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What do the following clinical paradigms have in common?

- Hormone replacement therapy and primary prevention for vascular disease
- The routine use of anti arrhythmic therapy and CV mortality
- Arthroscopic surgery for knee osteoarthritis

Today's update will be focusing on contemporary conventional wisdom concerning 1) Targeting serum glucose levels to decrease cardiovascular risk in type II diabetics; 2) Screening for CAD in asymptomatic type II diabetics and treating those with established CAD; 3) PSA screening in average risk men. 4) If I have time, I'll also try and tackle the use of BNP in managing patients with heart failure AND a P&P study from England AND the "evidence" on evidence based guidelines.

Type II Diabetes and CAD – targeting the glyco

With regards to the risk of coronary disease for type II diabetics, the conventional wisdom reads something like this: 1) CAD is the leading cause of death in pts with DM-II; 2) Since the primary metabolic abnormality in DM-II = elevated glucose; 3) Improving glucose control -> better CAD outcomes.

The ADA recommends: 1) Lowering A1C to below or around 7% for microvascular disease prevention for non-pregnant adults (A) 2) Until more evidence is available, the general goal of <7% appears reasonable for many adults for macrovascular risk reduction (B) 3) Less stringent goals may be appropriate for patients with a hx of severe hypoglycemia, limited life expectancy, advance microvascular or macrovascular complications, and extensive co-morbid conditions and those with long standing DM in whom the general goal is difficult to attain¹

The following several studies test the hypothesis that in type II DM, targeting glycohemoglobin to a level of somewhere ~ 7.0% (vs. somewhere ~ 8.0%) will improve morbidity and mortality from CAD.

1. EFFECTS OF INTENSIVE GLUCOSE LOWERING IN TYPE 2 DIABETES The Action to Control Cardiovascular Risk in Diabetes Study Group (**ACCORD**) N Engl J Med 358(24):2545, June 12, 2008 **BACKGROUND:** Despite substantial efforts to promote intensive glucose lowering in type 2 diabetics, there has never been evidence that this is beneficial. **METHODS:** In this multicenter trial, coordinated at Wake Forest University in Winston-Salem, NC, 10,251 type 2 diabetics (mean age 62.2) at high risk for cardiovascular disease and with a mean glycosylated hemoglobin (HbA1c) of 8.1% were randomized to intensive treatment (to a target HbA1c of below 6%) or to standard therapy (to a target HbA1c of 7.0-7.9%). The primary outcome was a composite of nonfatal myocardial infarction or stroke, or cardiovascular mortality. **RESULTS:** By one year, the mean HbA1c levels were 6.4% in the intensive treatment group and 7.5% in the standard treatment group, and these results remained stable throughout the remainder of the study (mean follow-up 3.5 years). Although there was a statistically insignificant trend in favor of the intensive treatment group with regard to the primary composite outcome (6.9% vs. 7.2% in the standard treatment group, hazard ratio [HR] 0.9, p=NS), a similar trend in the opposite direction was true for all-cause mortality (5% vs. 4%, HR 1.22, p=NS), prompting early discontinuation of intensive treatment. Adverse effects that were statistically more frequent in the intensive treatment group included hypoglycemia requiring assistance (16.2% vs. 5.1%), and weight gain in excess of 10kg (27.8% vs. 14.1%). **CONCLUSIONS:** In these patients with type 2 diabetes and at high cardiovascular risk, intensive glucose lowering did not reduce major cardiovascular effects and was associated with increased all-cause mortality and increased adverse effects. 25 references (bbyingto@wfubmc.edu for reprints) Copyright 2008 by Primary Care Medical Abstracts - All Rights Reserved 10/08 - #15

