

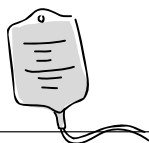
Diabetes 2007

From the 67th Annual Scientific Sessions of the American Diabetes Association ■ Chicago, IL

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Glucose in the Hospital



Important data on diabetes presented at the 67th Annual Scientific Sessions of the American Diabetes Association come to you in **Diabetes 2007**, a newsletter CME program that is being offered to you by Yale University School of Medicine with the support of Takeda Pharmaceuticals North America, Inc., Merck & Co., Inc., Novo Nordisk Inc., and Amylin Pharmaceuticals, Inc./Eli Lilly and Company. Fax or e-mail delivery to your office of **Diabetes 2007** will be followed by a **Diabetes 2007** booklet (ACC and ADA newsletters) in the mail. After successfully completing the quiz and evaluation therein contained, you will qualify for up to 5.5 Category 1 credits towards the Physician's Recognition Award of the American Medical Association to be issued by Yale University School of Medicine.

Diabetes 2007 is being offered to physicians practicing in the United States. After successfully completing this program, participants will be able to:

- Explain the pathogenesis of Type 2 diabetes, especially the coexisting roles of insulin resistance and insulin secretion.
- Recognize the clinical manifestations of the macrovascular and microvascular complications of diabetes and describe appropriate therapeutic interventions.
- Recognize the important association between insulin resistance/metabolic syndrome and atherosclerosis in patients with Type 2 diabetes.
- Identify evolving and emerging management strategies for diabetes (e.g., combination antihyperglycemic therapy, new insulin delivery systems, new glucose monitoring techniques, novel drugs).
- Describe the approach to managing dyslipidemia, hypertension, and cardiovascular risk factors in patients with diabetes.

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Over the past five years, there's been increasing interest in the inpatient management of hyperglycemia. Interest began after the publication of several randomized clinical trials demonstrating impressive benefit of tight control on certain patient outcomes. Over the past year, the field has become more controversial, since the presentation of the results of two European studies which suggested no benefit from intensive insulin therapy in the ICU. While we await the publication of these trials in final form, the "Hospital Management of Diabetes" was a hot topic at the ADA's Scientific Sessions. In an opening day symposium with this title, experts from several US centers updated the audience on progress at their home institutions in this arena. The session was moderated by Dr. Stephen Clement from Georgetown University.

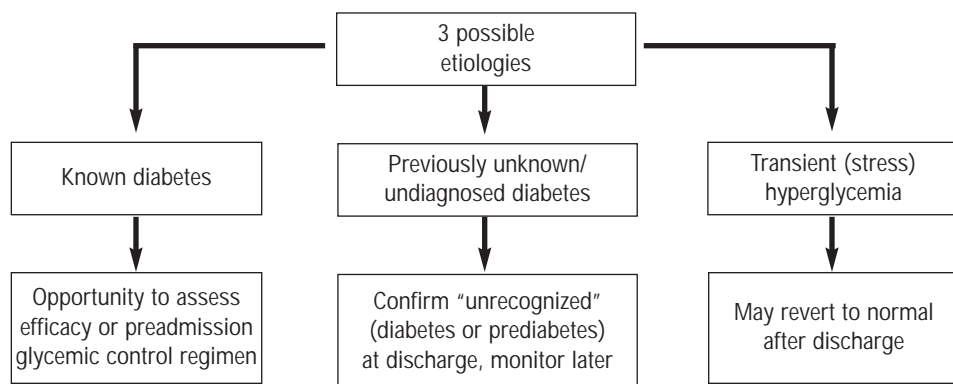
Dr. David Baldwin from Rush University Medical Center spoke on "Emerging Best Practices." Dr. Baldwin focused on six areas—treatment-induced hypoglycemia; transitioning patients from intravenous (IV) to subcutaneous insulin; initiating insulin therapy in the post-operative patient; the management of diabetes in steroid-treated patients; and the critical importance of HbA1c measurement in the hospital to facilitate proper discharge planning. Some key points from Dr. Baldwin's talk: To date, there is little evidence that hypoglycemia rates are different between computer-assisted IV insulin protocols vs. printed

algorithms. Accordingly, lack of access to computerized systems should not dissuade hospitals from implementing one of several published IV insulin protocols, which have been demonstrated to substantially improve glucose control in critically ill patients.

