National Academy of Clinical Biochemistry (NACB)

Laboratory Medicine Practice Guidelines (LMPG):

Evidence-Based Practice for Point-of-Care Testing

Diabetes Mellitus

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NACB: LMPG for POCT
diabetes mellitus

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EVIDENCE-BASED LABORATORY MEDICINE

"Absence of evidence is not evidence of absence"

Alderson BMJ 2004;328:476-7

Questions 1 and 2

- Does blood glucose self testing in a primary care setting lead to an improved patient (clinical) outcome or economic benefit in diabetes mellitus?

1. Who	2. What	3. Alternative	4. Outcome
[Primary care setting] #1 AND [Diabetes mellitus] #2	[Blood glucose self testing] #3		[Clinical outcome] #4 [Economic benefit] #5

Questions 3 and 4

- Does blood glucose point-of-care testing in the hospital (i.e. secondary care setting) lead to an improved patient (clinical) outcome in diabetes mellitus, when compared with central laboratory testing?

1. Who	2. What	3. Alternative	4. Outcome
[Secondary care setting] #6 AND [Diabetes mellitus] #2	[Point of care testing] #7	[Central laboratory testing] #8	[Clinical outcome] #4 [Economic benefit] #5

Questions 5 and 6

- Does blood glucose point-of-care testing (primary and secondary care) lead to an improved patient (clinical) outcome (mother and/or baby) in the case of the pregnant woman with gestational diabetes, when compared to central laboratory testing?

Question 7A

- What is the frequency of testing required to achieve the best patient (clinical) outcome in type 1 diabetes?
- Does more frequent testing lead to better outcomes?
- Does the optimal frequency of testing (more or less testing) lead to an economic benefit compared with less frequent testing?

Question 7B

- What is the frequency of testing required to achieve the best patient (clinical) outcome in type 2 diabetes?
- Does more frequent testing lead to better outcomes?
- Does the optimal frequency of testing (more or less testing) lead to an economic benefit compared with less frequent testing?

Question 9

- Is there a role for urine glucose self testing in the management of diabetes?

Question 10

- What is the analytical standard required for blood glucose testing for the screening and diagnosis of diabetes, and can this be achieved with point-of-care testing?

Question 11

- Are there technical limitations associated with point-of-care blood glucose testing which might limit its use in the management of diabetes e.g. extreme environments, extremes of temperature, oxygen levels, detection of hypoglycaemia

Question 12

- Does blood glucose testing at alternatives sites (e.g. forearm) lead to an improved patient (clinical) outcome in the management of diabetes?

Retrieved articles

- The questions were searched in PubMed (682 hits) and the Cochrane library (66 hits).
- 695 abstracts were found (53 duplicates)
- The abstracts were read by two reviewers to determine whether the articles should be retrieved or not. Disagreement was solved by consensus or by a third person.
- 88 articles were retrieved

For this preliminary review - Questions 1 -9 were dealt with:

- Articles dealing with SMBG
  - type I DM
  - type II DM
  - gestational DM
- POCT for glucose in the hospital setting

SMBG

Papers not included in the Coster review* were dealt with.

For hospital and POCT glucose all articles were selected.

Two persons made a rough sorting of the probable relevant full articles from the 88 retrieved articles. These were read thoroughly by two persons who selected and classified the relevant articles according to the forms in the Coster review.

* Coster S, Gulliford M C, Seed P T, Powrie J K, Swaminathan R. Monitoring blood glucose control in diabetes mellitus: a systematic review.
Health Technology Assessment Vol.4: No.12. The National Coordinating Centre
for Health Technology Assessment (NCCHTA). 13665278. 2000.

