Experiences of using routinely collected medical data in a cardiovascular safety trial?

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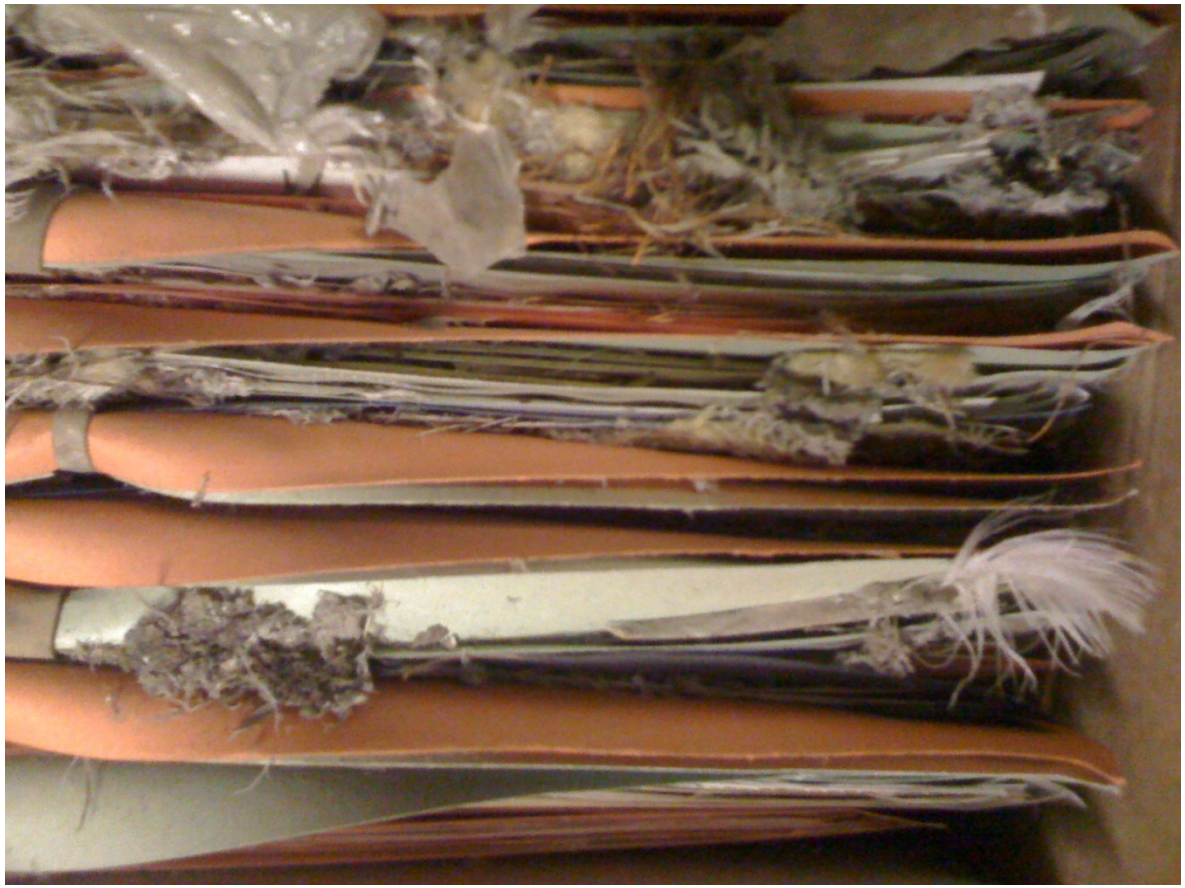
Issues in clinical trials

- Study feasibility
- Recruitment
- Data capture
- QA/ monitoring
- Pharmacovigilance
- Long-term follow-up within and after trial
- Desire to do large simple trials
  - Comparative safety
  - Comparative efficacy

University of Glasgow

NHS Greater Glasgow and Clyde

Data cleaning



eTRIALS: Trial Portals

15/04/2005 | Demonstration e-Trial | *Jane Aziz*

Main
- Home
- Mailer
- Forum
- Contacts

Trial Site

Enter Subject

Study drug

Subject Status

Subject Data

Data Management

Data Summaries

This web portal provides an interactive demonstration of some of the e-solutions provided by the Robertson Centre to aid in Clinical Trial data management.
Please select an option from the menu on the left to view that application.