2. INTENSIVE BLOOD GLUCOSE CONTROL AND VASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES: The ADVANCE Collaborative Group N Engl J Med 358(24):2560, June 12, 2008 **BACKGROUND:** Intensive blood glucose control has not been shown to improve vascular outcomes in patients with type 2 diabetes. **METHODS:** (DM-II, ≥ 30 yo at time of Dx; age > 55 at time of study entry, hx micro or macro vasc complication OR one other risk for CV dz; EXCL = need for long term insulin at start of study OR absolute indication for or against study drugs; 6 week run-in period – if compliant and tolerant were enrolled in the study) (f/u week 2 after randomization, then monthly 1-6, then q3months VS 3,4,6 months post randomization then q 6 months) In this manufacturer-sponsored factorial controlled trial from 215 centers in 20 countries and coordinated at the University of Sydney in Australia, 11,140 patients with type 2 diabetes were randomized to intensive treatment (modified-release gliclazide [a second-generation sulfonylurea] along with other drugs, to achieve an HbA1c of 6.5% or lower) or to standard treatment. Inclusion criteria were age above 55, type 2 diabetes diagnosed after age 30 and a history of major macrovascular or microvascular disease or other vascular risk factors. Endpoints were adjudicated by a committee blinded to the treatment assignment. **RESULTS:** (13.4% failed run in; both groups DM duration ~ 8yrs; ~ 32% with macro vasc dz; ~ 10% with microvasc dz; ~ 27% with microalbumin) After a median follow-up of five years, the mean HbA1c level was lower in the intensive treatment group (6.5% vs. 7.3%). There was no statistical difference in the incidence of major macrovascular events (cardiovascular death, or nonfatal MI or stroke) (hazard ratio [HR] 0.94, 95% CI 0.84-1.06), cardiovascular death (HR 0.88, 95% CI 0.74-1.04), or all-cause mortality (HR 0.93, 95% CI 0.83-1.06). There was a reduction in major microvascular events (9.4% vs. 10.9%), almost all of which involved a reduction in macroalbuminuria. Severe hypoglycemia was more common in the intensive intervention group (2.7% vs. 1.5%). **CONCLUSIONS:** Intensive glucose control over a period of five years did not improve patient-oriented outcomes in patients with type 2 diabetes, and increased the frequency of severe hypoglycemia. 34 references (apatel@george.org.au for reprints) Copyright 2008 by Primary Care Medical Abstracts - All Rights Reserved 10/08 - #16

3. GLUCOSE CONTROL AND VASCULAR COMPLICATIONS IN VETERANS WITH TYPE 2 DIABETES Duckworth, W., et al, N Engl J Med 360(2):129, January 8, 2009. **BACKGROUND:** Intensive glucose control is often recommended in type 2 diabetics, despite evidence that it is not beneficial. **METHODS:** In the **Veterans Affairs Diabetes Trial (VADT)**, funded by multiple pharmaceutical companies, 1,791 patients (mean age about 60) with poorly controlled type 2 diabetes were randomized to standard or intensive glucose control. Patients in the intensive control group were started on maximal doses of oral hypoglycemics and patients in the standard control group were started on half maximal doses. Insulin was added for failure to achieve an HbA1c level below 6% in the intensive treatment group and 9% in the standard treatment group. The treatment goal in the intensive management group was an absolute reduction of 1.5% as compared with the standard treatment group. **RESULTS:** The median duration of follow-up was 5.6 years. The median HbA1c level was 6.9% with intensive therapy and 8.4% with standard therapy. There were no differences between the groups in the primary outcome, a composite of myocardial infarction, stroke, cardiovascular mortality, congestive heart failure, surgery for vascular disease, inoperable coronary artery disease, and amputation for ischemic gangrene. There were, likewise, no intergroup differences in rates of death from individual cardiovascular causes or all-cause mortality. Overall rates of microvascular complications were similar. Hypoglycemia, the most common adverse event, was nearly four times more frequent in the intensive therapy group than in the standard treatment group. The percentage of patients experiencing at least one serious adverse event was 24.1% with intensive glucose control vs. 17.6% with standard treatment. **CONCLUSIONS:** In this study, as in others, there was no advantage of intensive glucose control in patients with type 2 diabetes. 26 references (william.duckworth@va.gov for reprints) Copyright 2009 by Primary Care Medical Abstracts - All Rights Reserved 6/09 - #9

You may remember the UKPDS study. The original study demonstrated that in Type II diabetics {diet vs intensive Rx (insulin or sulphonylurea), 10 yr follow up, mean A1C 7.0 v 7.9%; DM-related endpoints 12% lower in intensive gp – almost all due to need for retinal photocoagulation –however no difference in visual acuity between the groups; no diff in macrovascular dz; hypoglycemia 11-36% vs 1.2%). The following study suggests a “legacy” effect of early “intensive” control (control during the study but lost during follow up)

