0.0046$). Redrawn from UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998; 317:703.



Lower systolic pressure reduces complications in type 2 diabetes

Among 3642 patients with type 2 diabetes mellitus in the United Kingdom Prospective Diabetes Study (UKPDS), there was an inverse correlation between the updated mean systolic blood pressure and the aggregate end point for any complication related to diabetes (myocardial infarction, sudden death, angina, stroke, renal failure, lower extremity amputation or death from peripheral vascular disease, death from hyperglycemia or hypoglycemia, heart failure, vitreous hemorrhage, retinal photocoagulation, and cataract extraction). The lowest risk occurred at a systolic pressure below 120 mmHg. The values, adjusted for age, sex, and ethnic group, are expressed for white men aged 50 to 54 years at diagnosis with a mean duration of diabetes of ten years. (Data from Adler, AI, Stratton, IM, Neil, HA, et al, BMJ 2000; 321:412.)

HTN and DMII

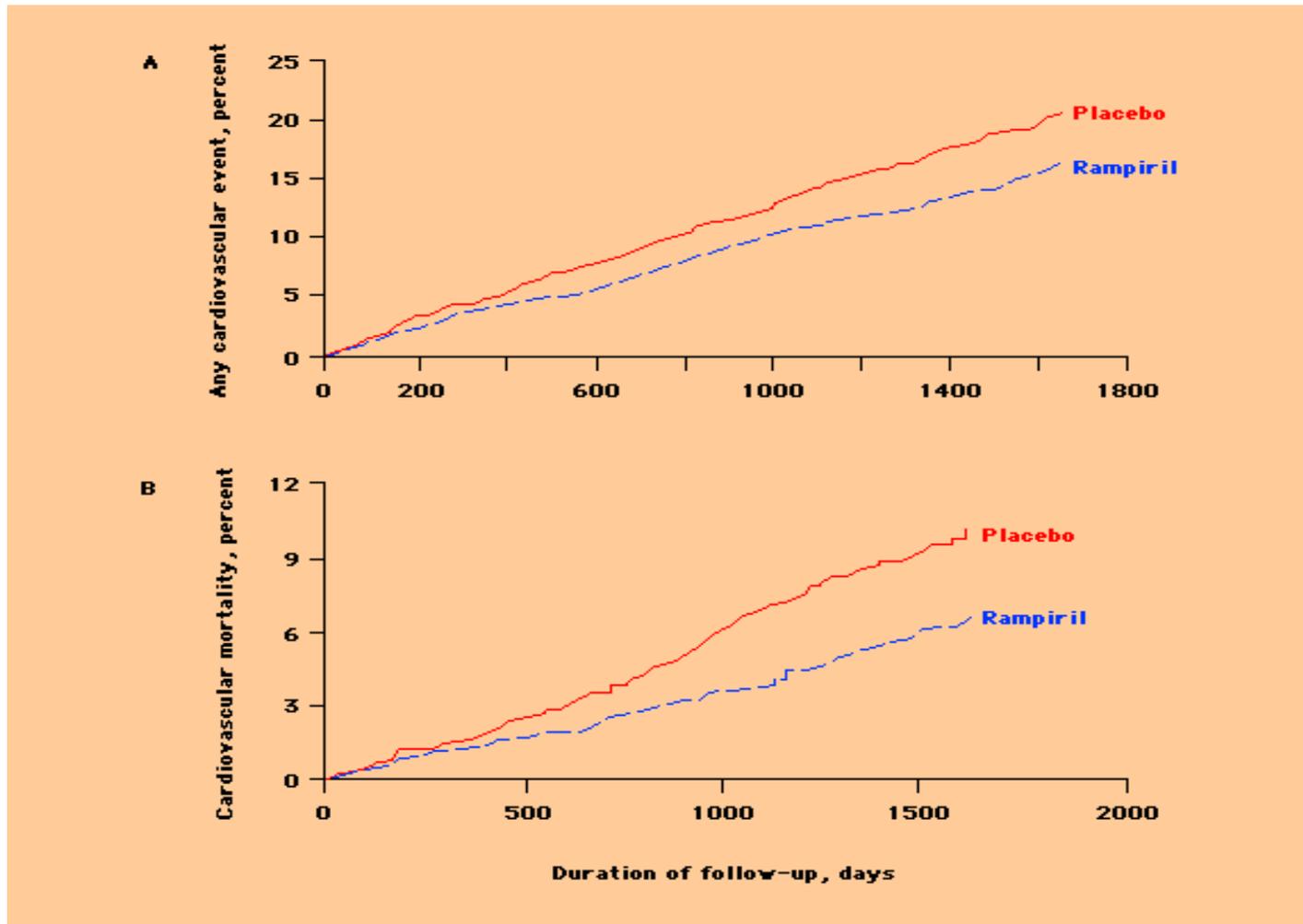
- HTN, occurs just before, and is associated with microalbuminuria
- Associated with obesity
- Hyper-insulin state increases systolic BP
- Hyperglycemia leads to Na retention
- Increased arterial stiffness
- Treat early and treat aggressively
- Bottom line...get them below 130/80