SMBG - Coster conclusions

Type 1

- SMBG well established and supported by DCCT
- pooled effect of HbA1c -0.57(-1.07 to -0.06)%
- unconfounded studies not provide convincing evidence
- propose prospective observational studies

- Type 2
- insufficient evidence to support SMBG
- pooled effect on HbA1c -0.25 (-0.61 to -0.10)%
- RCTs needed on new pts and discontinuing testing

Retrieved relevant articles - from the 88 retrieved:

- Articles dealing with SMBG and
  - type I DM - 12 - final selection 4
  - type II DM - 22 articles - final selection: 8 (7 after 2000)
  - gestational DM - none
- Secondary care setting (hospital) and POCT in the departments
  - 4 articles - final selection 3

Type II DM: research after 2000

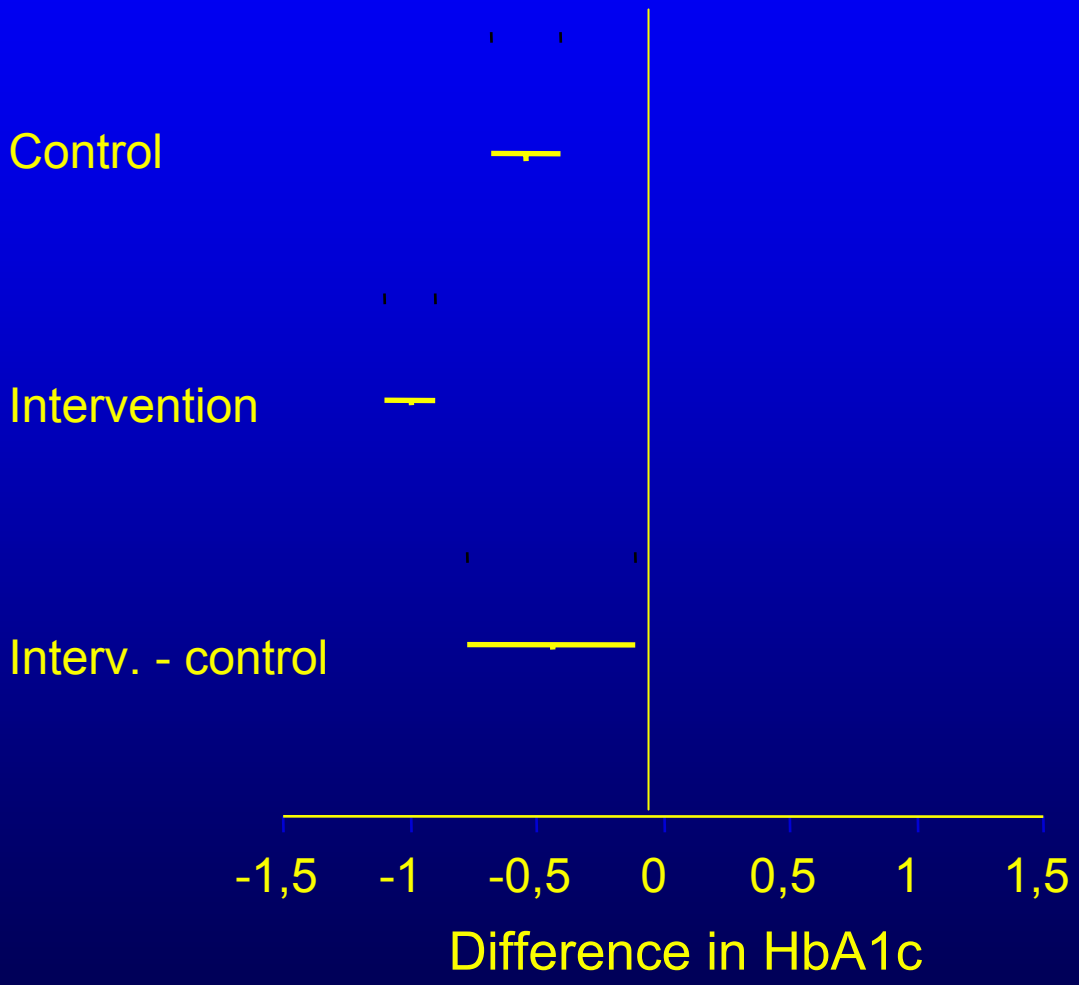
- One published RCT
- Six cross-sectional case control / cohort studies

