

## Update on Glycemic Control: Care Gap

### Abstract

Achieving A1C level of <7% in patients with type 1 and type 2 diabetes results in significant decrease in microvascular and macrovascular complications. (1-3).

To focus on type 2 diabetes, as it represents the majority of patients with this disease, information from the United Kingdom Prospective Diabetes Study (UKPDS) showed that at diagnosis a 3-months approach of life-style modification resulted in a decrease in mean A1C from 9 to 7%. This was however followed by a steady increase in A1C levels which lagged by about 1% in patients who continued life-style management alone compared to patients who were also started on monotherapy with sulfonylureas, metformin or insulin. Disappointedly however, even in patients in the intensive treatment policy of the UKPDS who were treated with the above pharmacological agents, there was a gradual and progressive increase in A1C levels over the more than 10-year duration of the study. The 1% difference in A1C between the 2 treatment groups resulted in 25-30% reduction in microvascular diabetes complications and a 16% reduction in myocardial infarction.

As a result of the above studies, evidence- based clinical practice guidelines advocate attaining an A1C of  $\leq 7\%$  as soon as possible after diagnosis. Studies looking at whether this target is attained found that  $\frac{1}{2}$  or fewer patients with diabetes reach such level (4-7).

Attaining target blood glucose levels is a difficult task (8). The reasons for this difficulty include:

1. The pathogenesis of hyperglycemia in type 2 diabetes is multi-factorial. Many of the pathogenetic factors are either progressive (beta-cells: decreased insulin production and increased apoptosis) or persistent (insulin resistance).
2. Environmental factors (obesity and lack of physical activity) add difficulty to glycemic control.
3. The pharmacological oral agents available for controlling blood glucose while effective initially given as monotherapy, soon fail to attain target glucose levels. Combination therapy is therefore needed and are recommended if monotherapy fails or if initial A1C levels are  $>9\%$ .
4. Most oral antihyperglycemic agents reduce A1C by about 1%, with more robust reduction if initial A1C is higher than 9%.
5. Combination therapy usually results in reductions in A1C of  $\geq 2\%$ .
6. Many oral antihyperglycemic agents given in combination at sub maximal doses result in better glycemic control with less side effects.
7. Optimization of oral pharmacological treatment is often delayed, with some studies showing lag periods of several months before adding a second agent (9)
8. Continuing to blame inadequate life-style management for poor control often leads to lack of action and ongoing hyperglycemia
9. Delay in insulin use either in addition to oral agents or by itself and lack of optimization of insulin regimens.

Are there any solutions?

1. Follow the diabetes clinical practice guidelines
2. Refer to diabetes care (education) centres: recruiting the help of other health care professionals in making sure patients follow treatment regimens
3. Linking compensation to attaining targets!

**References:**

1. DCCT. Diabetes Control & Complications Trial. N Engl J Med 1993
2. DCCT/EDIC. Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications. N Engl J Med 2005
3. Stratton, I.M. et al UKPDS 50, Diabetologia 2001;44:156
4. Harris M et al. Diabetes Care 1999; 22:403
5. Diabetes Registry To Improve Vascular Events, CHRC Drive Registry 2006
6. Harris, SB et al. DICE study. Diabetes Res Clin Pract 2005; 70: 90
7. Harris, M et al. Diabetes Care 1999; 22: 403
8. Gaede P, et al, NEJM 2003; 348(5):383-393. STENO-2 Study
9. Brown and Nichols. Diabetes 2003; 52 (suppl 1): A61

## Update on Glycemic Control: Care- Gap

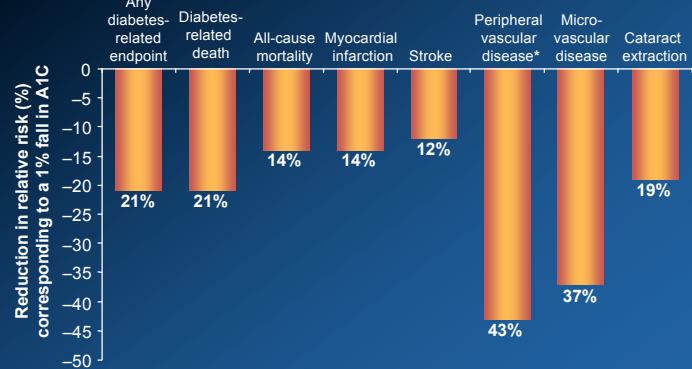
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## A1C < 7% Reduces Incidence of Complications

HbA <sub>1c</sub>	DCCT 9-7%	Kumamoto 9-7%	UKPDS 8-7%
Retinopathy	63%	69%	17-21%
Nephropathy	54%	70%	24-33%
Neuropathy	60%	-	-
Macrovascular disease	40%*	50%*	16%*

\* Not Statistically significant

## UKPDS: Reduced Micro- and Macrovascular Complications for a 1% Decrease in A1C



\*Lower extremity amputation or fatal peripheral vascular disease

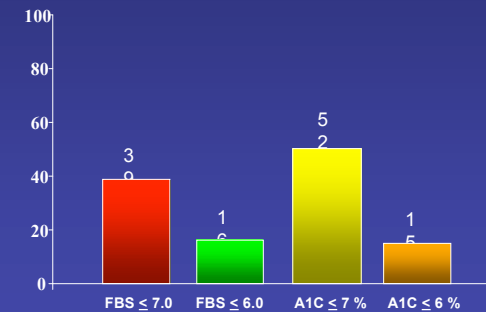
Adapted from Stratton IM et al. UKPDS 35. *BMJ* 2000; 321:405-12.