Considerations...

- ALLHAT showed us that lisinopril, amlodipine, and chlorthalidone provided similar protection from coronary death and nonfatal AMI among DM
- Thiazide outperformed ACEI and CaCB slightly
- ACEI offer other advantages
 - No adverse effect on lipids
 - May *lower* BS
 - May *prevent* DM (HOPE & LIFE trials)
 - Slow progression of nephropathy
 - May slow progress of retinopathy
 - Safe and well tolerated
 - Cheap
 - ARB's work as well (new data)
- Look for reasons to use ACEI's



HOPE Trial



Ramipril improves outcome in patients with diabetes Kaplan-Meier survival curves for 3755 patients with diabetes enrolled in the HOPE trials shows that ramipril significantly reduced both the incidence of any cardiovascular event (cardiovascular death, myocardial infarction, and stroke) compared to placebo (15.3 versus 19.8 percent) (panel A) and cardiovascular death (6.2 versus 9.7) (panel B). (Data from The Heart Outcomes Prevention Evaluation (HOPE) Study Investigators, *Lancet* 2000; 355:253).

Soccer

Football ITOOTR OGSO SOTG LOTG TRIAR
 All Ball! Assist Attacking Midfielder Back
 Back Defender Ball! Breakaway Offensive
 Central Defender Charge Defensive Outside
 Dribble Drive Drop Ball Far and Wide Forward
 Fullback Get It Out of There! Get Square Goal!
 Goalie Good Save! Hacking Halfback Hat Trick
 Header Juggling Keeper Kickoff Libero
 Midfielder Numbers Down Numbers Up
 Nutmeg Penalty Kick Red Card Send It! Shoot
 Starter Stay Wide! Steal Stopper Striker
 Sunday Shot Sweeper Unlucky Winger
 Yellow Card The Ball Has No Lungs Give & Go
 The Net Knows No Gender Deny, Delay & Destroy
 "You'll always miss 100% of the shots you don't take."

0 0 1 1 2 2 3 3 4 4
 5 5 6 6 7 7 8 8 9 9



JOCK TALK

Animal Quality and Fun Light The
 Jockey's Choice for the
 Jockey's Choice for the Jockey's Choice

Volleyball

Red Card Over the Net Rotation Beach Serve
 Power Server Co-Ed Set Ace Setter Assist
 Side Out Attack Six Pack Attacker Spike
 Backcourt Striker Back Set Strong Side
 Back Row Attack Weak Side Beach Dig Wipe
 Block Yellow Card Bump Campfire Center Line
 Closing the Block Cross Court Shot Cut Shot
 Decoy Deep Set Dig Dink Double Block
 Doubles Down Ball Floater Foul! Free Ball
 Hit Hitter Isolation Play Jungle Ball Jump Serve
 Key Kill Line Shot Middle-Back Middle-Up
 Outside Hitter Overhand Pass Jed Pancake
 Penetration Power Alley
 Quick Set Boom Chuck



JOCK TALK

Animal Quality and Fun Light The
 Jockey's Choice for the
 Jockey's Choice for the Jockey's Choice

Lipids...