4. 10-YEAR FOLLOW-UP OF INTENSIVE GLUCOSE CONTROL IN TYPE 2 DIABETES Holman, R.R., et al, N Engl J Med 359(15):1577, October 9, 2008 **BACKGROUND:** In the **United Kingdom Prospective Diabetes Study (UKPDS)**, patients with type 2 diabetes were randomized to “intensive” pharmacological therapy (metformin for patients more than 120% of ideal body weight, and a sulphonylurea and/or insulin for others) or to dietary therapy alone. The authors of this follow-up study claim that “tight control” led to a lower risk of microvascular complications, although the differences were at most marginal, and only for laser photocoagulation of the retina. **METHODS:** After the original trial was completed, patients returned to usual care, with no attempt to maintain the previously randomized therapies. This study reports on clinic or questionnaire follow-up for 3,277 of the original 4,209 subjects. **RESULTS:** Differences in glucose control disappeared by one year after the end of the trial such that patients in all the original treatment groups had similar hemoglobin A1C levels. Nevertheless, the authors report persistent (and even enhanced) benefit in any diabetes-related endpoint, microvascular disease, myocardial infarction, and all-cause mortality among patients originally randomized to metformin. They also report smaller relative benefits in patients originally randomized to a sulphonylurea, even though these were not present during the study itself, at the time that use of this class of drug was associated with “better” glucose control. **CONCLUSIONS:** The authors report continued long-term benefit in patients originally randomized to metformin, but also report the development of new (albeit smaller) benefits in patients originally randomized to a sulphonylurea, even though this group of patients had no different glucose control for almost that entire time. 25 references (rury.holman@dtu.ox.ac.uk for reprints) Copyright 2009 by Primary Care Medical Abstracts - All Rights Reserved 2/09 -

Hypoglycemia is obviously more common in those attempting intensive glucose control. In elderly patients, hypoglycemia is associated with an increase risk of dementia.

5. HYPOGLYCEMIC EPISODES AND RISK OF DEMENTIA IN OLDER PATIENTS WITH TYPE 2 DM. JAMA 2009 Apr 15;301(15):1565-72 **CONTEXT:** Although acute hypoglycemia may be associated with cognitive impairment in children with type 1 diabetes, no studies to date have evaluated whether hypoglycemia is a risk factor for dementia in older patients with type 2 diabetes. **OBJECTIVE:** To determine if hypoglycemic episodes severe enough to require hospitalization are associated with an increased risk of dementia in a population of older patients with type 2 diabetes followed up for 27 years. **DESIGN, SETTING, AND PATIENTS:** A longitudinal cohort study from 1980-2007 of 16,667 patients with a mean age of 65 years and type 2 diabetes who are members of an integrated health care delivery system in northern California. **MAIN OUTCOME MEASURE:** Hypoglycemic events from 1980-2002 were collected and reviewed using hospital discharge and emergency department diagnoses. Cohort members with no prior diagnoses of dementia, mild cognitive impairment, or general memory complaints as of January 1, 2003, were followed up for a dementia diagnosis through January 15, 2007. Dementia risk was examined using Cox proportional hazard regression models, adjusted for age, sex, race/ethnicity, education, body mass index, duration of diabetes, 7-year mean glycated hemoglobin, diabetes treatment, duration of insulin use, hyperlipidemia, hypertension, cardiovascular disease, stroke, transient cerebral ischemia, and end-stage renal disease. **RESULTS:** At least 1 episode of hypoglycemia was diagnosed in 1465 patients (8.8%) and dementia was diagnosed in 1822 patients (11%) during follow-up; 250 patients had both dementia and at least 1 episode of hypoglycemia (16.95%). Compared with patients with no hypoglycemia, patients with single or multiple episodes had a graded increase in risk with fully adjusted hazard ratios (HRs): for 1 episode (HR, 1.26; 95% confidence interval [CI], 1.10-1.49); 2 episodes (HR, 1.80; 95% CI, 1.37-2.36); and 3 or more episodes (HR, 1.94; 95% CI, 1.42-2.64). The attributable risk of dementia between individuals with and without a history of hypoglycemia was 2.39% per year (95% CI, 1.72%-3.01%). Results were not attenuated when medical utilization rates, length of health plan membership, or time since initial diabetes diagnosis were added to the model. When examining emergency department admissions for hypoglycemia for association with risk of dementia (535 episodes), results were similar (compared with patients with 0 episodes) with fully adjusted HRs: for 1 episode (HR, 1.42; 95% CI, 1.12-1.78) and for 2 or more episodes (HR, 2.36; 95% CI, 1.57-3.55). **CONCLUSIONS:** Among older patients with type 2 diabetes, a history of severe hypoglycemic episodes was associated with a greater risk of dementia. Whether minor hypoglycemic episodes increase risk of dementia is unknown.