Virtually all diabetic patients on IV insulin should be transitioned to subcutaneous regimens once out of the critical care unit. The basal-bolus insulin approach is preferred, such as with a long-acting analogue (i.e., glargine, detemir) or NPH BID, with rapid-acting analogues (aspart, lispro, glulisine) added at mealtime. Individual patient characteristics will guide therapy as well. In those patients not previously recognized as having diabetes and whose stress hyperglycemia in the critical care setting necessitated insulin infusion, approximately 50% will ultimately *not* require insulin, or for that matter, any antihyperglycemic therapy upon discharge. Measuring HbA1c is invaluable in making this distinction (Figure 1). That is, those patients with normal or near-normal values will likely be those who can be transitioned to diet therapy and monitoring alone.

When choosing a subcutaneous insulin dose for patients on IV insulin, Dr. Baldwin endorsed multiplying the stable hourly rate over the terminal three hours by 20 to calculate the total daily basal insulin dose. This, in effect, provides 80% of the former IV dose as basal insulin.

Figure 1. Hyperglycemia in Hospitalized Patients: Discharge Planning



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So-called 'correction insulin' in the form of a rapid analogue is then added every six hours; when the patient begins to eat, prandial insulin (of the same type as correction) is then initiated at a dose of 0.05 units/kg/meal. In patients new to insulin, an initial dose of 0.3 units/kg was suggested for the total daily amount of basal insulin, with 0.05 units/kg/meal of rapid acting insulin analogue administered prandially.

In steroid-treated patients, NPH was recommended as the preferred insulin. When patients receive large doses of glucocorticoids intravenously several times per day, administering NPH BID allows for more rapid increases in the dose as may be required by persistent hyperglycemia. Adjustments can then be made every 12 hours vs. the less frequent modifications allowable by a once daily basal insulin. In addition, once the patient is transitioned to oral prednisone QAM, NPH dosed in the morning is best positioned to address hyperglycemia, which tends to occur over the first 12-18 hours, dissipating by the next morning. In contrast, long-acting analogues may have a duration of action that is simply too long for these patients.

In the second lecture, Dr. Gregory Maynard, a hospitalist from the University of San Diego, reported on his efforts to improve the quality of care provided by his institution to hyperglycemic inpatients. Dr. Maynard spearheaded a local quality improvement project focused on systems changes, including automatic ordering of insulin protocols and algorithms, making it easier for clinicians to implement more aggressive strategies. He underscored the importance of collaboration by physician leaders with other key stake holders, including nurses, pharmacists, and nutritionists. Dr. Maynard also emphasized that any system change in the complex, modern American hospital requires ongoing feedback and refinement, based on the successes as well as the failures along the way. His program has been adapted to a unique resource room on the Society of Hospital Medicine's website, <http://www.hospitalmedicine.org>.

Dr. Silvio Inzucchi from Yale University next introduced the concept of "glucometrics" for inpatient diabetes care. He reminded the audience that there was no HbA1c equivalent for the inpatient arena—that is, no single test can assess the quality of inpatient glucose management. Tens of thousands of fingerstick glucose readings are generated at most hospitals every month. To optimally collect, sort, analyze, and present these data is an overwhelming task, especially

Table 1. Effect of Insulin Glargine vs. Regular Insulin Sliding Scale on Glycemia and Triglycerides

	<i>Glargine + RISS</i>	<i>RISS ± NPH</i>	<i>p-value</i>
Mean CBG during study, mg/dl	163 ± 31	161 ± 30	0.75
Mean Nadir CBG, mg/dl	125 ± 29	120 ± 21	0.51
Mean Peak CBG, mg/dl	206 ± 49	207 ± 52	0.95
Hypoglycemia/patient days, %	2.7	4.8	0.34
Hyperglycemia/patient days, %	49.3	47.6	0.77
Baseline Triglycerides, mg/dl	142 ± 46	139 ± 68	0.52
Study-end Triglycerides, mg/dl	144 ± 44	145 ± 48	0.95

CBG=capillary blood glucose; RISS=regular insulin sliding scale.

given that there are no accepted standards to assess the quality of glucose control in this setting. Dr. Inzucchi proposed the use of the "patient-day" model of analysis, where mean or median blood glucose for each patient's hospital day is the analytical unit. In this way, rates of hypoglycemic or hyperglycemic events can be more fairly compared. Analysis by patient day also appears to be the most actionable method of assessing inpatient glycemic management. The audience was invited to use a free website at Yale University, <http://www.glucometrics.med.yale.edu>, where de-identified hospital glucose data can be uploaded, and then automatically deciphered and analyzed. Another new inpatient glucose resource room within the website of the American Association of Clinical Endocrinologists (<http://www.aace.com>) was also highlighted.