- ATPIII study declared DMII and previous MI as equal in risk for a macro-vascular event (CHD equivalent)
- Hyperglycemia leads to glycation of ApoB, increasing LDL $\frac{1}{2}$ life, which is taken up peripherally by macrophages. These foam cells collect in atherosclerotic plaque making it unstable and at risk of rupture

Lipids...

- The CARE, LIPID, and 4S Trials showed STATIN therapy decreased the risk of cardiovascular events (RR 0.76, 95 percent CI 0.59 to 0.93) with an absolute risk reduction of 7 percent. The number of patients needed to treat for benefit was 13 to 14.
- ADA, ATP III, and Hrt Protection Study recommends LDL < 100
- 2004 update adds recommendation to lower LDL 30% even if this is under 100
- ATP 2003 update recommends lowering LDL to < 70 with “active CAD”
- UpToDate states... “we recommend an LDL goal of 80 in DM”
- Lower is better, diet goes without saying, start STATINS early, Niacin reasonable 2nd agent (but may increase BS initially)



What is next
for our
patient?

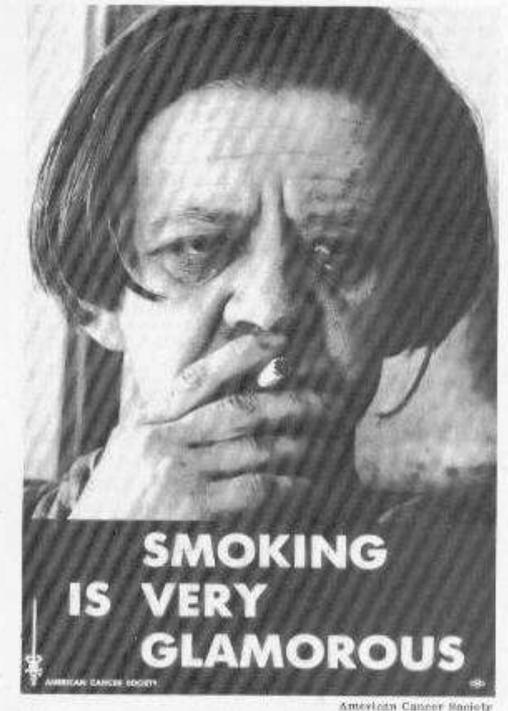
CNN FILE

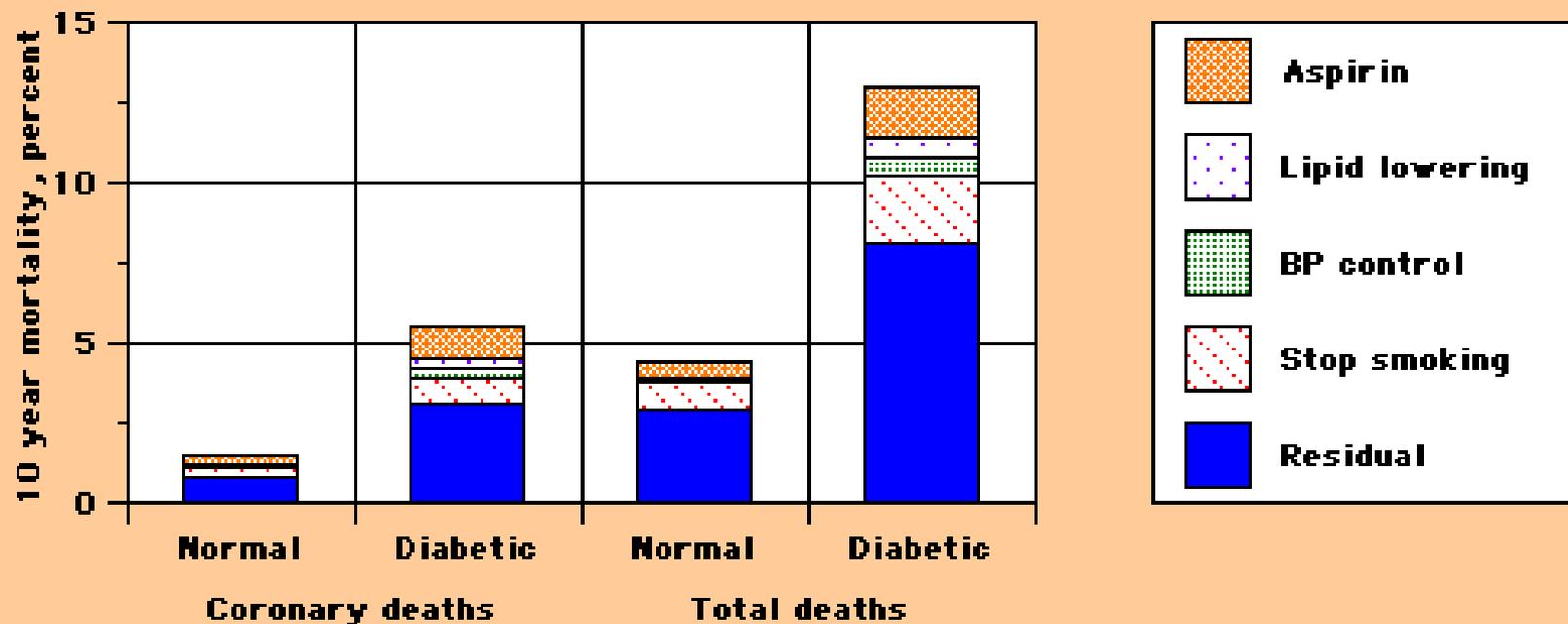
Next...“smoking has got to go before it smokes me!”



DM: “Smoking is bad for you” Why?

- Independent risk factor all-cause mortality
- Mortality increases with dose and duration
- Risk returns to baseline at 10 years
- Increases LDL, VLDL, and lowers HDL
- Makes insulin resistance worse
- Harder to control BS's
- Makes neuropathy worse
- Cessation is the most beneficial intervention on survival outperforming any other single intervention