Site 1

Western Infirmary

Total Randomised:	6
First Subject Randomised:	06/04/2005
Last Subject Randomised:	14/04/2005

Site 2

Glasgow Royal Infirmary University NHS Trust

Total Randomised:	0
First Subject Randomised:	N/A
Last Subject Randomised:	N/A

Site 3

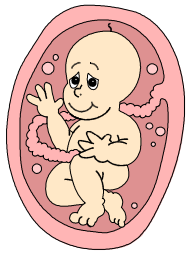
The Royal Hospital for Sick Children

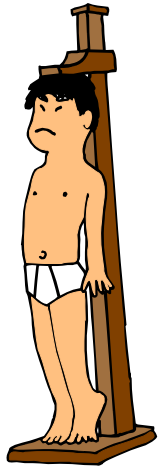
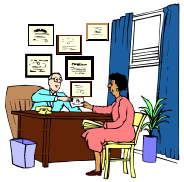
Total Randomised:	1
First Subject Randomised:	14/04/2005
Last Subject Randomised:	14/04/2005

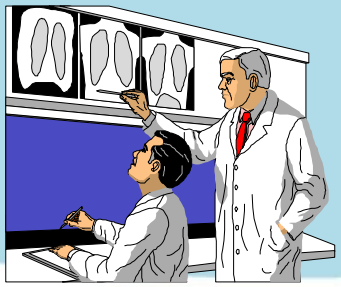
1

From conception to death...

- Mothers ante-natal records
- Maternity
- Neonatal record
- Register birth - NHS number
- Register with GP - CHI
- GP Appointments
- Dental Appointments
- Outpatients
- A&E attendance
- General hospital admission
- Prescribing
- Cancer registration
- Cancer treatment
- Community care
- Death



