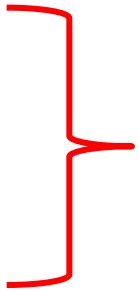
HbA_{1c} is the only measure of glycaemia needed for most patients with diabetes

Michael Mansfield
Leeds Teaching Hospitals

Measures of glycaemia

bioassay	ketosis and death
	symptoms & vascular complications
chemical assay	self monitoring of urine glucose
	self monitoring of blood glucose
	glycated haemoglobin (HbA1c)



Areas of agreement

Some type 2 diabetes patients at some stages of life should be encouraged to self-monitor glucose, for example:

- insulin-treated patients
- patients subject to actual symptomatic or troublesome hypoglycaemia
- in pregnancy
- severe intercurrent illness and/ or some medication eg steroids

Real question

Should SMBG be part of usual care for the vast majority of patients outside these scenarios ?

Or is HbA1c, the NICE target, adequate for most ?

HbA1c, glycated haemoglobin

reflects glycaemia over prior 6-8 weeks
50% glycation from prior month
25% the month before that
25% the 3 months before that
averaging effect probably not affected by glucose instability

strong correlation with mean glucose from 7 point profiles in DCCT (r=0.82)

lab measured, quality assured and standardised to DCCT

DCCT & UKPDS

predictor of microvascular complications in type 1 and type 2 diabetes
less strong predictor of macrovascular risk but epidemiological analysis supportive

NICE 2008

HbA1c recommended as primary glucose control measure for type 2 diabetes

HbA1c, glycated haemoglobin

target not useful for patients between consults ∴ disempowers patients

same "mean" glucose levels may produce different HbA1c in different patients

relationship between "mean" glucose and HbA1c may be confounded by:

- increased red cell turnover / production / transfusion
- carbamylation of haemoglobin in renal failure
- haemoglobin variants

the way in which HbA1c values are reported may be about to change

- more specific assay reporting values some 1.5 - 2% lower
- suggested change in units to mmol HbA1c/mol HbA0
- suggested change in units and emphasis to mean plasma glucose equivalent

Review of evidence: SMBG v none

cross-sectional, longitudinal, non-randomised

meta-analyses of very small randomised studies

recent moderately sized randomised studies

Confounders: concurrent education, powerful placebo effect

main endpoint usually HbA1c !

hypoglycaemia detection confounded

QoL outcome may depend on question asked

HbA1c strengths and weaknesses

Other perspectives

Longitudinal Study of New and Prevalent Use of Self-Monitoring of Blood Glucose

ANDREW J. KARTER, PHD[1]
MELISSA M. PARKER, MS[1]
HOWARD H. MOFFET, MPH[1]
MICHELE M. SPENCE, PHD[2]
JAMES CHAN, PHARMD, PHD[2]
SUSAN L. ETTNER, PHD[3]
JOE V. SELBY, MD[1]

OBJECTIVE — We sought to assess longitudinal association between self-monitoring of blood glucose (SMBG) and glycemic control in diabetic patients from an integrated health plan (Kaiser Permanente Northern California).

c16000 diabetes patients on Kaiser Permanente database

RESULTS — Greater SMBG practice frequency among new users was associated with a graded decrease in A1C (relative to nonusers) regardless of diabetes therapy ($P < 0.0001$). Changes in SMBG frequency among prevalent users were associated with an inverse graded change in A1C only among pharmacologically treated patients ($P < 0.0001$).

CONCLUSIONS — These observational findings are consistent with short-term benefits of initiating SMBG practice for all patients but continuing benefits only for pharmacologically treated patients. Differences in effectiveness between new versus prevalent users of SMBG have implications for guideline development and interpretation of observational outcomes data.