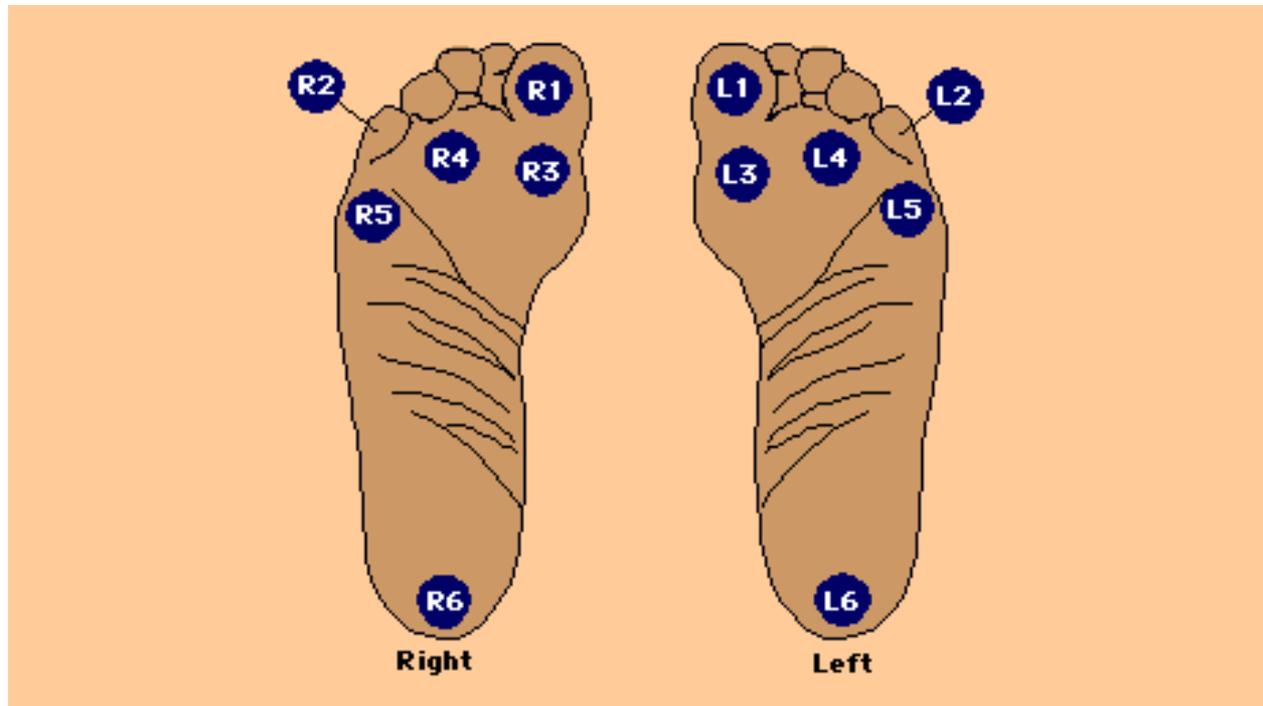


Increased cardiovascular risk in type 2 diabetes Calculated effects of different interventions on coronary and total deaths in 1000 normal and 1000 men with type 2 diabetes aged 35 to 57 years without a history of myocardial infarction. Although risk was reduced by the therapeutic interventions (particularly cessation of smoking), there was a residual three to four fold increase in mortality in the diabetic men, due presumably to the effects of hyperglycemia or hyperinsulinemia. (Data from Yudkin, JS, BMJ 1993; 306:1313.)

RE: Micro-vascular disease,
What do you screen for in our
patient?...and how?