DRIVE  
Diabetes Registry  
to Improve  
Vascular Events

## FBS and A1C Achieved

Registry

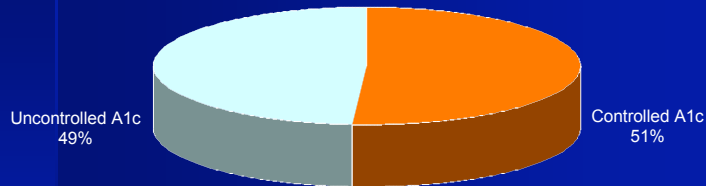
% of Patients



## Glycemic Control in Canada (DICE)

- One in two type 2 diabetes patients in Canada are poorly controlled

Most recent A1C test results (N= 2337)



DICE Study

## Glycemic Management

- Half of type 2 diabetes patients are not receiving a sufficiently aggressive treatment approach.

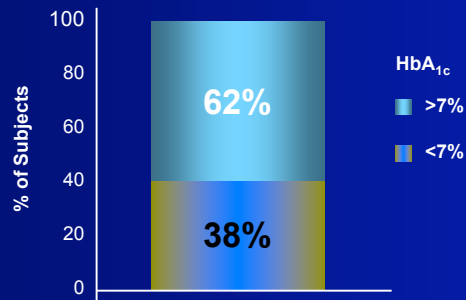
Sample	Total
Lifestyle	15%
1 oral agent - no insulin	36%
2 oral agents - no insulin	30%
3+ oral agents - no insulin	8%
Insulin only - No oral agents	6%
1 oral agent + insulin	3%
2+ oral agents + insulin	2%

51% of patients using lifestyle modifications or only one oral agent

DICE Study

## Majority of Type 2 Diabetes Patients in US Have Inadequate Glycemic Control

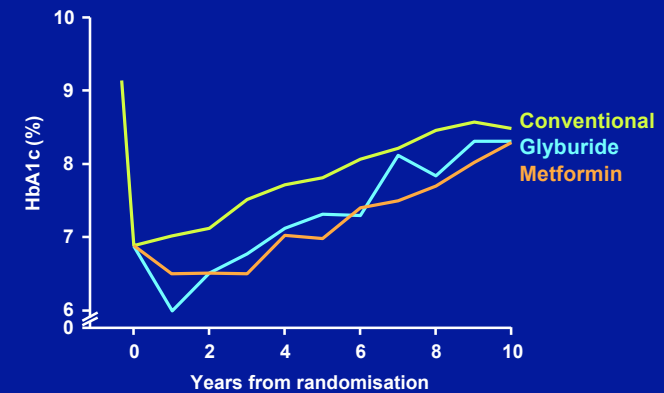
NHANES III (1988-1994)



62% of patients on oral therapy are not at ADA goal of HbA<sub>1c</sub> <7%

Harris MI et al. *Diabetes Care*. 1999;22:403-408.

## Progressive Hyperglycaemia on Monotherapy in Type 2 Diabetes

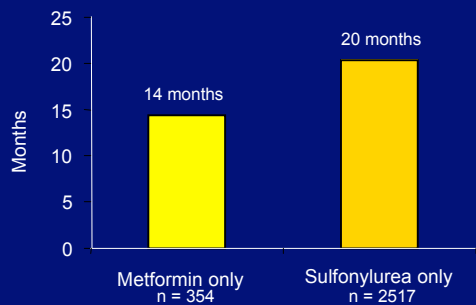


ADOPT

Adapted from UKPDS 34. *Lancet* 1998; 352:854-65

## Limitations of sequential (step-wise) treatment

Length of time between first monotherapy  
HbA<sub>1c</sub> > 8.0%\* and switch/addition in therapy\*



\*May include up-titration. Length of time between first HbA<sub>1c</sub> > 8% and switch/addition in therapy could include periods where patients had subsequent HbA<sub>1c</sub> test values below 8%. Based on nonrandomized retrospective database analysis. Data from Kaiser Permanente Northwest 1994-2002. Patients had to be continuously enrolled for 12 months with HbA<sub>1c</sub> lab values

Adapted from Brown & Nichols. *Diabetes* 2003; 52 (Suppl 1):A61

## Conclusions

- **A significant care gap continues to exist in the management of type 2 diabetes in Canada and greater adherence to guidelines is required in order to achieve optimal outcomes.**
- **Approach to improve glycemic control:**
  - Follow diabetes clinical practice guidelines
  - Refer to diabetes care (education) centres: recruiting the help of other health care professionals in making sure patients follow treatment regimens
  - Linking compensation to attaining targets!