Finally, Dr. Christopher Newton from Brody School of Medicine at East Carolina University, NC spoke on the finances of inpatient diabetes care. He reviewed the extraordinary costs involved in diabetes management in the US, with over \$92 billion dollars in direct costs annually, 44% of which is spent in the inpatient setting. Dr. Newton also reviewed the anticipated cost savings to hospitals from controlling blood glucose aggressively. Several published data sets suggest that, at least in the ICU setting, the very modest costs of IV insulin infusion (less than \$150 per patient) are enormously offset by the anticipated savings of several thousand dollars per patient, mainly due to reduced morbidity and decreased length of stay. During the first year of the Brody inpatient diabetes program, which consists of five specially trained nurses to help manage hyperglycemia in the hospital, length of stay was reduced by 0.26 days per patient. Because this allowed for an increase in admission volume of nearly 350 cases for that year, the net increased revenue to the hospital was calculated to exceed \$2.2 million. This proved to be a "return on investment" of 467%!

In the question and answer period, several important issues were raised. Dr. Molitch from the Northwestern University in Chicago emphasized the important role of a skilled clinician, usually a nurse, to modify or adapt standardized protocols to an individual patient's specific needs. Others commented that system change in hospitals is difficult without buy-in from key groups, including surgeons and critical care physicians. The transition to outpatient care was a concern of several audience members—often patients are placed on complex insulin regimens in the hospital but lack the outpatient resources upon discharge to optimally monitor their progress.

Dozens of abstracts were presented at the 67th Scientific Sessions on this topic area as well. Korytkowski and colleagues from Pittsburgh, PA (2293-PO) presented data from a single institution's hypoglycemic treatment protocol. This standardized nursing approach to the patient with any blood glucose <70 mg/dl reduced the frequency and severity of hypoglycemia hospital-wide. Each institution should standardize its approach to this common problem, including how many carbohydrates to provide the patient, when to give IV dextrose, the frequency of subsequent monitoring, and what should be done with the patient's antihyperglycemic regimen after he or she has been stabilized. In another abstract from this group (564-P), 50 patients with Type 2 diabetes receiving enteral feeding were randomized to glargine + regular insulin sliding scale (RISS) vs. RISS alone, with NPH added for persistent hyperglycemia. No difference in overall glucose outcomes could be demonstrated (see Table 1). The authors concluded that both regimens were equally effective in controlling blood glucose to <180 mg/dl, with an overall low risk of hypoglycemia. We would point out, however, that, because of the NPH "rescue" allowed in RISS patients, this study should not be considered an adequate comparison of basal insulin vs. sliding scales. It would have been of interest to compare the RISS patients' blood glucose data *prior to* initiating NPH.

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Matheny *et al.* from the US (2207-PO) reported on treatment intensification for blood glucose in the hospital. Over a period of 20 months, 3613 non-ICU diabetic patients were tracked during their hospitalizations. Hyperglycemia was documented in 82.5% (defined as a blood glucose >180 mg/dl). Yet, in only 22% of hospital days was treatment actually intensified. When implemented, intensification of either scheduled or sliding scale insulin was associated with a respective 10.1 mg/dl ($p < 0.0001$) and 9.6 mg/dl ($p = 0.0002$) lowering of mean blood glucose. In contrast, the use of oral medications was associated with no reduction in hyperglycemia. There was a low level of hypoglycemia, occurring in only 2.2% of hospital days following intensification.