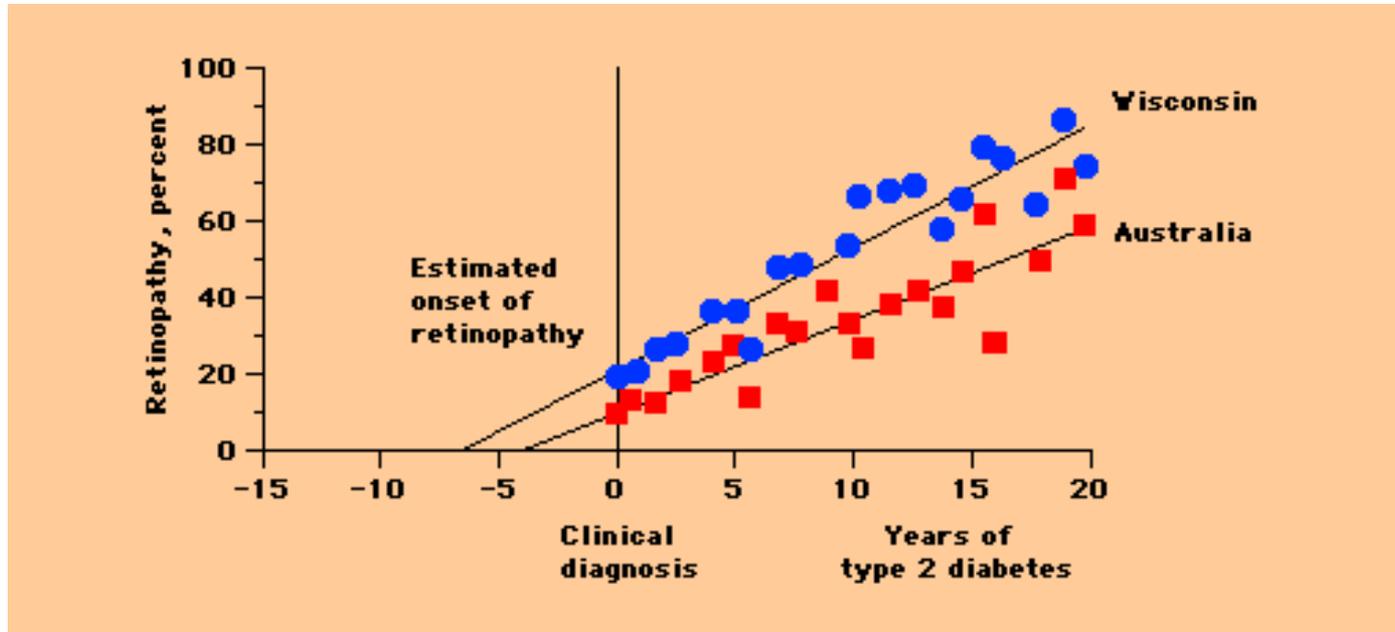
Neuropathy- the foot exam



Testing sites for pressure sensation in evaluation of diabetic foot The monofilament used to evaluate pressure sensation should be tested at each of the 12 sites shown, which represent the most common sites of ulcer formation. Failure to detect cutaneous pressure at any site indicates that the patient is at high risk for future ulceration.

Semmes-Weinstein 5.07 (10-g) monofilament

Retinopathy- referral annually



Onset of retinopathy precedes diagnosis of type 2 diabetes

Prevalence of retinopathy in relation to years after onset of diabetes among patients in southern Wisconsin (blue circles) and rural western Australia (red squares). At diagnosis (year zero), retinopathy was already present in 10 to 20 percent of patients. The lines extrapolate back to an estimated onset of