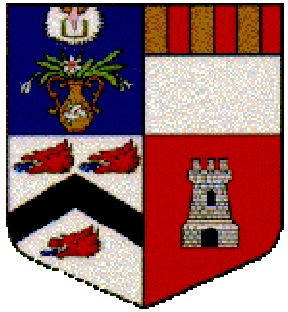






UNIVERSITY OF
DUNDEE


THE UNIVERSITY OF EDINBURGH


VIA VERITAS VITA




THE UNIVERSITY OF NOTTINGHAM

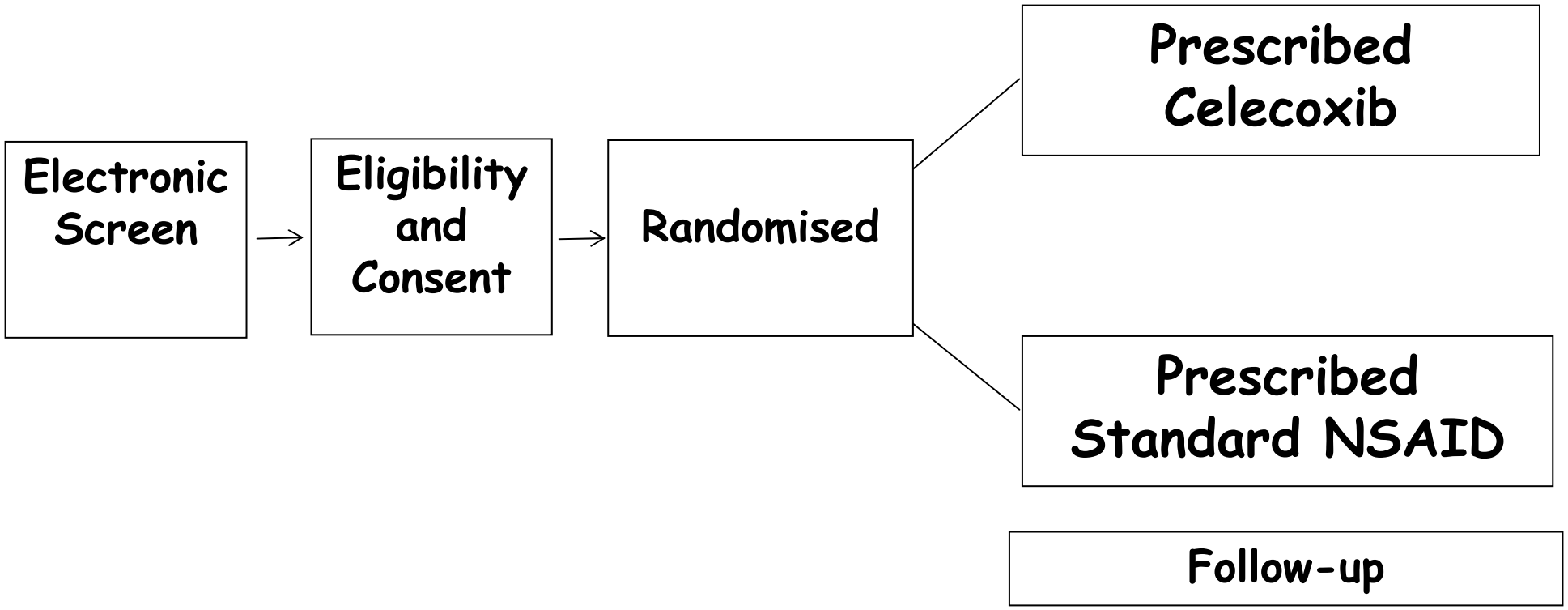

UNIVERSITAS OTHINIENSIS


SCOT

Inclusion / Exclusion

- Inclusion
  - Patients with OA or RA taking NSAIDS (>90 days in previous year)
  - Aged 60 years or over
- Exclusion
  - History of vascular disease

Design


Electronic Screen
Eligibility and Consent
Randomised
Prescribed Celecoxib
Prescribed Standard NSAID
Follow-up

Endpoints

- Primary
  - CV death, MI, stroke
- Secondary
  - GI hospitalisation

Design

- Non-inferiority trial
  - Non-inferiority limit set at HR = 1.3
- Pragmatic trial
  - PROBE design

Design

- Sponsor: University of Dundee
- CI: Prof Tom MacDonald
- Target recruits: 13,682 (611 primary endpoints)
- Recruitment from primary care
- Initial Countries: Scotland, Denmark