Diabetes Care 29:1757–1763, 2006

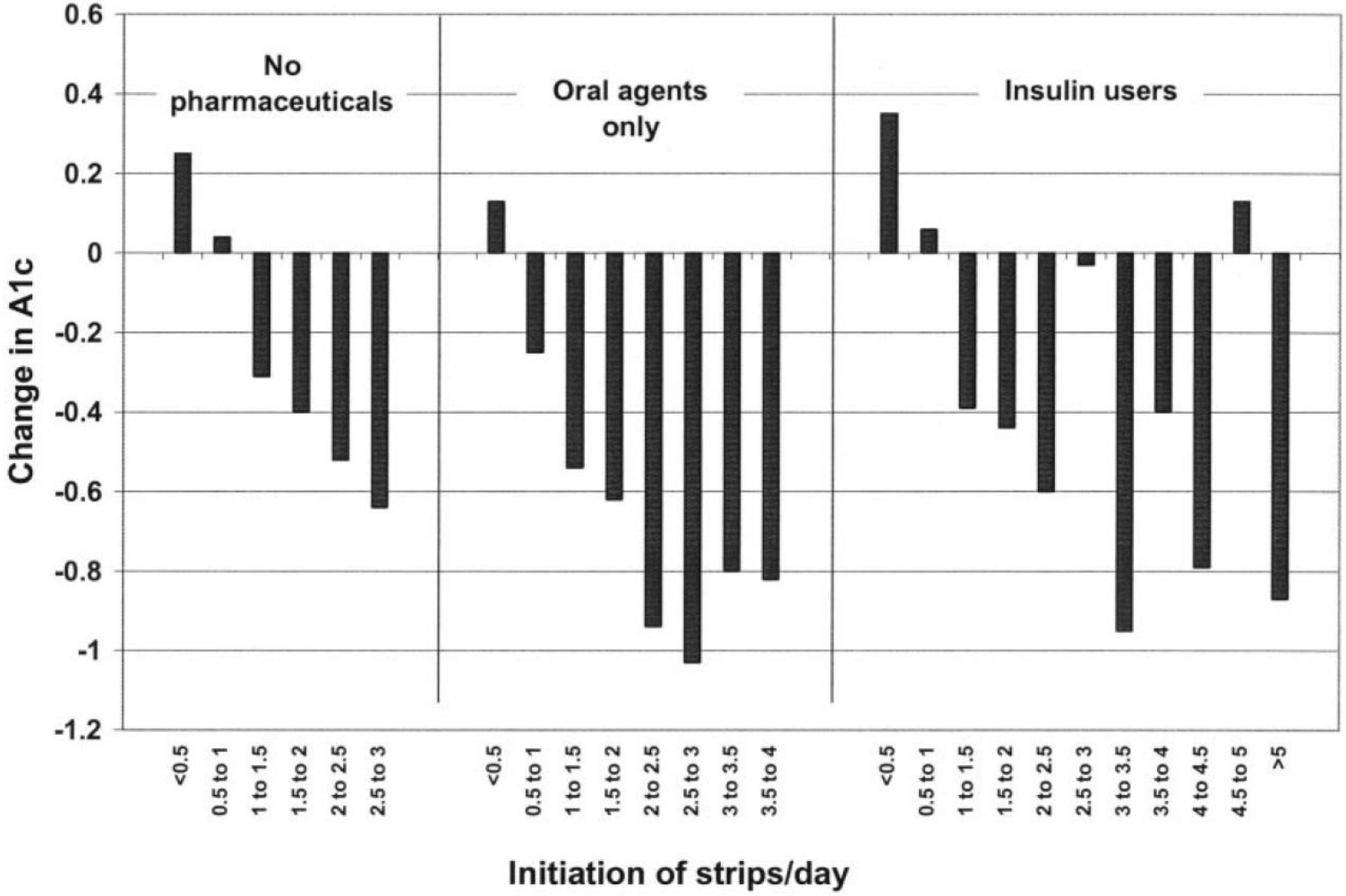


Figure 1—*Adjusted dose-responsive change in A1C associated with SMBG initiation among patients not previously using SMBG and not treated pharmacologically* (n = *7,872), treated with an oral agent only* (n = *5,546), and patients treated with insulin* (n = *840). Patients-switching-therapy changes were excluded. Therapy changes were excluded. Models adjusted for age, sex, insulin injection frequency (insulin model only), comorbidity index, oral medication refill adherence (OHA model only), appointment keeping, inpatient and outpatient utilization, smoking status, type of primary care provider, socioeconomic status indicators, timing of A1C test, and baseline A1C.*

Is Self-Monitoring of Blood Glucose Appropriate for All Type 2 Diabetic Patients?

The Fremantle Diabetes Study

WENDY A. DAVIS, PHD
DAVID G. BRUCE, MD
TIMOTHY M.E. DAVIS, DPHIL

Table 1—*Univariate associates of SMBG at study entry*

	No SMBG	Any SMBG	*P* value
n	386	900	
Age (years)	66.1 ± 12.3	63.2 ± 10.7	<0.001
Sex (male)	47.4	49.3	0.54
Diabetes duration (years)	4.0 (1.4–10.0)	3.9 (0.9–8.9)	0.08
BMI (kg/m^2)	29.7 ± 6.1	29.5 ± 5.2	0.65
A1C (%)	7.6 (6.4–8.9)	7.3 (6.4–8.8)	0.12
FPG (mmol/l)	8.4 (6.9–11.3)	8.5 (6.8–10.7)	0.35
Diabetes control			
Diet and exercise	35.9	30.4	0.06
OHA	56.8	55.7	0.76
Insulin (±OHA)	7.3	13.9	0.001
Self-reported hypoglycemia	21.3	33.5	<0.001
Ever attended diabetes education	40.7	79.3	<0.001