Falciglia *et al.* from Cincinnati, OH (673-P) collected data on a cohort of 259,040 ICU admissions from 114 geographically diverse VA hospitals between 2002-05 and compared findings to a previous cohort from 1996-97. The investigators' specific concern was the management of hyperglycemia in those with diabetes and cardiovascular diseases. The distribution of glucose values in these two cohorts is shown in Table 2. Improvement in glycemic control for these critically ill patients was demonstrated with severe hyperglycemia decreasing from 42% to 22% of patients (derived as the mean glucose for the entire ICU stay) and rates of normoglycemia increasing from 10% to 16%. These data suggest that, at least in the VA system, significant improvements have been made in the management of hyperglycemia in critically ill patients with cardiovascular diseases.

In a second presentation from this group, the concept of the severity of illness being a major determinant of hyperglycemia in the critically ill was challenged (669-P). Using the same database, the authors identified 181,073 first admissions to ICUs at these VA hospitals. The severity of illness was calculated for each patient with a validated ICU logistic regression model that uses age, admission diagnosis, co-morbidities, and laboratory variables. The association between severity of illness and glucose was then determined using a linear regression model with mean glucose as the dependent variable. The correlation coefficient (R^2) was calculated to be 0.007—signifying that the contribution of illness severity to the variance in blood glucose was only 0.7%. This surprising finding calls into question the widely held notion that hyperglycemia during illness is mainly related to surges in stress hormones that reflect underlying acute

Table 2. Improvement in Glycemic Management in VA ICUs, 1996-2005

		Mean Blood Glucose (mg/dl)			
		70-110	111-145	146-199	>200
Diabetes	1996-1997	9.6	18.5	29.5	42.4
	2002-2005	15.9	28.2	34.2	21.7
No diabetes	1996-1997	34.5	39.5	19.8	6.2
	2002-2005	39.7	38.0	17.3	5.1

illness severity. Instead, the authors proposed that hyperglycemia in this setting is more likely linked to the patients' underlying metabolic tendencies.

UCLA investigators (Sadhu *et al.*; 1204-P) reported on their Targeted Insulin Therapy to Improve Hospital Outcomes (TRIUMPH) program. 6719 adult patients admitted between 2003-05 to one of five ICUs received intervention from the TRIUMPH team, which used insulin infusion and aggressive glucose targets as defined by the AACE guidelines (80-110 mg/dl). Outcomes are presented in Table 3. This intervention, compared to historical controls, had several patient care and financial benefits, as has been reported by other groups. Statistical significance was achieved, however, only for length of ICU stay.

Derr *et al.* from Baltimore (965-P) conducted a nonconcurrent, prospective cohort study of 382 adult patients undergoing bone marrow transplantation who developed neutropenia, only 25 (6.5%) of whom had a prior diagnosis of diabetes. No patient had evidence of infection prior to the development of their neutropenia. After the drop in white cell count, 84 patients (22%) showed evidence of at least one infection, 51 of whom had bacteremia. The median blood glucose prior to the development of neutropenia in the entire group was 108 mg/dl (range 83-255 mg/dl). For every 10 mg/dl increase in mean pre-neutropenia glycemia, the risk of any infection increased by 11% (95% confidence interval [CI], 2-21%, $p = 0.016$) and bloodstream infection by 18% (95% CI, 7-29%, $p = 0.001$). In those patients with at least one glucose result ≥ 200 mg/dl ($n = 71$), the odds ratio for any infection and bloodstream infection was 1.99 (1.10-3.59, $p = 0.023$) and 2.45 (1.24-4.89, $p = 0.010$), respectively. Cause and effect relationships between illness and glucose are difficult to decipher in such studies. Strengths of this study, however, include the prospective design, the lack of any evidence of infection prior to the development of neutropenia, and the fact that the glucose abnormalities were recorded prior to any fall in white cell count. This suggests that hyperglycemia may have predisposed to infection as opposed to simply being an innocent marker of

Table 3. Change in Outcome with Intensive Insulin Therapy (n=6,719)

Total costs	-\$4,746 (-\$10,509, \$1,832)
Direct variable costs	-\$2,210 (-\$5,593, \$1,584)
Total ICU costs	-\$5,231 (-\$13,775, \$3,591)
Direct variable ICU costs	-\$1,143 (-\$4,096, \$2,068)
Total days	-0.47 (-1.87, 1.02)
ICU days	-1.19 (-1.93, -0.43)*
Mortality	-0.011 (-0.05, 0.03)

* $p \leq 0.05$

disease severity. Randomized clinical trials designed to show a benefit from tight glucose control in bone marrow transplant patients are needed.