OK, I suspect many of you have fond feelings concerning the effectiveness of home glucose monitoring in your Type II diabetics. Again the ADA recommends that “ Self-monitoring of blood glucose (SMBG) may be useful as a guide to the success of therapy for patients using ... noninsulin therapies, or medical nutrition therapy and physical activity alone” And, after all, what harm could there be to getting the patient more involved in monitoring their blood sugars on a regular (daily, hourly, weekly, etc) basis?

6. EFFICACY OF SELF MONITORING OF BLOOD GLUCOSE IN PATIENTS WITH NEWLY DIAGNOSED TYPE 2 DIABETES (ESMON STUDY): RANDOMISED CONTROLLED TRIAL O'Kane, M.J., et al, Br Med J 336:1174, May 24, 2008 **BACKGROUND:** Although self-monitoring of blood sugar is often encouraged for patients with type 2 diabetes who do not require insulin, the value of this practice is uncertain. **METHODS:** In this controlled Irish study, 184 patients with newly diagnosed type 2 diabetes were randomized to self-monitoring of blood glucose or no self-monitoring (controls). The self-monitoring group was provided with glucose monitors and instructed in their use and the appropriate response to high or low blood sugar readings. Both groups received diabetes instruction and were seen by a physician at three-month intervals for one year. **RESULTS:** Baseline characteristics were similar in the two groups. There were no significant differences between the groups in HbA1c levels at any time during the study (6.9% in both groups at one year). By one year, patients in the self-monitoring group had a 6% higher mean score on a depression subscale of a well-being questionnaire than patients in the control group ($p=0.01$), and tended to have higher anxiety scores. There were no differences between the groups on other well-being subscales, or in satisfaction with treatment or attitudes about diabetes. **CONCLUSIONS:** In these patients with newly diagnosed type 2 diabetes, self-monitoring of blood glucose had no beneficial effect on glycemic control, measures of well-being or satisfaction with care, and tended to be associated with more depression and anxiety. 25 references (Maurice.OKane@westerntrust.hscni.net - no reprints) Copyright 2008 by Primary Care Medical Abstracts - All Rights Reserved 10/08 - #18

OK, if targeting the glycohemoglobin has no palpable effect on Type II diabetics risk of macrovascular disease (and may worsen the risk), and if CAD is commonly asymptomatic in DMII pts (until it's too late); then we should screen for asymptomatic CAD in type II diabetics, right!

7. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. Young LH, et al. DIAD Investigators. JAMA. 2009 Apr 15;301(15):1547-55. **CONTEXT:** Coronary artery disease (CAD) is the major cause of mortality and morbidity in patients with type 2 diabetes. But the utility of screening patients with type 2 diabetes for asymptomatic CAD is controversial. **OBJECTIVE:** To assess whether routine screening for CAD identifies patients with type 2 diabetes as being at high cardiac risk and whether it affects their cardiac outcomes. **DESIGN, SETTING, AND PATIENTS:** The Detection of Ischemia in Asymptomatic Diabetics (DIAD) study is a randomized controlled trial in which 1123 participants with type 2 diabetes and no symptoms of CAD were randomly assigned to be screened with adenosine-stress radionuclide myocardial perfusion imaging (MPI) or not to be screened. Participants were recruited from diabetes clinics and practices and prospectively followed up from August 2000 to September 2007. **MAIN OUTCOME MEASURE:** Cardiac death or nonfatal myocardial infarction (MI). **RESULTS:** The cumulative cardiac event rate was 2.9% over a mean (SD) follow-up of 4.8 (0.9) years for an average of 0.6% per year. Seven nonfatal MIs and 8 cardiac deaths (2.7%) occurred among the screened group and 10 nonfatal MIs and 7 cardiac deaths (3.0%) among the not-screened group (hazard ratio [HR], 0.88; 95% confidence interval [CI], 0.44-1.88; $P = .73$). Of those in the screened group, 409 participants with normal results and 50 with small MPI defects had lower event rates than the 33 with moderate or large MPI defects; 0.4% per year vs 2.4% per year (HR, 6.3; 95% CI, 1.9-20.1; $P = .001$). Nevertheless, the positive predictive value of having moderate or large MPI defects was only 12%. The overall rate of coronary revascularization was low in both groups: 31 (5.5%) in the screened group and 44 (7.8%) in the unscreened group (HR, 0.71; 95% CI, 0.45-1.1; $P = .14$). During the course of study there was a significant and equivalent increase in primary medical prevention in both groups. **CONCLUSION:** In this contemporary study population of patients with diabetes, the cardiac event rates were low and were not significantly reduced by MPI screening for myocardial ischemia over 4.8 years. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00769275

If tight glucose control and screening for CAD in DM-II has minimal benefit, then if we discover CAD in a type II diabetic, then surely revascularization procedures (vs aggressive medical management) will improve survival, correct!?

8. A randomized trial of therapies for type 2 diabetes and coronary artery disease. BARI 2D Study Group N Engl J Med. 2009 Jun 11;360(24):2503-15. Epub 2009 Jun 7. **BACKGROUND:** Optimal treatment for patients with both type 2 diabetes mellitus and stable ischemic heart disease has not been established. **METHODS:** We randomly assigned 2368 patients with both type 2 diabetes and heart disease to undergo either prompt revascularization with intensive medical therapy or intensive medical therapy alone and to undergo either insulin-sensitization or insulin-provision therapy. Primary end points were the rate of death and a composite of death, myocardial infarction, or stroke (major cardiovascular events). Randomization was stratified according to the choice of percutaneous coronary intervention (PCI) or coronary-artery bypass grafting (CABG) as the more appropriate intervention. **RESULTS:** At 5 years, rates of survival did not differ significantly between the revascularization group (88.3%) and the medical-therapy group (87.8%, $P=0.97$) or between the insulin-sensitization group (88.2%) and the insulin-provision group (87.9%, $P=0.89$). The rates of freedom from major cardiovascular events also did not differ significantly among the groups: 77.2% in the revascularization group and 75.9% in the medical-treatment group ($P=0.70$) and 77.7% in the insulin-sensitization group and 75.4% in the insulin-provision group ($P=0.13$). In the PCI stratum, there was no significant difference in primary end points between the revascularization group and the medical-therapy group. In the CABG stratum, the rate of major cardiovascular events was significantly lower in the revascularization group (22.4%) than in the medical-therapy group (30.5%, $P=0.01$; $P=0.002$ for interaction between stratum and study group). Adverse events and serious adverse events were generally similar among the groups, although severe hypoglycemia was more frequent in the insulin-provision group (9.2%) than in the insulin-sensitization group (5.9%, $P=0.003$). **CONCLUSIONS:** Overall, there was no significant difference in the rates of death and major cardiovascular events between patients undergoing prompt revascularization and those undergoing medical therapy or between strategies of insulin sensitization and insulin provision. (ClinicalTrials.gov number, NCT00006305.) 2009 Massachusetts Medical Society

PROSTATE CANCER SCREENING

Perhaps the problems with conventional wisdom are disease specific. Surely, identifying early prostate cancer and killing before it can cause havoc improves prostate cancer related outcomes in men?!

