

# Self-monitoring of Blood Glucose: Individual patient data

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# Health Technology Assessment

## March 2010

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- Health Technology Assessment – March 2010
  - Effect of Self-management of Blood glucose (SMBG): HbA1c reduction of 0.21%
  - Education might have an important role
  - SMBG could be effective if linked to self-adjustment of treatment

# SM BG – a Complex Intervention

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- Variations in
  - Intervention components
  - target population
  - reporting methods
- Aim: to examine these factors within the trials of SMBG through an individual patient data analysis (IPD)

# What is an IPD Meta-analysis?

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- Central collection, checking and analysis of **updated** individual patient data
- Include **all** RCTs
- Include **all** patients using ITT analysis

# What is an IPD Meta-analysis?

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## Formal Collaboration

Common aims  
and objectives

Joint Publication  
policy

Confidentiality

# Key Principles

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- All data sent will
  - be secure and with strict confidence
  - not be used without permission of trialist
- All published reports will
  - be in the name of the Collaborative Group
  - be circulated to all members for comment and approval
  - Focus on presentation of results (rather than interpretation)

# Advantages of an IPD

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- Only practical way to do subgroup analyses
- Update follow up information
- More balanced interpretation of results
- Wider endorsement and dissemination of results
- Better clarification of further research
- Collaboration on further research

# Protocol

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- Formal protocol
  - Allows a meta-analysis to be designed with the same rigour as a randomised trial
    - specify rationale behind project
    - set out main aims and objectives
    - specify a priori hypotheses and methods
  - Clarifies issues
    - Identifies potential problems
    - Explain project to collaborators



# Timeline of Research

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- Form Collaboration
- Circulate meta-analysis protocol
- Submission of MA protocol
- Collect trial protocol and data
- Data management and Analysis
- Presentation of results to Collaboration
- Manuscript created and distributed
- Submission of research article

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# IPD aims

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- to estimate the effect of SMBG on glycaemic control for patients with non-insulin treated type 2 diabetes;
- to estimate the effect of self-monitoring of blood glucose in pre-defined sub-groups of patients by baseline HbA1c, age and duration of disease at the outset

# IPD aims (cont...)

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- to identify differences in trial outcomes based on intensity of intervention using sub-group and meta-regression analyses;
- to systematically report the interventions used in the pooled trials of SMBG, including educational training, educational materials, and monitoring schedules.

# IPD Methods

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- Data Checking
- Quality Assessment
- Statistical Analysis plan
  - Dummy Randomisation
- Subgroup analyses
- Software for data handling and statistical analyses

# Data Checking

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- **Not** to centrally police trials or to expose fraud
- Improve accuracy of data
- Improve follow-up
- Ensure intention-to-treat analysis
- Ensure all randomised patients are included
- Assess quality of trial
  - Integrity of randomisation procedure
  - Integrity of follow-up procedure

# Quality Assessment

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- Quality scoring systems largely relate to trial publications
- IPD allows for very detailed checking
- Aim is to 'clean' all data sets to be of high quality

# Statistical Analysis Plan

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- Based on the Published Protocol
- Detailed description of the Methods used
- Distributed across the collaboration – iterative process
  - Use all randomised patients
  - Adhere to Intention-to-treat principle
  - ‘Up-to-date’ analysis

# Subgroup Analyses

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- Aim: sufficient power to detect effect differences in any patient subgroups

But...

- Still **exploratory** analyses - interpreted cautiously
- Should be a reasonable biological explanation for any observed interactions