RCT: meal related structured SMBG

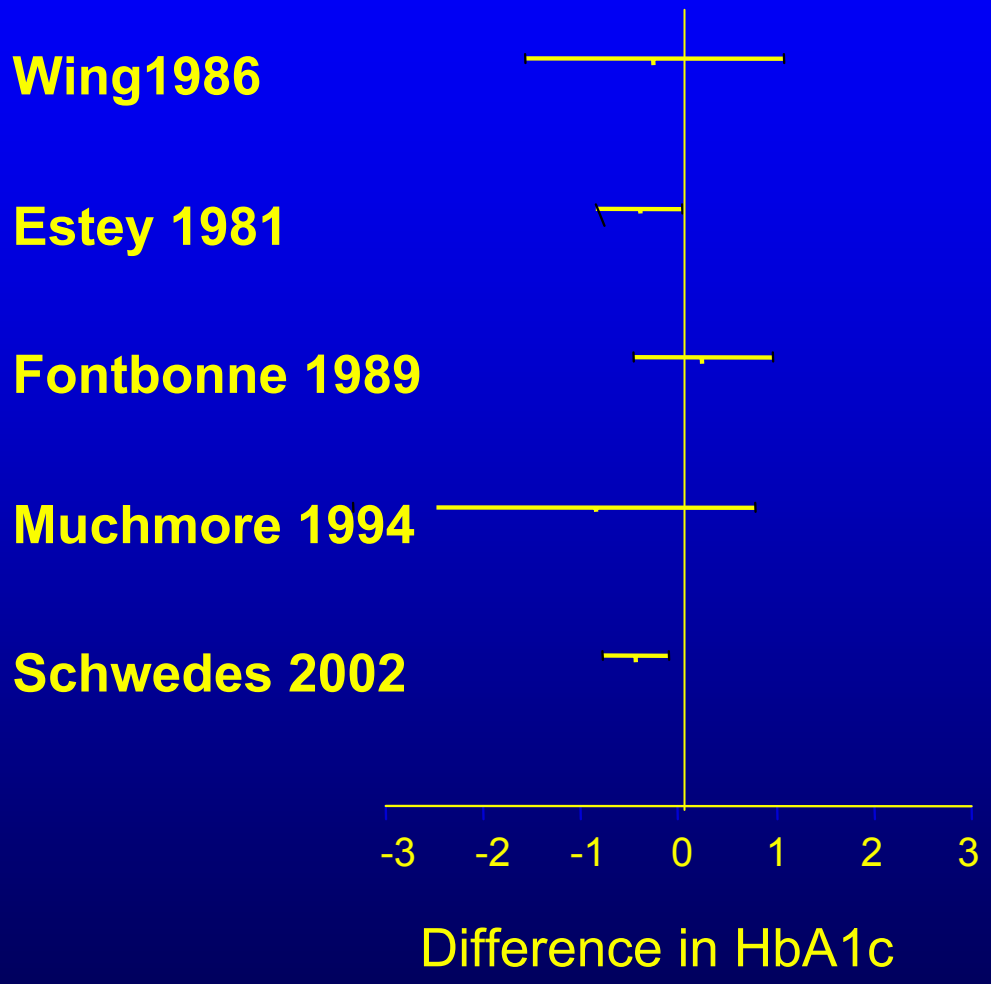
Schwedes et al. Diabetes Care 2002; 25:1928-32

- SMBG six times (before and 1h after main meals) on two days per week. Diary with blood glucose and eating habits. Patients were seen every 4 weeks / counselling algorithms. Nurses assessed the correct use of SMBG.
- Controls received non standard counselling
- 250 patients, 10% excluded because of non-compliance. 6 months intervention and 6 months follow up.
- Main outcome: HbA1c