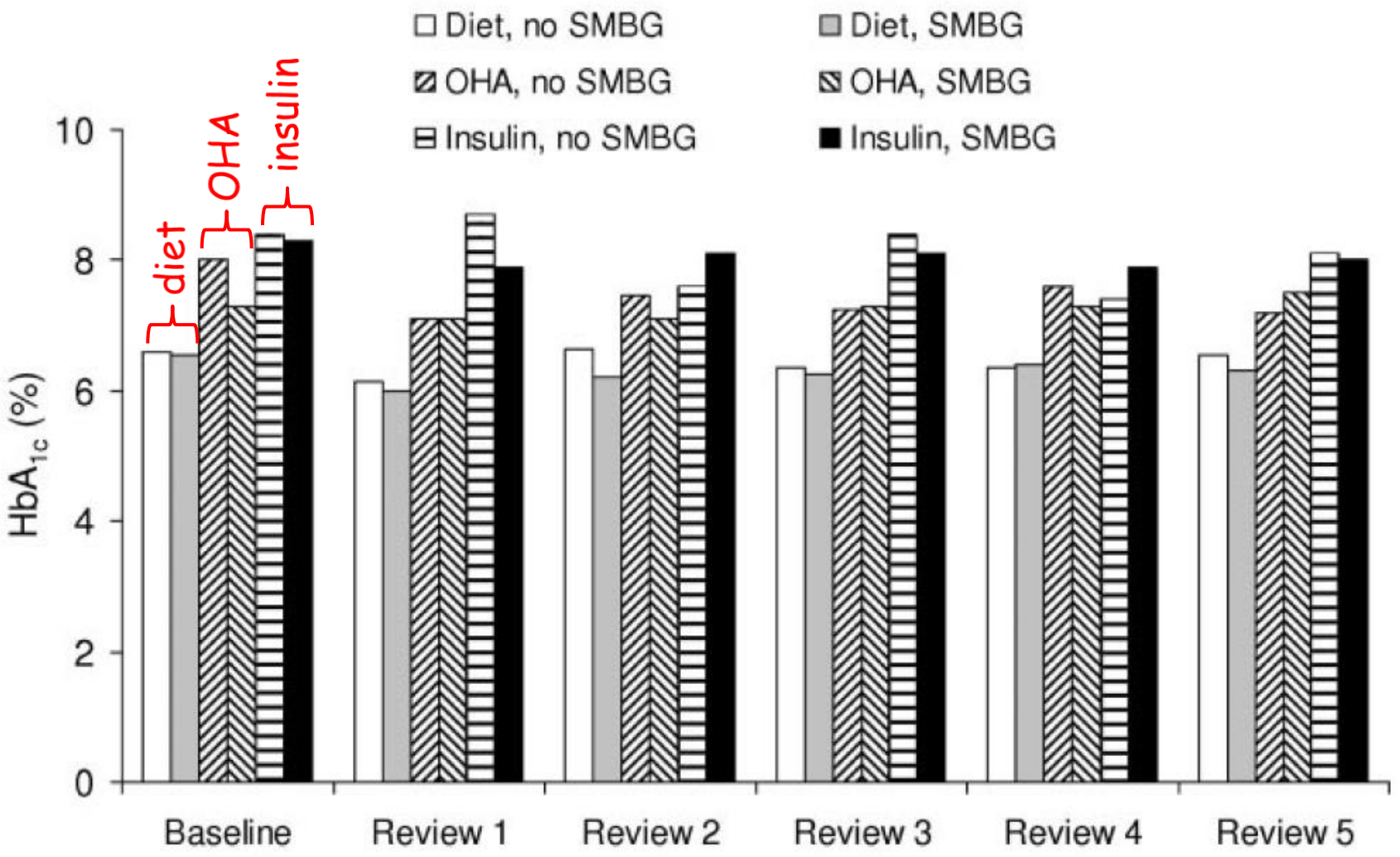


Figure 1—*A1C by diabetes treatment type, year of follow-up, and SMBG status for the 531 FDS participants with type 2 diabetes who attended at least six annual assessments.*

Frequency of blood glucose monitoring in relation to glycaemic control: observational study with diabetes database

Josie M M Evans, Ray W Newton, Danny A Ruta, Thomas M MacDonald, Richard J Stevenson, Andrew D Morris

Table 4 Linear regression models in 290 patients with type 2 diabetes who were using insulin, with haemoglobin A_{1c} concentration as outcome variable

Factors in univariate analysis	Regression coefficient	P value
Age (+10 years)	–0.0003	0.997
Total strips dispensed (+180)	–0.108	0.357
Duration (+1 year)	0.007	0.616
Deprivation score (+1 category)	–0.018	0.796
Sex (female *v* male)	0.217	0.283
Body mass index (+1 SD)	0.145	0.216

The Impact of Blood Glucose Self-Monitoring on Metabolic Control and Quality of Life in Type 2 Diabetic Patients

An urgent need for better educational strategies

MONICA FRANCIOSI, MSC (BIOL)[1]
FABIO PELLEGRINI, MS[1]
GIORGIA DE BERARDIS, MSC (CHEM)[1]
MAURIZIO BELFIGLIO, MD[1]
DONATELLA CAVALIERE, MD[1]
BARBARA DI NARDO, HSDIP[1]
SHELDON GREENFIELD, MD[2]
SHERRIE H. KAPLAN, PHD, MPH[2]
MICHELE SACCO, MD[1]
GIANNI TOGNONI, MD[1]
MIRIAM VALENTINI, MD[1]
ANTONIO NICOLUCCI, MD[1]
FOR THE QUED STUDY GROUP

3567 t2DM patients

2855 pts with SMBG data

38% did no SMBG

Table 2—*Results of multilevel linear regression for HbA_{1c} levels*

	Non–insulin-treated patients		Insulin-treated patients	
Fixed effects	β	*P*	β	*P*
Level 1 covariates				
Women	0.22	0.001	0.33	0.038
BMI	0.02	0.003	0.04	0.050
Diabetes duration	0.02	<0.001	0.01	0.320
Diabetes treatment				
Diet alone versus oral agents (rc)	−0.71	<0.001	—	—
SMBG frequency				
≥1/day	0.30	0.008	—	—
≥1/week	0.27	<0.001	—	—
<1/week or never (rc)	—	—		
Combined effect of SMBG and ISM				
ISM yes/SMBG ≥1/day			−0.55	0.015
ISM yes/SMBG ≥1/week	—	—	−0.31	0.178
ISM yes/SMBG <1/week	—	—	−0.33	0.244
ISM no/SMBG any (rc)			—	—

ISM: insulin dose self-management

Table 3—*QoL scores according to the frequency of SMBG*

QoL domain	Frequency of SMBG				*P**
	≥1/day	≥1/week	<1/week	Never	
n	471	899	414	1,071	
Diabetes-related stress	51.6 ± 20.5	47.7 ± 19.9	49.5 ± 19.0	44.1 ± 19.2	0.0001
Diabetes health distress	44.1 ± 26.0	37.9 ± 25.8	37.1 ± 25.6	28.5 ± 24.5	0.0001
Diabetes-related worries	60.6 ± 24.6	53.7 ± 27.1	50.2 ± 28.2	48.5 ± 28.6	0.0001
Depressive symptoms (CES-D)	23.3 ± 10.7	20.9 ± 10.8	21.6 ± 10.4	19.9 ± 10.4	0.0001

Data are means ± SEM unless otherwise indicated. *Kruskall-Wallis one-way analysis of variance.