9. MORTALITY RESULTS FROM A RANDOMIZED PROSTATE-CANCER SCREENING TRIAL Andriole, G.L., et al, N Engl J Med 360(13):1310, March 26, 2009 **BACKGROUND:** Screening for prostate cancer has been widely adopted, but it is not certain if screening confers a mortality benefit. **METHODS:** The multicentered "Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial" was coordinated by the National Institutes of Health. In one arm of the trial, 76,693 men aged 55-74 were randomized to be offered annual PSA

testing for six years and annual DRE for four years, or to a control group to which usual care was offered (which sometimes included screening). **RESULTS:** The study group was followed for a median of 11.5 years. In the group offered screening, compliance was about 85% for PSA measurement and DRE. By year six, about 50% of the control subjects had undergone PSA measurement and DRE had been performed in 46%. By seven years, the incidence of prostate cancer was 116 per 10,000 person-years in the screening group and 95 per 10,000 person-years in controls (rate ratio 1.22). Rates of stage III or IV tumors were similar in the two groups, although control subjects had a higher rate of cancers with Gleason scores of 8-10. By seven years, rates of prostate cancer-specific mortality (the primary outcome) were 2.0 per 10,000 person-years in the screening group and 1.7 per 10,000 person-years in controls (rate ratio 1.13). By ten years, with 67% of data complete, prostate cancer mortality was similar to that reported at seven years (rate ratio in the screening group, 1.11). The rate of medical complications due to the diagnostic process after positive screening was 68 per 10,000 diagnostic evaluations. **CONCLUSIONS:** After seven and ten years of follow-up in this large study, the prostate cancer mortality rate was low, and screening did not appear to confer a mortality benefit. 31 references (bergc@mail.nih.gov for reprints) Copyright 2009 by Primary Care Medical Abstracts - All Rights Reserved 7/09 - #14

10. SCREENING AND PROSTATE-CANCER MORTALITY IN A RANDOMIZED EUROPEAN STUDY Schroder, F.H., et al, N Engl J Med 360(13):1320, March 26, 2009 **METHODS:** The multinational "European Randomized Study of Screening for Prostate Cancer" (ERSPC) trial, coordinated in the Netherlands, was initiated in the 1990s to evaluate the effect of PSA screening on prostate cancer mortality. In this study, 162,243 men aged 55-69 in seven European countries were randomized to a group that was offered PSA screening at an average of once every four years, or to a control group that was not offered such screening. The primary outcome was death due to prostate cancer. Mortality follow-up for the two study groups was identical, and ended on December 31, 2006. **RESULTS:** Most (82%) of the men in the group offered screening were screened with the PSA test on at least one occasion. Over a median follow-up of nine years, the cumulative incidence of diagnosed prostate cancer was 8.2% in the screening group and 4.8% in the control group. The rate of death due to prostate cancer was marginally lower in the screening group compared with the control group, with an absolute risk difference of 0.71 deaths per 1000 men. As such, 1,410 men would need to be offered screening (with 1,068 men actually undergoing screening), with the treatment of 48 additional cases of prostate cancer, in order to prevent one death from prostate cancer. **CONCLUSIONS:** PSA screening only marginally reduced the rate of death due to prostate cancer over a median follow-up of nine years, and was associated with a high risk of overdiagnosis. 38 references (secr.schroder@erasmusmc.nl for reprints) Copyright 2009 by Primary Care Medical Abstracts - All Rights Reserved 7/09 - #

BNP and CHF

The use of BNP in acutely dyspneic patients and in patients with chronic CHF is common. The effect of the use of BNP in clinical outcomes and resources utilization in both of these groups suggests that BNP has little effect on clinical outcomes and resource utilization.

11. BNP-GUIDED VS. SYMPTOM-GUIDED HEART FAILURE THERAPY: THE TRIAL OF INTENSIFIED VS. STANDARD MEDICAL THERAPY IN ELDERLY PATIENTS WITH CONGESTIVE HEART FAILURE (TIME-CHF) RANDOMIZED TRIAL. Pfisterer, M., et al, JAMA 301(4):383, January 28, 2009 **METHODS:** In this 15-center European study, partially funded by multiple pharmaceutical companies, 499 patients aged 60 or older with NYHA class II or higher congestive heart failure (CHF) were randomized to treatment decisions guided by symptoms alone, or by periodic BNP measurements in addition to symptoms. Escalation of treatment was performed during the first six months of the study according to a predefined strategy, and follow-up was continued for an additional twelve months. **RESULTS:** By six months, up-titration of treatment was much more common in the BNP-guided group, but there were no differences between the groups in symptomatic improvement. By 18 months, there was likewise no between-group difference in the primary study outcome, survival free of all-cause hospital admission (40% with symptom-guided therapy and 41% with BNP-guided therapy), or in measures of quality of life. The authors note a decrease in "hospitalization for CHF" in the BNP-guided group, but this was balanced by an equivalent increase in hospitalization ascribed to another cause. Similarly, although multiple subgroup analyses identified a "potential benefit" of BNP-guided therapy in one subgroup (patients aged 60-74), the opposite ("potential harm") was observed in another subgroup (older patients), almost certainly reflecting a set of chance associations. **CONCLUSIONS:** BNP-guided therapy for CHF was not more effective than symptom-guided therapy for any patient-oriented outcome, including quality of life, all-cause hospitalization, or survival. 31 references (pfisterer@email.ch - no reprints) Copyright 2009 by Primary Care Medical Abstracts - All Rights Reserved 6/09 - #1