Schwedes et al 2002



All RCTs concerning Type II DM



Cross-sectional / case control / cohort studies:

- Harris et al 2001: no association HbA1c and SMBG (1988-94)
- Blonde et al 2002: More SMBG users in groups with low HbA1c.
- Franciosi et al 2001:Higher HbA1c with more frequent SMBG for all. However lower in group of insulin treated patients.
- Evans et al 1999: no association with frequency of SMBG(1993-95)
- Karter et al 2001: strong association with frequency of SMBG in all groups of persons with DM (1996/97)
- Meyer et al 2002: no change in HbA1c when reducing number of strips from average 1.4 to 0.7 per day

Evidence for SMBG in Type II patients all papers:

total number of articles/new articles

- RCTs n=9 /1 (5/1)
  - One study showed effect, 4 did not
- Cross sectional, n=10 /4
  - 6 no effect, 3 effects only on insulin treated patients and one on all type II patients.
- Case control, n=2 /1
  - Possible association in one, one showing no effect
- Prospective Cohort (n=4 / 1)
  - 2 showing effect and 2 showing no effect

Recommendations Type II DM - insulin treated

- *Evidence* grade II-2 or II-3
- *Recommendation*: C.
  We make no recommendation for or against routinely using SMBG
- Comment: if SMBG is going to be used, good instruments should be used and patients must be educated in the use and instructed in how to use the results to monitor their therapy.

Recommendations Type II DM - not insulin treated

- *Evidence* grade I, II-2 or II-3
- *Recommendation:* D
  We recommend against using SMBG routinely
- Comment: if SMBG is going to be used, good instruments should be used and patients must be educated in the use and instructed in how to use the results to monitor their therapy.

  - Additional information: one big RCT is in progress and will be finished mid 2006(Andrew Farmer)

Gestational DM
no new articles found

- RCTs n=5 /0
  - Conflicting result, one showed lower costs with SMBG. Small studies
- Case series (3 with historical controls), n=6 / 0
  - only 3 with GDB, the others with type I DM.
  - conflicting results

Gestational DM - recommendations

- *Evidence* grade I (but not very good), II-3 and III
- *Recommendation*: C.
  We make no recommendation for or against routinely using SMBG
- Comment: if SMBG is going to be used, good instruments should be used and patients must be educated in the use and instructed in how to use the results to monitor their therapy.

Type I DM

- RCTs n=9 /1
  - Two studies showed effect, 6 did not
- Cross sectional, n=3 /0.
- Case series, n=2 /0
- Prospective Cohort (n=8 / 2)
- Other (2/0)
  - All different designs: conflicting results

Type I DM

- *Evidence* grade I (not very good) II and III
- *Recommendation*: C (B). We make no recommendation for or against routinely using SMBG.
- Comments:
  - The consensus agreement among experts is very strong (e.g. ADA), and it is difficult to advice against SMBG.
  - There is fair evidence that SMBG can improve health outcome. The balance between benefits and costs must be evaluated in each single environment.
  - If SMBG is going to be used, good instruments should be used patients must be educated in the use and instructed in how to use the results to monitor their insulin therapy.

POCT for glucose in hospital

- Three articles were retrieved
  - Lee-Lewandrowski et al, 1994: POCT was not inherently more expensive but can be relatively more costly if utilization is low.
  - Nosanchuk et al, 1995: POCT more expensive than central laboratory analysis
  - Parvin et al, 1996: Length of stay unchanged compared to when analyses were performed in the central laboratory

Recommendations - POCT for glucose in hospital

- *Evidence* grade II (economical and practical)
- *Recommendation*: C
  We make no recommendation for or against routinely using SMBG.
- Comments:
  - There is no evidence for clinical or economical / practical benefit.
  - The utility is probably very dependent on the local environment and how testing is organised.