Bozzo *et al.* from New Haven, CT (576-P) reported on the success of an Inpatient Diabetes Management Team, which is primarily nurse practitioner-driven. In the first 11 months of activity, 620 patients were evaluated, with a mean length of stay of 13.5 days—indicative of a high acuity of illness. As compared to before consultation, the mean blood glucose by patient-day was reduced by 42.4 mg/dl. The number of days with severe hyperglycemia (>300 mg/dl) was cut in half (-51.2%), with no change in the number of days with hypoglycemia (<70 mg/dl; -13% of patient days). The percentage of patient days with a mean glucose between 70-149 mg/dl more than doubled (+111.4%). The investigators next compared this group of patients to a contemporaneously hospitalized control group, matched for several clinical variables including diagnosis and length of stay, not managed by the team (i.e., usual care). In this comparison, the differences in mean glucose over time were -49.5 mg/dl ($p < 0.01$ from baseline) in team patients vs. only -16.4 mg/dl ($p = \text{NS}$ from baseline) in controls. Such a "hyperglycemia SWAT team" is but one approach that's been used to address the problem of hyperglycemia in the hospital.

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Faingold and collaborators from Argentina (530-P) retrospectively assessed the effects of hyperglycemia in the post-cardiac surgery setting, focusing on patients with "off-pump" coronary artery bypass grafting (CABG). The association between hyperglycemia and CABG using cardiopulmonary bypass has been well documented, with greater adverse outcomes, including mortality, in those patients with the highest post-operative glucose. These researchers included 465 consecutively operated patients admitted to the ICU in 2004 and 2005. 163 patients (35%) had post-operative hyperglycemia, which was arbitrarily defined as a glucose of ≥ 200 mg/dl. In the diabetic subgroup, the prevalence of hyperglycemia was 58%. In all, those with post-operative hyperglycemia experienced greater hospital mortality (4.3% vs. 0.2%, $p=0.002$) and infections (17.4% vs. 7.4%, $p=0.02$).

When adjustments were made for other prognostic factors, including diabetes, previous myocardial infarction and non-elective surgery, post-operative hyperglycemia remained an independent predictor of both infection ($p<0.001$)

and mortality ($p<0.001$). Each 10 mg/dl increment of blood glucose increased mortality by 30% and infection by 20%. Therefore, in off-pump CABG patients, hyperglycemia remains a powerful risk factor for post-operative complications.

In a related abstract, Gianchandani & Puttnam from Ann Arbor, MI (2226-PO) reported on deep sternal wound infection (DSWI) rates in their cardiothoracic surgery patients before and after initiation of a rigorous, 72-hour post-operative insulin infusion protocol targeting a blood glucose of 100-140 mg/dl. Before the protocol was initiated, the mean blood glucose levels were 153.1, 157.2, and 163.2 mg/dl on the day of surgery and on post-operative days 1 and 2, respectively. Corresponding blood glucoses in the protocol patients were 131.1, 125.0, and 127.2 mg/dl, respectively. Rates of DSWI were 2.3% before and 1.8% after initiation of the protocol. Patients receiving the insulin infusion protocol experienced a lower rate of requiring two or more readmissions for DSWI (23% vs. 37%). The authors concluded that mediastinitis is reduced with aggressive glucose lowering after cardiac surgery. Given the non-randomized design of this study, such a conclusion is not entirely justified, although these data are in

keeping with those from the Portland cardiothoracic surgery program (Furnary *et al.*, *Ann Thorac Surg* 2004), an often cited study which also happened to use historical controls.

Finally, Ghandi and international colleagues (539-P) performed a systematic review and meta-analysis of 58 randomized controlled trials of *perioperative* insulin infusion. A random-effects meta-analysis of 26 trials which assessed mortality showed that, compared with the control group ($n=2,354$, 98 deaths), those receiving perioperative insulin infusion ($n=2,391$, 68 deaths) experienced 31% less mortality (RR=0.69 [0.51-0.94]). Hypoglycemia was more common, however (RR 2.07 [1.29-3.32]). When a single trial that was stopped prematurely was excluded from the analysis, the mortality benefit essentially disappeared ($n=3197$; 33 [insulin infusion] vs. 35 deaths [control], RR=0.92, 0.57-1.48). The authors concluded that there remains significant uncertainty regarding the potential benefits and risks of perioperative insulin use.