12. B-TYP NATRIURETIC PEPTIDE TESTING, CLINICAL OUTCOMES, AND HEALTH SERVICES USE IN EMERGENCY DEPARTMENT PATIENTS WITH DYSPNEA: A RCT. Schneider HG, et al. Ann Intern Med. 2009 Mar 17;150(6):365-71. **BACKGROUND:** B-type natriuretic peptide (BNP) is used to diagnose heart failure, but the effects of using the test on all dyspneic patients is uncertain. **OBJECTIVE:** To assess whether BNP testing alters clinical outcomes and health services use of acutely dyspneic patients. **DESIGN:** Randomized, single-blind study. Patients were assigned to a treatment group through randomized numbers in a sealed envelope. Patients were blinded to the intervention, but clinicians and those who assessed trial outcomes were not. **SETTING:** 2 Australian teaching hospital emergency departments. **PATIENTS:** 612 consecutive patients who presented with acute severe dyspnea from August 2005 to March 2007. **INTERVENTION:** BNP testing (n = 306) or no testing (n = 306). **MEASUREMENTS:** Admission rates, length of stay, and emergency department medications (primary outcomes); mortality and readmission rates (secondary outcomes). **RESULTS:** There were no between-group differences in hospital admission rates (85.6% [BNP group] vs. 86.6% [control group]; difference, -1.0 percentage point [95% CI, -6.5 to 4.5 percentage points]; P = 0.73), length of admission (median, 4.4 days [interquartile range, 2 to 9 days] vs. 5.0 days [interquartile range, 2 to 9 days]; P = 0.94), or management of patients in the emergency department. Test discrimination was good (area under the receiver-operating characteristic curve, 0.87 [CI, 0.83 to 0.91]). Adverse events were not measured. **LIMITATION:** Most patients were very short of breath and required hospitalization; the findings might not apply for evaluating patients with milder degrees of breathlessness. **CONCLUSION:** Measurement of BNP in all emergency department patients with severe shortness of breath had no apparent effects on clinical outcomes or use of health services. The findings do not support routine use of BNP testing in all severely dyspneic patients in the emergency department. PRIMARY FUNDING SOURCE: Janssen-Cilag.

P4P

13. EFFECTS OF PAY FOR PERFORMANCE ON THE QUALITY OF PRIMARY CARE IN ENGLAND Campbell SM, et al. *N Engl J Med.* 2009 Jul 23;361(4):368-78. **BACKGROUND:** A pay-for-performance scheme based on meeting targets for the quality of clinical care was introduced to family practice in England in 2004. **METHODS:** We conducted an interrupted time-series analysis of the quality of care in 42 representative family practices, with data collected at two time points before implementation of the scheme (1998 and 2003) and at two time points after implementation (2005 and 2007). At each time point, data on the care of patients with asthma, diabetes, or coronary heart disease were extracted from medical records; data on patients' perceptions of access to care, continuity of care, and interpersonal aspects of care were collected from questionnaires. The analysis included aspects of care that were and those that were not associated with incentives. **RESULTS:** Between 2003 and 2005, the rate of improvement in the quality of care increased for asthma and diabetes ($P < 0.001$) but not for heart disease. By 2007, the rate of improvement had slowed for all three conditions ($P < 0.001$), and the quality of those aspects of care that were not associated with an incentive had declined for patients with asthma or heart disease. As compared with the period before the pay-for-performance scheme was introduced, the improvement rate after 2005 was unchanged for asthma or diabetes and was reduced for heart disease ($P = 0.02$). No significant changes were seen in patients' reports on access to care or on interpersonal aspects of care. The level of the continuity of care, which had been constant, showed a reduction immediately after the introduction of the pay-for-performance scheme ($P < 0.001$) and then continued at that reduced level. **CONCLUSIONS:** Against a background of increases in the quality of care before the pay-for-performance scheme was introduced, the scheme accelerated improvements in quality for two of three chronic conditions in the short term. However, once targets were reached, the improvement in the quality of care for patients with these conditions slowed, and the quality of care declined for two conditions that had not been linked to incentives. Continuity of care was reduced after the introduction of the scheme. 2009 Massachusetts Medical Society