Nature and Style of Questions

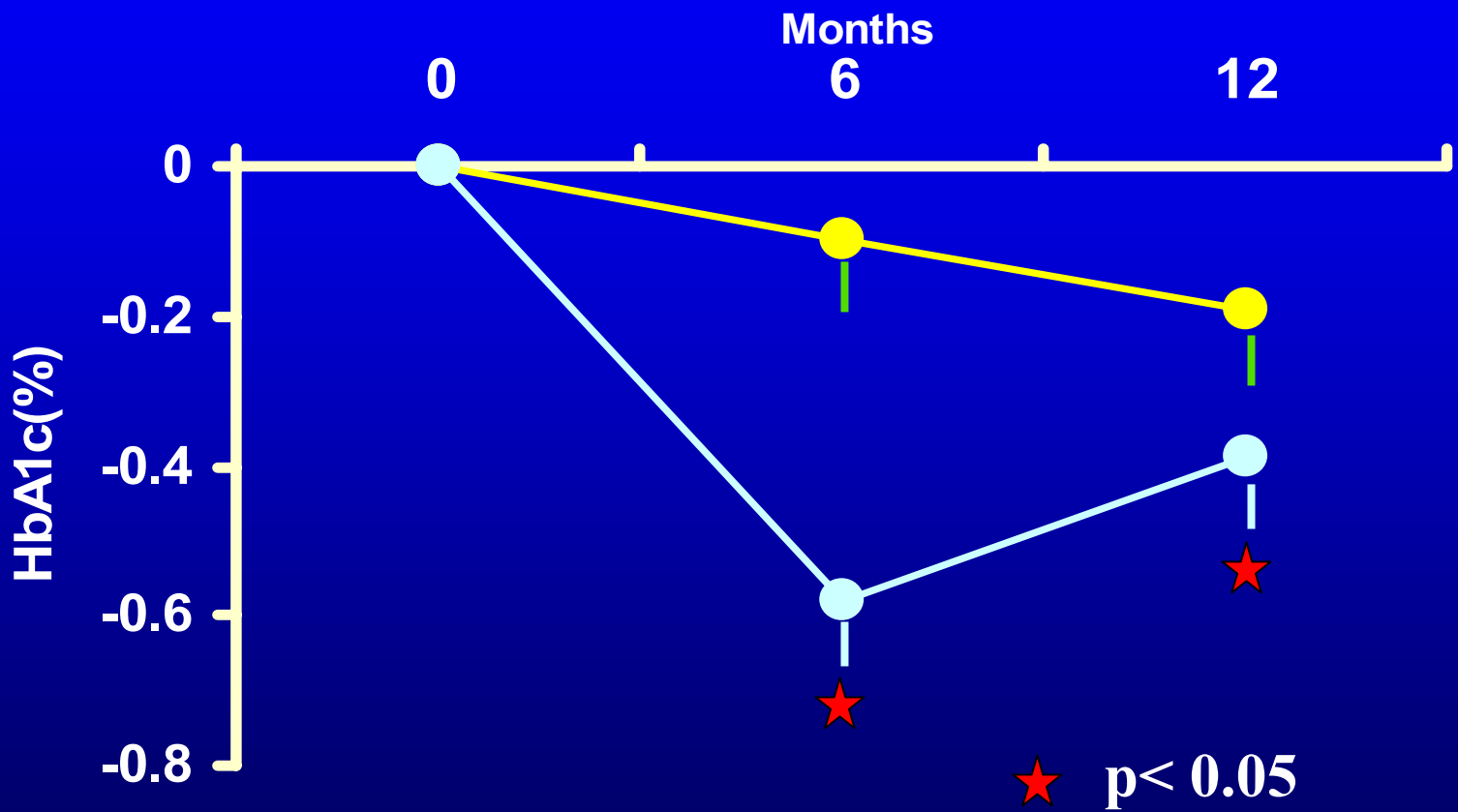
HbA1c, fructosamine, microalbuminuria

- does POCT improve the clinical outcome compared with central laboratory testing
- ….economic outcome….
- ….self testing….clinical….
- ….frequency of testing….clinical….