Cross-sectional / observational non-randomised studies

Not a great way to address the clinical value of SMBG

No consistent indication of a positive impact on HbA1c

Where benefit seen it may wane with time in some patient groups

Some suggestion of a negative psychological impact

Randomised interventional studies.....meta-analyses

Urine or blood monitoring compared with no monitoring

Trial	Number of subjects	Intervention effect GHb (%)
Wing [13]	23/22	-0.25 (-1.56 to 1.08)
Estey [7]	28/25	-0.40 (-0.85 to 0.05)
Fontbonne [8]	110/54	0.25 (-0.46 to 0.97)
Muchmore [11]	12/11	-0.85 (-2.47 to 0.78)
Pooled effect		**-0.25 (-0.61 to 0.10)**

Blood monitoring compared with urine monitoring

Allen [6]	27/27	0.00 (-1.60 to 1.60)
Fontbonne [8]	56/54	-0.23 (-1.05 to 0.59)
Miles [10]	58/56	0.10 (-0.57 to 0.77)
Pooled effect		**-0.03 (-0.52 to 0.47)**

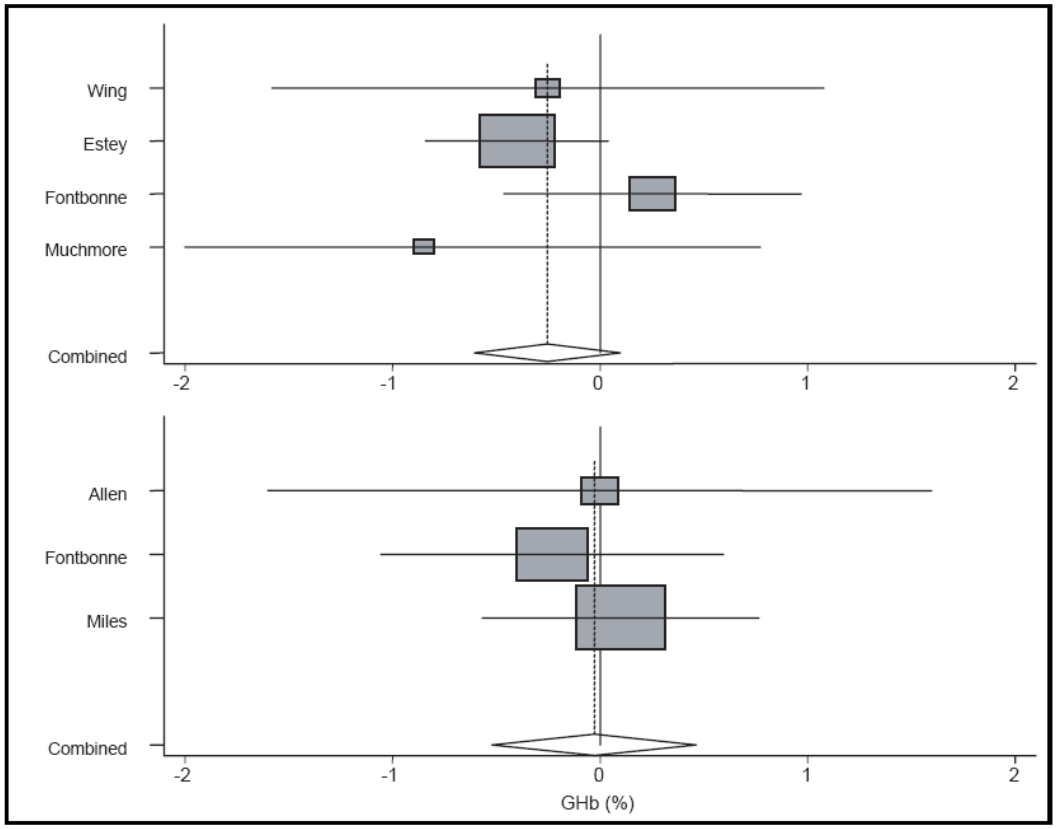


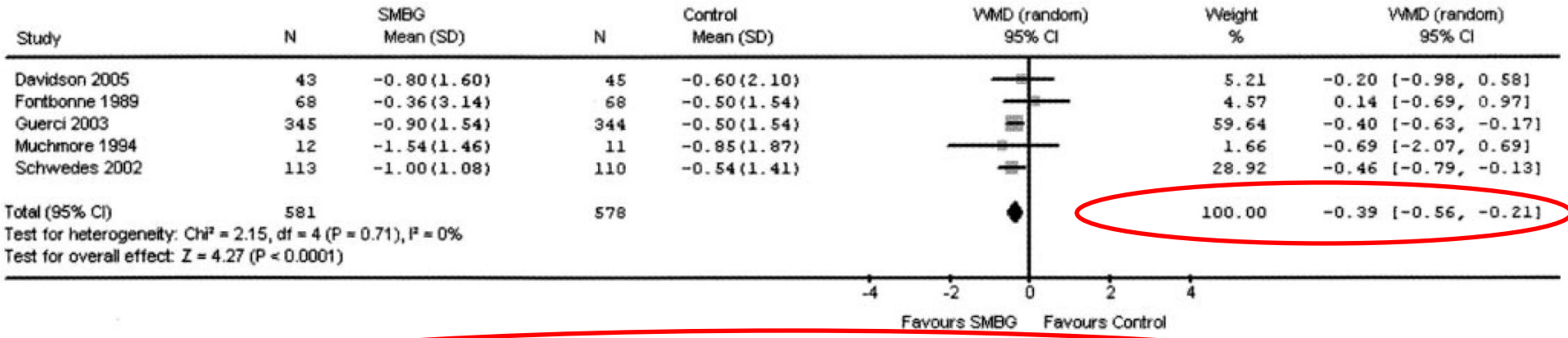
Figure 2 Results of meta-analysis.