Committees

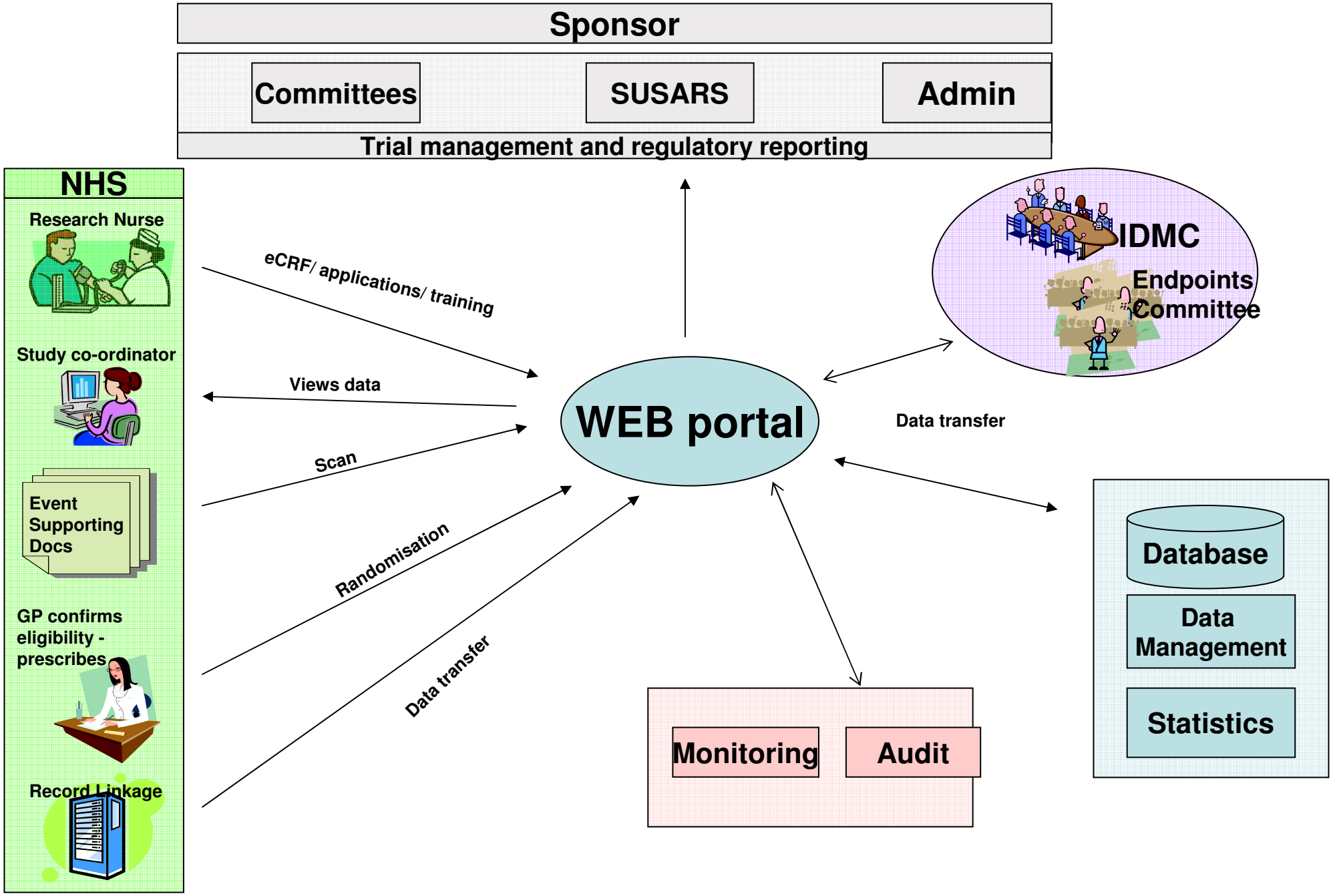
- Executive
- Steering
- IDMC
- CV endpoints
- GI endpoints

Processes (Scotland)

- Pre-screen GP electronic records
- Invite potentially eligible patients for screening
- Consent
- Check inclusion/exclusion
- Record baseline characteristics on eCRF
- Randomise
- Prescribe
- Follow up off-line

Data Collections systems

- Primary Care
  - Electronic search tool
  - Data extract to upload prescription data
- Lab data
- Randomisation
  - IVRS
- E-CRF
  - Screening
- Follow-up data
  - Record linkage (deaths, hospital admissions, cancer registry)
- Pharmacovigilance


Sponsor
Committees
SUSARS
Admin
Trial management and regulatory reporting
NHS
Research Nurse
Study co-ordinator
Event Supporting Docs
GP confirms eligibility - prescribes
Record Linkage
eCRF/ applications/ training
Views data
Scan
Randomisation
Data transfer
WEB portal
IDMC
Endpoints Committee
Data transfer
Database
Data Management
Statistics
Monitoring
Audit

Why e-Searching

Pros

- Reduces the amount of manual review
- Tracks each stage in the screening process
- Metrics available earlier in the trial