POCT for HbA1c
summary of studies

Cagliero	RCT	Secondary I and II	164	I 0.29±0.95% ↓ (0.07%) II 0.84±1.86% ↓ (0.16%)
Thaler	CT	Secondary	574	8.9±0.2% → 9.6±0.37
		II	>7.0%	9.2±0.2% → 9.3±0.27
Miller	CT	Primary	597	9.7±0.3 → 9.1±0.3%
		II	>7.0%	10.1±0.2 → 9.1±0.2%
Grieve	cohort	Secondary	1591	POCT 7.79± 0.058% LAB 8.66±0.056%
Ferenczi	cohort	Secondary	115	1.03±0.33% 0.33±0.83%

POCT for HbA1c in Diabetes Clinic



Cagliero et al 1999

POCT for HbA1c
diabetes clinics

- mean HbA_{1c} ↓ POCT cohort
- POCT costs ↑ cfd laboratory
- clinic visits ↓ (2.28 → 1.81 per annum)

Grieve et al. 1999

POCT for HbA1c
recommendations

- POCT improves clinical outcome (I/A)
- POCT improves economic outcome (II-2/B)
- no data on self testing (I)
- only opinion on frequency of testing (III/B)

Fructosamine POCT

- FDA approved POCT device (LXN InCharge) for home-monitoring of serum fructosamine
- CLIA-waived
- POCT device evaluated in a few studies - compared value of addition of fructosamine to SMBG
- POCT device no longer available

Value of Fructosamine POCT

- Only 3 published studies adequately examined effect of home POCT fructosamine as adjunct to SMBG
- Study of 25 patients (14 glucose only, 11 glucose plus fructosamine) showed at 3 months that fructosamine improved glycemic control
- Two other studies (comprising 60 and 140 patients) showed no benefit of fructosamine on glycemic control

POCT for fructosamine
recommendations

- no data on clinical outcome (III/I)
- no data on economic outcome (III/I)
- data does not support self testing (II-2/D)
- no data on frequency of testing (I)

POCT Ketone Body Analysis

key issues

- acetoacetate/acetone and β - hydroxybutyrate are reciprocal
- no single method measures both ketone groups
- acetoacetate/acetone usually measured in urine (semiquant)
  - **IS KETONE TESTING (any modality) CLINICALLY APPROPRIATE IN DIABETES?**

Results

- No study that compared patient outcomes associated with **PERFORMANCE vs. NON-PERFORMANCE** of serum ketone measurement in diabetic patients any modality (POCT or reference laboratory)
- Three studies supported argument that serum BOHB measurement did not provide additional information already given by DKA associated biochemical parameters (T**CO_2, pH)**
- **No ABSOLUTE indications supported in the literature**
- However RELATIVE indications are supported by the biochemical physiology of poorly controlled diabetes

POCT for blood ketones
recommendations

- no data related to clinical outcome (I)
- no data related to economic outcome (I)
- no data on self testing (I)

POCT for Microalbuminuria

- microalbuminuria is an important marker of incipient nephropathy
- clinical intervention (e.g., improved metabolic control & antihypertensives) decreases risk of ESRD development
- **POCT: MAU dipstick (Micral II, Immunodip vs. device (DCA2000+, Clinitek)**