Clearly, there continues to be intense interest but also intense controversy in the management of hyperglycemia in the hospitalized patient.



Prevention of Type 2 Diabetes



In a symposium chaired by Dr. Steven Edelman of University of California, San Diego, strategies for Type 2 diabetes prevention were addressed. Dr. Jaakko Tuomilehto of Finland shared three-year follow-up data to the Finnish Diabetes Prevention Study. The original four-year study demonstrated a 58% reduction in the risk of developing diabetes ($p<0.001$) in middle-aged, overweight individuals with impaired glucose tolerance (IGT) from intensive lifestyle intervention. Specific targets included: weight loss, decreased total fat, decreased unsaturated fat, increased dietary fiber, and increased exercise. Impressively, not a single subject meeting all five treatment targets went on to develop diabetes. Those remaining free of diabetes were followed for an additional three years to determine if the impact of lifestyle intervention might be sustained despite discontinuing active intervention. Upon analysis of the long-term (~seven years) data, the original intervention group had a 43% relative risk reduction ($p=0.0001$) when compared with the control group. The total number of intervention targets met continued to correlate with the likelihood of developing diabetes. If four of five were achieved, then the likelihood of

developing diabetes was two in 100, whereas if only one target was met, then diabetes developed in seven out of 100. Although there were no differences with respect to gender or baseline body mass index (BMI), older subjects (>61 years) were more likely to benefit from intervention ($p=0.013$). Dr. Tuomilehto also commented that despite cessation of the trial and active intervention, approximately 2/3 of subjects continued with a healthy lifestyle. The unanswered question posed by Dr. Tuomilehto is whether diabetes is truly being prevented or delayed.

Dr. Hertzler Gerstein from McMaster University in Canada continued the discussion on diabetes prevention specifically focusing on the DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medications) trial results. Although it was a 2x2 factorial design trial ($n=5,269$) evaluating rosiglitazone and ramipril, comments were limited to the rosiglitazone arm of the study. This multicenter (191 sites) trial representing 21 countries demonstrated that 8 mg daily of rosiglitazone was associated with a 62% decreased risk of developing diabetes (HR=0.38, 95% CI 0.33-0.44, $p<0.0001$) when compared

with placebo in patients considered at risk (i.e., impaired fasting glucose [IFG], IGT or both). Additionally, 50.5% of rosiglitazone patients versus 30.3% on placebo achieved the secondary outcome of regression to normoglycemia ($p<0.0001$). Additional findings included statistically significant decreases in fasting plasma glucose, two-hour plasma glucose during oral glucose tolerance testing, systolic and diastolic blood pressures, and ALT with rosiglitazone versus placebo (each $p<0.0001$). The rosiglitazone arm did experience an increase in weight and BMI ($p<0.0001$) when compared with placebo. However, the waist-to-hip ratio increased in patients receiving placebo and remained unchanged in those on rosiglitazone ($p<0.0001$), supporting the well described increase in subcutaneous fat deposition associated with thiazolidinediones (TZDs). There were no differences in risk reduction when compared by gender, age, or underlying risk. Cardiovascular outcomes (composite, myocardial infarction, stroke, cardiovascular death, new angina, and revascularization) were similar in both groups with the exception of hospitalization for congestive heart failure (CHF). The rosiglitazone group had

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14 CHF hospitalizations as compared with two in the placebo arm ($p=0.01$). The overall results of the DREAM trial show that for every 1000 persons treated for three years with rosiglitazone, 144 cases of diabetes are prevented. Dr. Gerstein acknowledged the recent meta-analysis by Dr. Steven Nissen (*NEJM*, 2007) implicating rosiglitazone with an increased risk of cardiovascular events. He proceeded to share the interim analysis of the RECORD (Rosiglitazone Evaluated for Cardiovascular Outcomes) trial. At this point in the trial, 3.75 years, there are no statistically significant differences between rosiglitazone and placebo with respect to cardiovascular hospitalizations and/or death. However, as has been previously described, the incidence of CHF is increased in the rosiglitazone group (1.7%) when compared with placebo (0.76%) ($HR=2.24, p=0.06$). He concluded that, when taken together, the available evidence is as yet insufficient to determine the impact of rosiglitazone on ischemic heart disease and/or cardiac death.