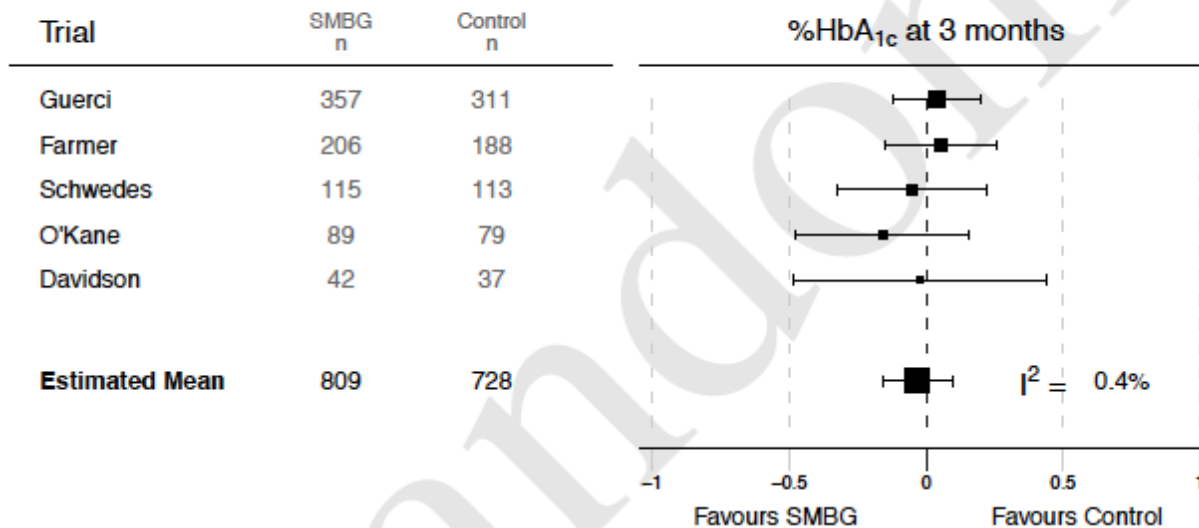
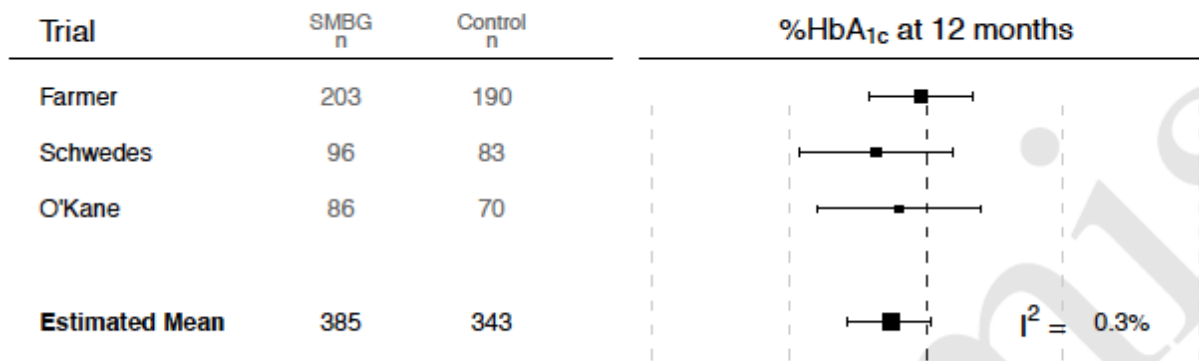
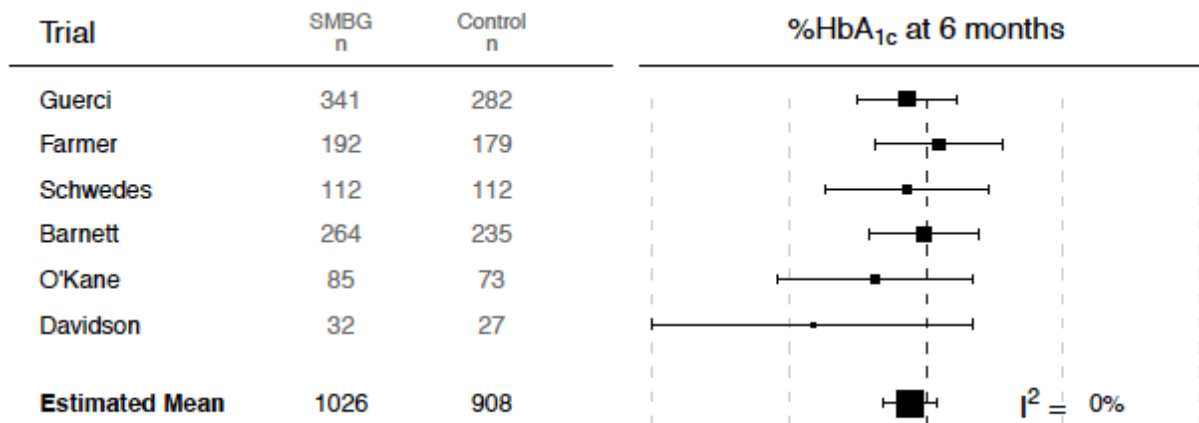
# Software

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- SPSS for Data management
  - Recoding
  - Appending
  - Merging
- STATA and R for Statistical Analysis
  - Syntax for analysis based on dummy randomisation
  - Tested across both packages to test for robustness and consistency of models