POCT for Microalbuminuria

- Systematic review of literature

- 141 peer reviewed articles

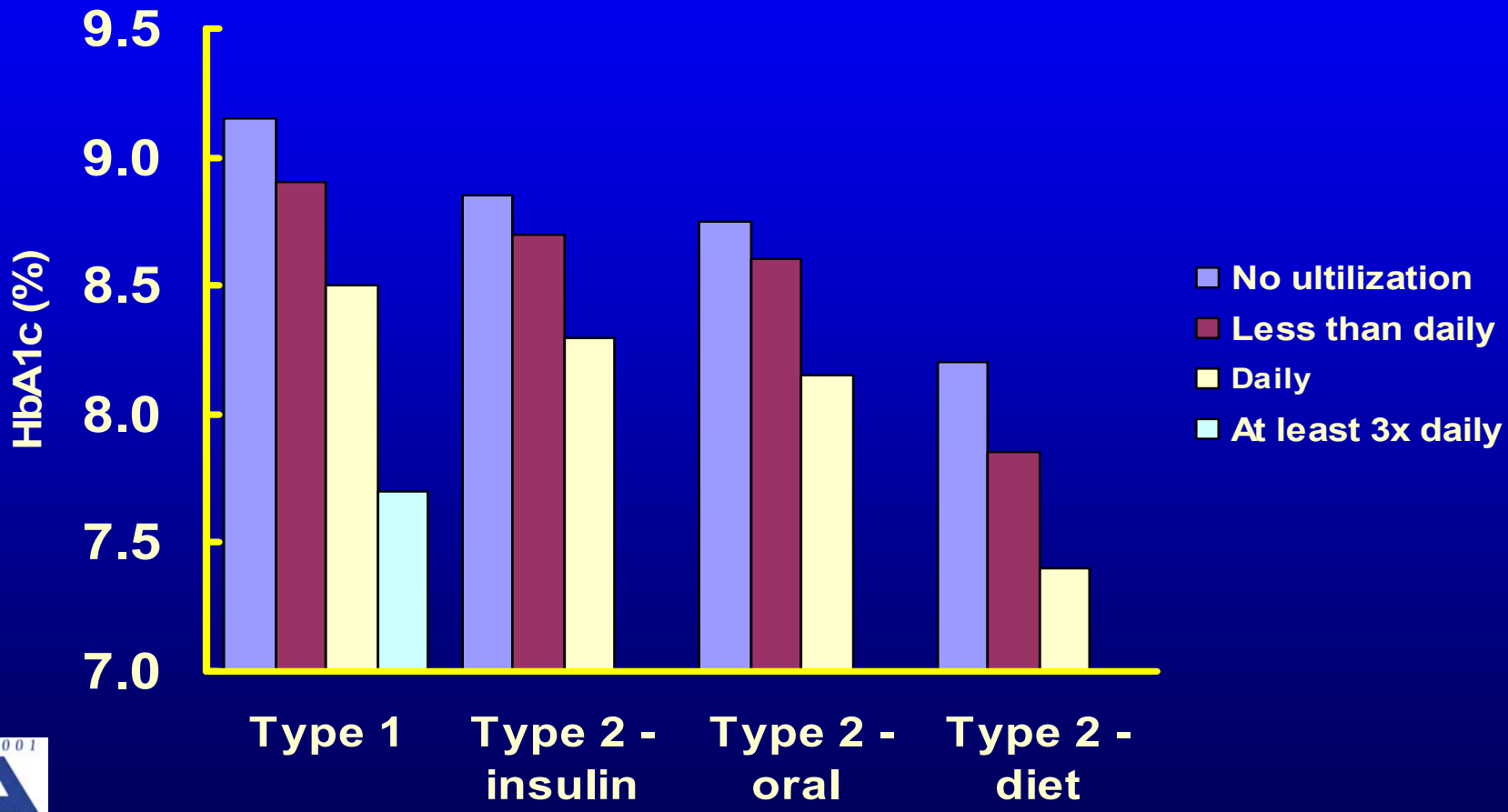
- 4 review articles

- Clinical: no articles comparing clinical outcome for POCT and central lab testing
- Economic: on cost per test basis POCT is 35% more expensive, but…….

POCT for microalbuminuria
recommendations

- no data on clinical outcome (III/I)
- no data on economic outcome (II-2/C)
- no data on self testing (I)
- only opinion on frequency of testing (III/C)

Outcomes from POCT
some current challenges



Karter et al 2001

NACB: LMPG for POCT
diabetes mellitus
considerations and challenges

- study designs
- recommendations
- practice guidelines
- care pathways
- role of audit
- further research
- ethics