What is the evidence supporting guidelines?

14. SCIENTIFIC EVIDENCE UNDERLYING THE ACC/AHA CLINICAL PRACTICE GUIDELINES. Tricoci P, et al. 1: *JAMA.* 2009 Feb 25;301(8):831-41. Erratum in: *JAMA.* 2009 Apr 15;301(15):1544. **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 determined. The subset of guidelines that were current as of September 2008 was evaluated to describe changes in recommendations between the first and current versions as well as patterns in levels of evidence used in the current versions. **RESULTS:** Among guidelines with at least 1 revision or update by September 2008, the number of recommendations increased from 1330 to 1973 (+48%) from the first to the current version, with the largest increase observed in use of class II recommendations. Considering the 16 current guidelines reporting levels of evidence, only 314 recommendations of 2711 total are classified as level of evidence A (median, 11%), whereas 1246 (median, 48%) are level of evidence C. Level of evidence significantly varies across categories of guidelines (disease, intervention, or diagnostic) and across individual guidelines. Recommendations with level of evidence A are mostly concentrated in class I, but only 245 of 1305 class I recommendations have level of evidence A (median, 19%). **CONCLUSIONS:** Recommendations issued in current ACC/AHA clinical practice guidelines are largely developed from lower levels of evidence or expert opinion. The proportion of recommendations for which there is no conclusive evidence is also growing. These findings highlight the need to improve the process of writing guidelines and to expand the evidence base from which clinical practice guidelines are derived. PMID: 19244190 [PubMed - indexed for MEDLINE]

CONCLUSIONS

1. Three recent large RCT's (ACCORD; ADVANCE, VADT) concluded that intensive glucose control (Glyco targeted to 6-7% for 3.5 – 5.5 years) does not improve macrovascular outcomes in patients with type II DM.
2. Microvascular events (mostly macroalbuminuria) were less common in the intensive treatment group (NNT = 66) in ADVANCE but not VADT.
3. Hypoglycemia was 1.3 to 3.2 times more likely in the intensive Rx group
4. Hypoglycemia is assoc with a risk for the development of dementia in older (> 65) year old diabetics
5. Screening for CAD in asymptomatic type II diabetics with myocardial perfusion imaging (MPI) had no effect on the rates of cardiac deaths, non-fatal MI, unstable angina, CHF, CVA and coronary revascularization compared to those not screened after a follow up of 4.8 years
6. No differences exist in the 5 year rate of death and major cardiovascular events in patients with type II DM and angiographically proven CAD treated with revascularization vs. medical therapy, or treated with insulin sensitizing medications vs. insulin provision.
7. The effect of screening for PRC with PSA on disease-specific mortality is negligible after 9 – 11 years. The number needed to screen to prevent one PRC death is 1000 – 1400.
8. The use of BNP on clinical outcomes and resource utilization in acutely dyspneic patients and those with chronic CHF is negligible.
9. P4P likely improves measurable aspects of care that are incentivized, however decreases in the quality for non-incentivized aspects of care may be an unintended consequence (at least in England)
10. Approximately 50% of the current ACC/AHA guideline recommendations are C level (expert opinion, case study or standard of care). Only 11% of the ACC/AHA recommendations are supported by A level evidence (multiple RCT's or meta-analyses)

References:

1. Executive Summary: Standards of Medical Care in Diabetes – 2009. *Diabetes Care* 2009; 32(suppl 1):s6