retinopathy four to seven years before the clinical diagnosis was made. (Data from Harris, MI, Klein, R, Welborn, TA, Knudman, MW, Diabetes Care 1992; 15:815.)

Why? Because laser therapy prevents visual loss

Nephropathy-Microalbumin/Crt ratio



MA = 30 is micro-proteinuria, suggests nephropathy

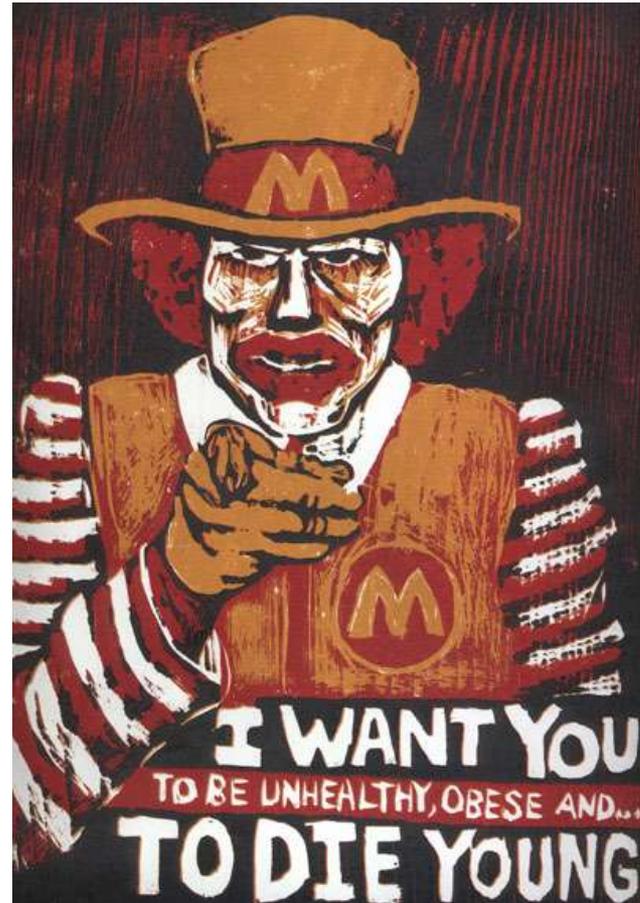
- Confirm with 2nd test
- Start ACEI or ARB
- Glucemic control

MA = 300 is macro-proteinuria

- Glycemic control
- Prep for dialysis

Top Priority for CRR in DM should be

1. Smoking cessation
2. ASA
3. BP
4. Lipids
5. Diet
6. Exercise
7. ACEI



How do you help patients participate, succeed, and then “maintain the gains”?

- Self-management support
- Collaborative goal setting
- Knowledge/nutrition
- Promote physical activity
- Involve family
- Problem solving
- Depression scn and management
- BBSWAR



Part II, 12/05