Pooled effect on HbA1c **-0.25 (-0.61 to 0.10) %**

Self-Monitoring of Blood Glucose in Patients With Type 2 Diabetes Who Are Not Using Insulin

A systematic review 2005

LAURA M.C. WELSCHEN, MSC[1,2]
EVELIEN BLOEMENDAL, MSC[1,2]
GIEL NIJPELS, MD, PHD[1,2]
JACQUELINE M. DEKKER, PHD[1]
ROBERT J. HEINE, MD, PHD[1,3]
WIM A.B. STALMAN, MD, PHD[1,2]
LEX M. BOUTER, PHD[1]



pooled effect on HbA1c -0.39 (-0.56 to -0.21) %

2 additional studies: (considered of low quality by the review authors)

Guerci n=345, effect –0.40 (-0.63 to -0.17) %, drop-out rate >40%

Schwedes n=113, effect -0.46 (-0.79 to -0.13) %, much more counselling, not ITT

BMJ

RESEARCH

DIGEM study

Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial

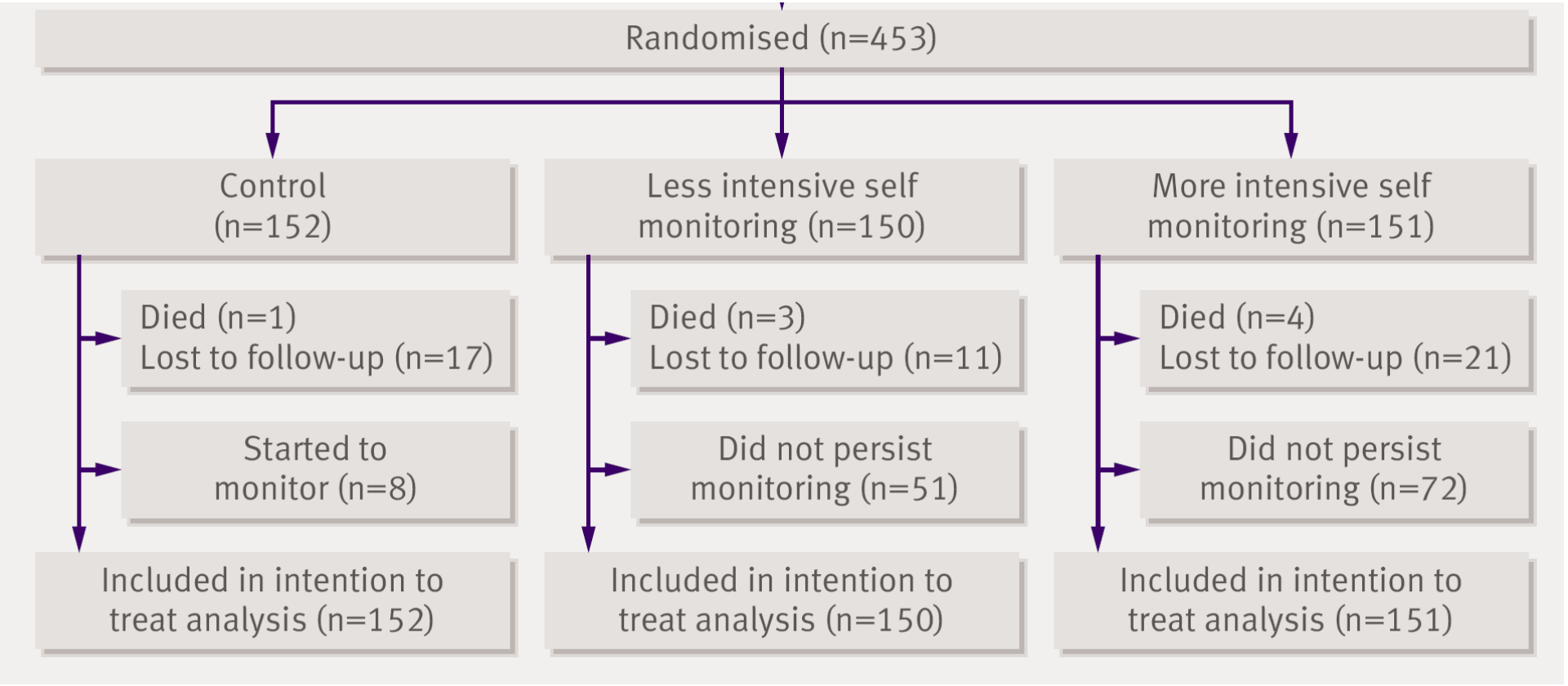
Andrew Farmer, lecturer,[1] Alisha Wade, resident,[2] Elizabeth Goyder, reader,[3] Patricia Yudkin, reader,[1] David French, reader,[4] Anthea Craven, trial manager,[1] Rury Holman, professor,[5] Ann-Louise Kinmonth, professor,[6] Andrew Neil, professor,[7] on behalf of the Diabetes Glycaemic Education and Monitoring Trial Group

general-practice based study
32% identified as eligible responded to invite and ½ of these had meter already

age: mean 66, SD 10 years
men: 57%
duration of diagnosed diabetes: median 3, IQR 2-6 years

diet only 27%
one drug 38%
more drugs 34%

baseline HbA1c mean 7.5, SD 1.1%



intention to treat analysis

12.6% of pts lost from follow-up (equal across the groups)

DIGEM groups

control: standardised	usual care, goal setting and review informed of HbA1c result 2 weeks before consults
less intensive self-monitoring	as above PLUS: given meter asked to measure glucose three times a day twice a week target 4-6 mmol/L pre-meal, 6-8 mmol/L post-meal consider contacting Dr if >15 or < 4 mmol/L no other info on interpretation of SMBG values separate diaries for SMBG and other activities
more intensive self-monitoring	usual care, goal setting given meter & training and support in timing, interpreting encouraged to reflect on and use results to plan activities single diary to record SMBG and other activites

for all groups medication adjusted according to (previous) NICE guidance

Variable	Control group* (n=152)	Meter group, less intensive self monitoring (n=150)	Meter group, more intensive self monitoring (n=151)
HbA_{1c} (%):			
Baseline	7.49 (1.09)	7.41 (1.02)	7.53 (1.12)
Follow-up	7.49 (1.20)	7.28 (0.88)	7.36 (1.05)
Change	−0.00 (1.02)	−0.14 (0.82)	−0.17 (0.73)