Dr. Bernard Zinman from the University of Toronto, next addressed how diabetes prevention might be implemented on a broad scale. Given the size of the diabetes epidemic, primary prevention should be the principle focus of management. Zinman continued to share the deliberation and recommendations from the recently published ADA Consensus statement regarding prevention in patients with IFG or IGT. There is ample evidence supporting diabetes prevention either by lifestyle modification or pharmacologic means (Table 4). Studies assessing additional modalities are ongoing such as ACT-NOW (pioglitazone), NAVIGATOR (nateglinide/valsartan), and CANOE (low-dose metformin + rosiglitazone). Although uniform agreement is lacking relative to populations suitable for screening as well as the precise mode of prevention, all the major diabetes organizations concur that lifestyle intervention remains the primary option. The ADA has provided guidance for when pharmacologic therapy is indicated and recommends metformin be considered in certain patients,

Table 4. Studies Supporting Diabetes Prevention

Study Name	Population	Intervention	Risk Reduction
Finnish DPS	IGT	lifestyle	58%
DPP	IGT	lifestyle metformin	58% 31%
STOP-NIDDM	IGT	acarbose	25%
TRIPOD	History gestational diabetes	trogliptazone	55%
XENDOS	Obese	orlistat	37%
DREAM	IGT, IFG	rosiglitazone	62%

given the available evidence combined with its long history of safety (Table 5). Outcome studies are needed to truly delineate the ideal therapeutic strategy, including a potential newer paradigm of prevention: low-dose combination pharmacologic therapies. Zinman summed up the presentation stating, "We need to do whatever it takes to prevent this disease."

William Herman, MD, MPH from Michigan closed the session with a discussion on the cost effectiveness of diabetes prevention. The factors influencing this include cost of the intervention, quality of life issues, the intervention's actual effectiveness, and safety concerns. He shared an analysis identifying \$56,000 per 18 quality-adjusted life-years as the "cost" of usual care for individuals with IGT. Utilizing simulation modeling, several studies have evaluated the economic impact of lifestyle, metformin, or acarbose on diabetes prevention. Dr. Herman concluded his presentation by stating, from a payer's perspective, each of the interventions represents reasonably good value for the money, when one considers the costs of managing diabetes and its related complications.

Our own sense is that lifestyle intervention should continue to be the paramount method by which at-risk patients prevent diabetes. It is proven relatively inexpensive, certainly safe, and carries with it other cardiovascular benefits. We are less comfortable with the wholesale use of medications for this purpose. The most potent agents would appear to be the TZDs—but they

Table 5. ADA Consensus Recommendations for Diabetes Prevention

Risk	Intervention
IFG or IGT	Lifestyle modification (e.g., weight loss, physical activity)
IFG or IGT and one of the following:	Lifestyle modification + metformin
■ <60 years	
■ BMI ≥ 35 kg/m ²	
■ Family history in first degree relative	
■ Decreased HDL	
■ Hypertension	
■ HbA1c $>6.0\%$	

(Nathan *et al.*, *Diabetes Care*, 2007)

have certain well established side effects and some new concerns. While metformin is not an unreasonable choice, follow-up of the Diabetes Prevention Program cohort randomized to metformin showed that a sizable proportion had diabetic indices soon after the drug was discontinued, raising the question of true prevention of diabetes or simple masking of hyperglycemia. In addition, no one has yet demonstrated a measurable benefit to treating pre-diabetes with drugs versus simply waiting for diabetes to develop and then initiating early, aggressive treatment.



So Many Posters, So Little Time....



A New Antihypertensive Drug Class

Taylor and American coworkers conducted a pooled analysis of data from 10 randomized, double-blind trials of hypertensive patients ($n=9,503$; diastolic blood pressure 95-110 mmHg,

14.9% Type 1/Type 2 diabetes, 21% ≥ 65 years) who received monotherapy with aliskiren, a direct renin inhibitor, for eight to 12 weeks (abstract 483-P). In an intent-to-treat analysis, there was a statistically significant treatment effect vs. placebo

based on blood pressure lowering, with the effect in the diabetes sub-group (change in systolic/diastolic: -13.2/-10.4 mmHg with 150 mg [$n=98$] and -14.8/-12.2 with 300 mg [$n=393$]) similar to that in the overall population.

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