# Proposed Analyses

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|                                 | Number of trials | SMBG n | Control n | Unadjusted estimate | Confidence Interval | Adjusted estimate | Confidence Interval |
|---------------------------------|------------------|--------|-----------|---------------------|---------------------|-------------------|---------------------|
| <b>Primary Outcome</b>          |                  |        |           |                     |                     |                   |                     |
| HbA <sub>1c</sub> 6 months (%)  | 6                | 1026   | 908       | -0.06               | (-0.16, 0.04)       | -0.07             | (-0.17, 0.03)       |
| <b>Secondary Outcomes</b>       |                  |        |           |                     |                     |                   |                     |
| HbA <sub>1c</sub> 12 months (%) | 3                | 385    | 343       | -0.13               | (-0.29, 0.02)       | -0.15             | (-0.31, 0.01)       |
| HbA <sub>1c</sub> 3 months (%)  | 5                | 809    | 728       | -0.031              | (-0.158, 0.095)     | -0.03             | (-0.136, 0.076)     |
| Systolic Blood Pressure (mmHg)  | 3                | 854    | 754       | -0.28               | (-1.46, 0.91)       | -0.33             | (-1.53, 0.87)       |
| Diastolic Blood Pressure (mmHg) | 3                | 853    | 754       | -0.34               | (-1.05, 0.38)       | -0.46             | (-1.18, 0.26)       |
| Total Cholesterol (mmol/l)      | 3                | 343    | 301       | -0.002              | (-0.134, 0.129)     | 0.002             | (-0.132, 0.137)     |

## Intervention Effect

### Age, in years

<=45

>45-55

>55-65

>65-75

>75

### Sex

Female

Male

### %HbA<sub>1c</sub> Baseline

<=8

>8-9

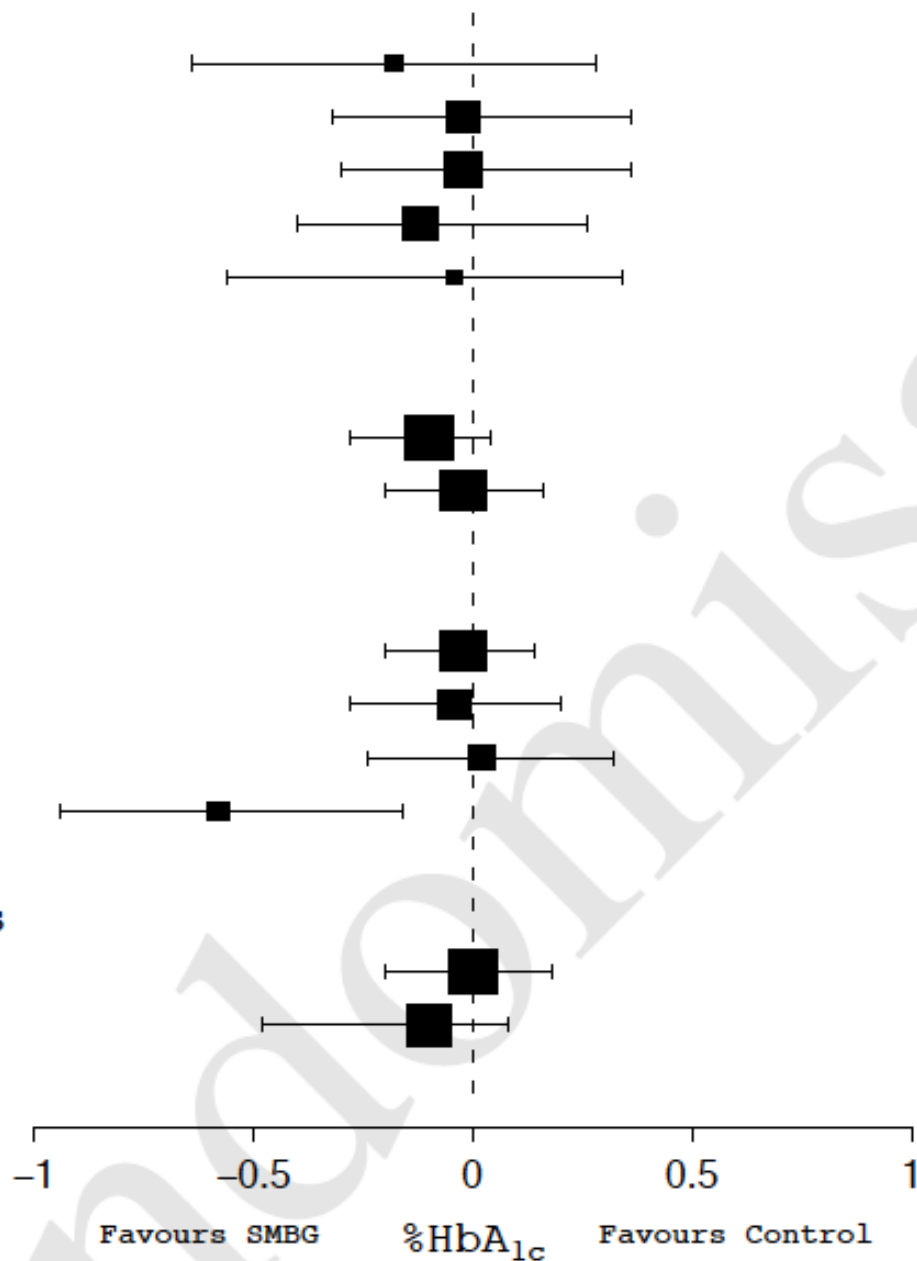
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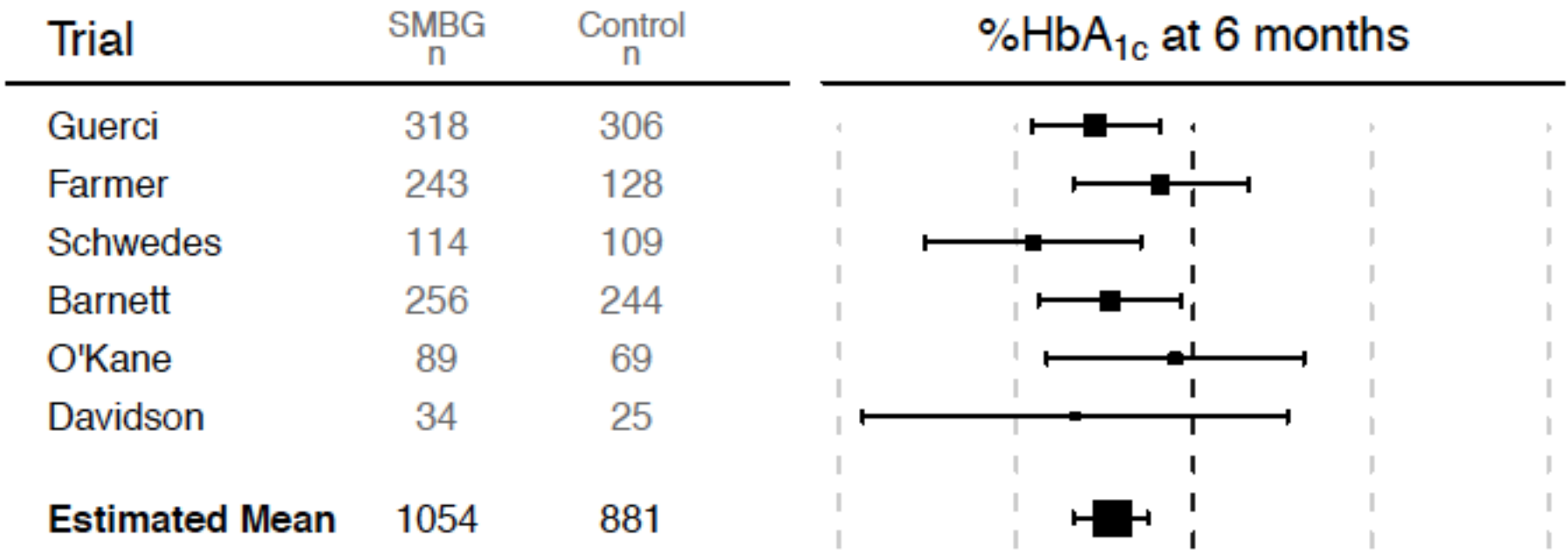
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### Duration of Diabetes