Episodes of hypoglycaemia:

grade 2: mild symptoms requiring minor intervention

grade 3: moderate symptoms requiring immediate third party intervention

grade 4: unconscious

During study at least one grade 2 episode experienced by:

control group	14 patients
less intense intervention	33 patients
more intense interv'tion	43 patients

Grade 3 episodes: only 1 patient in control group

BMJ

RESEARCH

Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): randomised controlled trial 2008

Maurice J O'Kane, consultant,[1] Brendan Bunting, professor,[2] Margaret Copeland, trial manager,[3] Vivien E Coates, professor,[3] on behalf of the ESMON study group

hospital clinic based study

age: mean 59, SD 11 years
men: 60%
newly diagnosed type 2 diabetes

baseline HbA1c mean 8.7, SD 2.1%

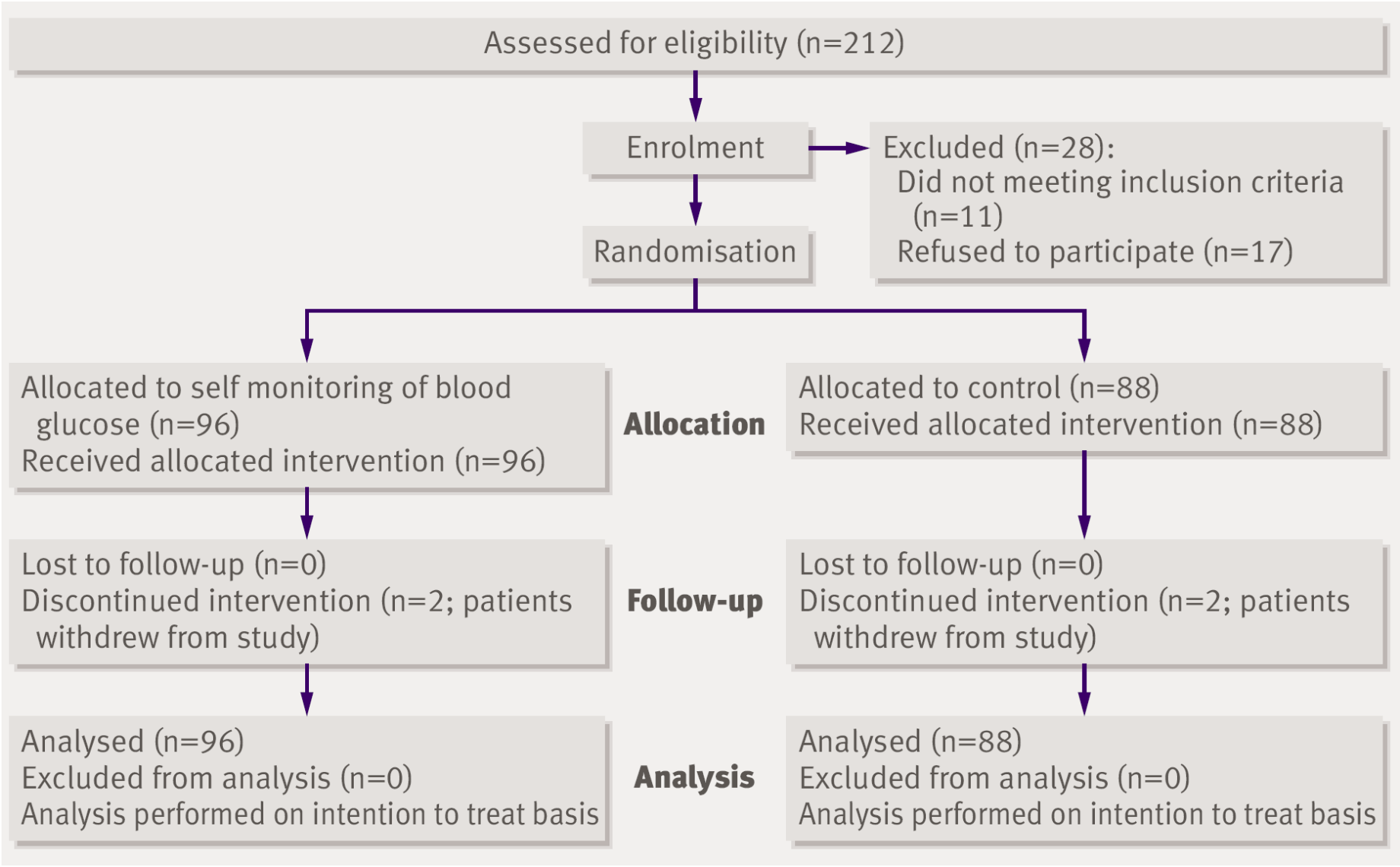

Assessed for eligibility (n=212)
Enrolment
Excluded (n=28):
Did not meeting inclusion criteria (n=11)
Refused to participate (n=17)
Randomisation
Allocated to self monitoring of blood glucose (n=96)
Received allocated intervention (n=96)
Allocation
Allocated to control (n=88)
Received allocated intervention (n=88)
Lost to follow-up (n=0)
Discontinued intervention (n=2; patients withdrew from study)
Follow-up
Lost to follow-up (n=0)
Discontinued intervention (n=2; patients withdrew from study)
Analysed (n=96)
Excluded from analysis (n=0)
Analysis performed on intention to treat basis
Analysis
Analysed (n=88)
Excluded from analysis (n=0)
Analysis performed on intention to treat basis

Table 2 | Mean (SD) HbA_{1c} in patients with newly diagnosed diabetes according to self monitoring or no monitoring (control) of blood glucose

Time (months)	Monitoring	Control	P value	Mean difference (95% CI)
0	8.8 (2.1)	8.6 (2.3)	0.68	−0.33 (−0.77 to 0.51)
3	7.2 (1.1)	7.1 (1.2)	0.50	0.18 (−0.47 to 0.23)
6	7.0 (0.9)	7.0 (1.1)	0.82	0.04 (−0.27 to 0.35)
9	6.9 (0.8)	7.1 (1.4)	0.30	0.19 (−0.16 to 0.54)
12	6.9 (0.8)	6.9 (1.2)	0.69	0.07 (−0.25 to 0.38)

Table 3 | Analysis of covariance for effect of monitoring on psychological variables (baseline and end point), adjusted for sex

Item	β coefficient* (SE)	P value
Depression	6.05 (2.37)	0.011
Anxiety	5.86 (3.19)	0.07
Positive wellbeing	4.16 (2.88)	0.15
Energy	−0.84 (2.83)	0.77

These recent studies suggest

no clear benefit in terms of 12 month HbA1c from SMBG

recently diagnosed type 2 diabetes
patients not on insulin
with baseline HbA1c around 7-8%

but, were these typical patients ?

2006/07 QOF Clinical Indicators for Diabetes

	diabetes prevalence aged 17+ (%)	% pts in whom last HbA1c is 7.5% or less in last 15 months
Leeds	4.0	69.7
North Yorkshire	4.0	67.9
Yorks & Humber	4.6	68.5
England	4.5	67.6

qualitative work on blood glucose self-monitoring:

from longitudinal & repeated interviews with patients

can empower patients
viewed by patients as complex and inconvenient
painful
repeated "bad" results lead to frustration, guilt, learned helplessness

fewer patients monitor over time (seen also in DIGEM)
those who continue to monitor do so less often
patients uncertain about meaning of results & how to act on them

concerns voiced about value health professionals place on SMBG readings

self-monitoring of blood glucose: why ?

patient:

- patient empowerment

healthcare professional:

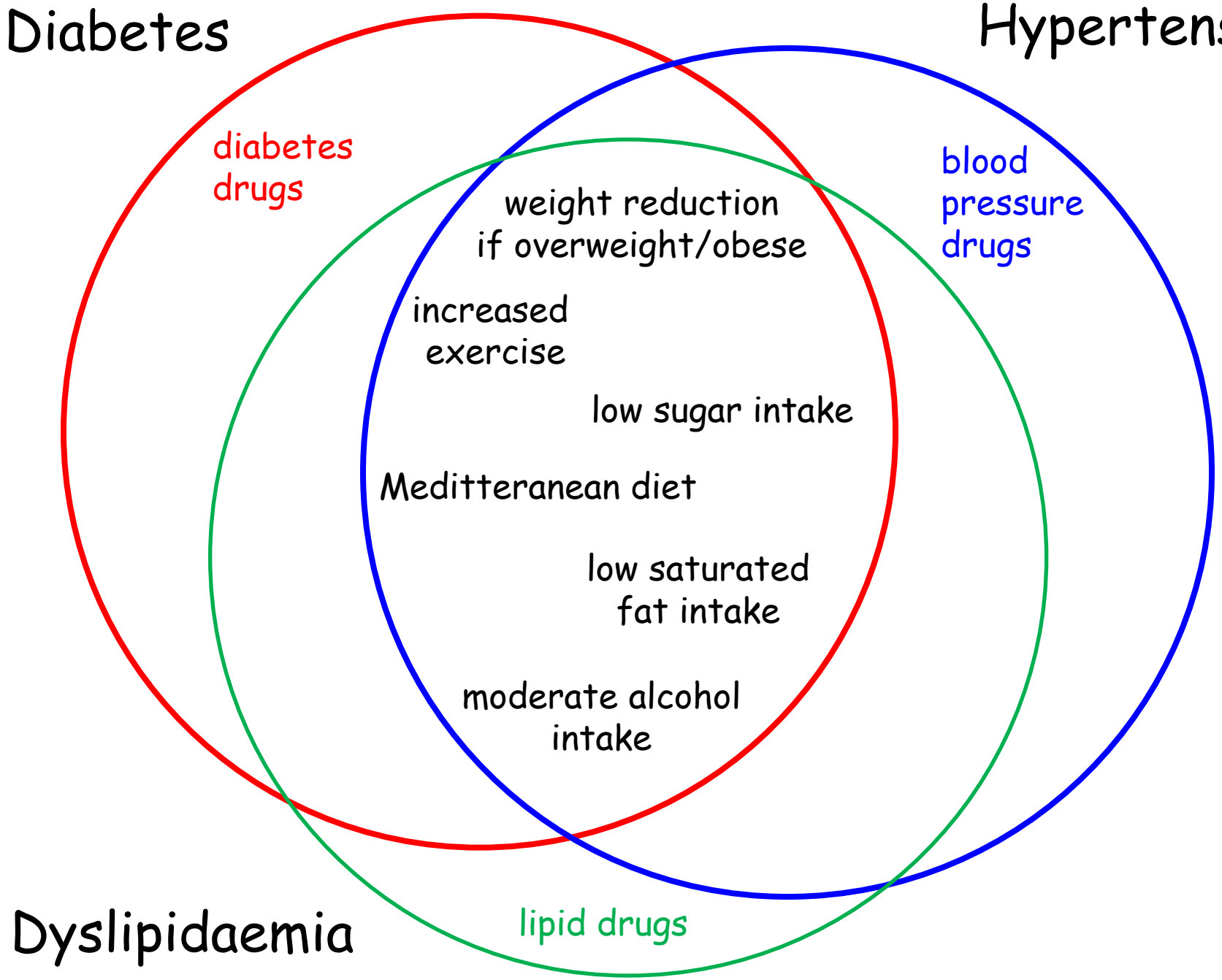
- something to discuss at consultations
- treatment titration
- technophilia

wider perspective:

- commercial pressure and interests

historical context:

- <u>hypoglycaemia avoidance</u>


Diabetes
Hypertension
diabetes drugs
blood pressure drugs
weight reduction if overweight/obese
increased exercise
low sugar intake
Meditteranean diet
low saturated fat intake
moderate alcohol intake
Dyslipidaemia
lipid drugs

Ames reflectance meter 1971

The Accu-Chek Aviva Meter

Display – Shows results, messages, and results stored in memory.