<=24 months

>24 months





| Number of trials | SMBG n | Control n | Unadjusted estimate | Confidence Interval | Adjusted estimate | Confidence Interval |
|------------------|--------|-----------|---------------------|---------------------|-------------------|---------------------|
|------------------|--------|-----------|---------------------|---------------------|-------------------|---------------------|

**Primary Outcome**

|                                |   |      |     |       |                |       |                |
|--------------------------------|---|------|-----|-------|----------------|-------|----------------|
| HbA <sub>1c</sub> 6 months (%) | 6 | 1054 | 881 | -0.23 | (-0.34, -0.13) | -0.25 | (-0.35, -0.14) |
|--------------------------------|---|------|-----|-------|----------------|-------|----------------|

# Acknowledgements

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- Anthony Barnett
- Mayer Davidson
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- Andrew Farmer
- Alison Ward
- Carl Heneghan
- Jason Oke
- Alice Fuller
- Clare Bankhead
- Richard Stevens

# Inclusion criteria

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- Published and unpublished RCTs where
  - main intended effect to improve disease outcomes through incorporating SMBG into self-management regimen of non-insulin treated patients with type 2 diabetes, and
  - trial not confounded with respect to this intervention, no other differences in modification of risk factors or behaviour between the relevant treatment groups were intended; and
  - trial aimed to recruit 80 participants or more with follow up duration lasting at least six months.