Right and Left Arrow Buttons – Press to enter memory, adjust settings, and scroll through results.

Test Strip Slot – Insert test strip here.

Infrared (IR) Window – Transfers data from the meter to a computer or PDA.

On/Off/Set Button – Turns the meter on or off and sets options.

Battery Door – Flip open the battery door by pushing the tab in the direction of the arrow.

Code Chip Slot – Insert code chip into

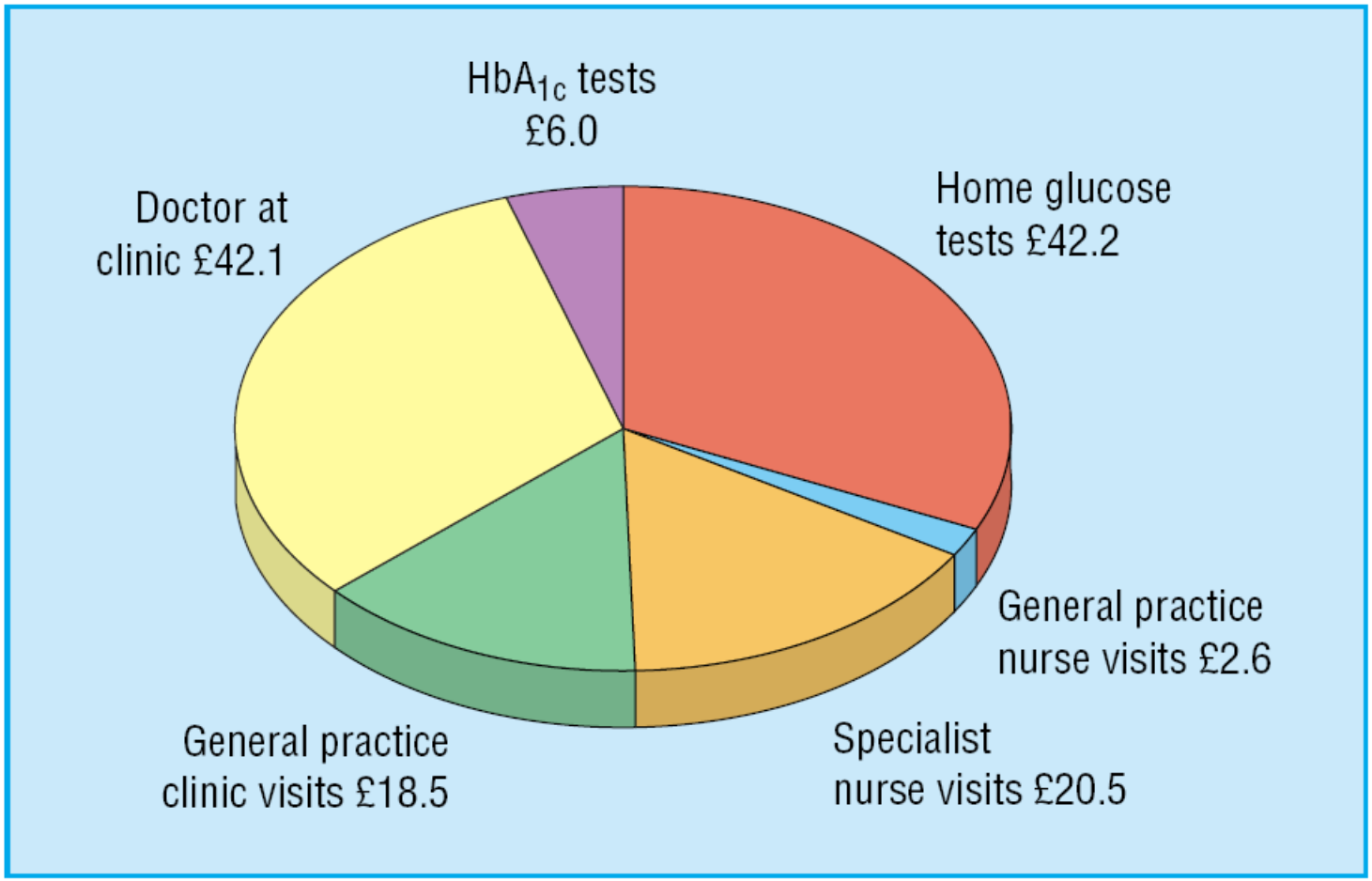
Strategies for managing type 2 diabetes which do not disturb physiological protection against hypoglycaemia

healthy eating
calorie restriction
physical exercise

metformin
acarbose
thiazolidinediones
DDP-4 inhibitors
GLP-1 analogs

(orlistat)
(sibutramine)

(? higher target HbA1c eg 7.5% instead of 6.5%)



Estimated additional management costs (£m, at 1999 prices) of adopting policies in England for more intensive control of blood glucose and blood pressure by category of resource use (total=£132m)

Expense

£14 to £14-50 per 50 strip pack

28 pence per strip

once daily use £102 per year per person

approximately 0.4 bikes/year/person

Cost to NHS estimated at £100 million per annum:

more than the spend on diabetes tablets or insulin in many PCTs

just over 0.1% of the total English NHS budget of £92 billion

equivalent to about 1400 nurse consultants; 9 for each PCT in England

.....or about 700 consultants at various salary points

Blood glucose monitoring
why not ?

patient focus
hassle & painful
"poor" results lead to discouragement
can lead to dependency on health care professionals
reduced quality of life

number focus
focusing on numbers can distract from the real changes needed
may be difficult to interpret figures

consultation focus
monitoring to please the health care professional
can distract from the real agendas

population focus
leaves less money for other more important interventions in diabetes

poor evidence
most studies suggest no benefit or only modest benefit on HbA1c
no hard outcome studies