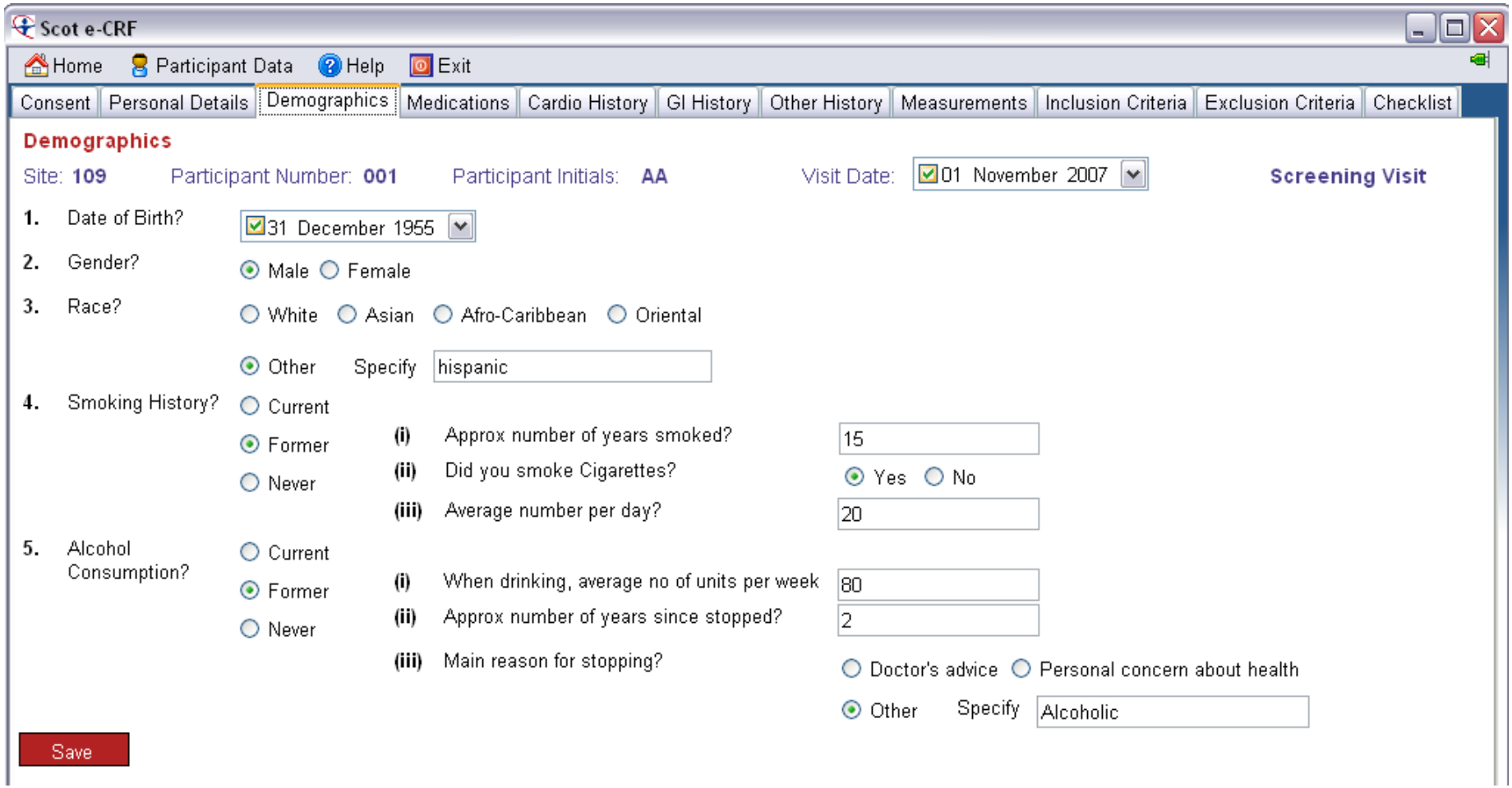
Cons

- Many varieties of GP system that the software has to work in!

START

- Streamlined Trial Adaptable Recruitment Toolset
  - Identify potential participants
  - Facilitates letter of invitation generation
  - Track screening process
  - Generate files for upload

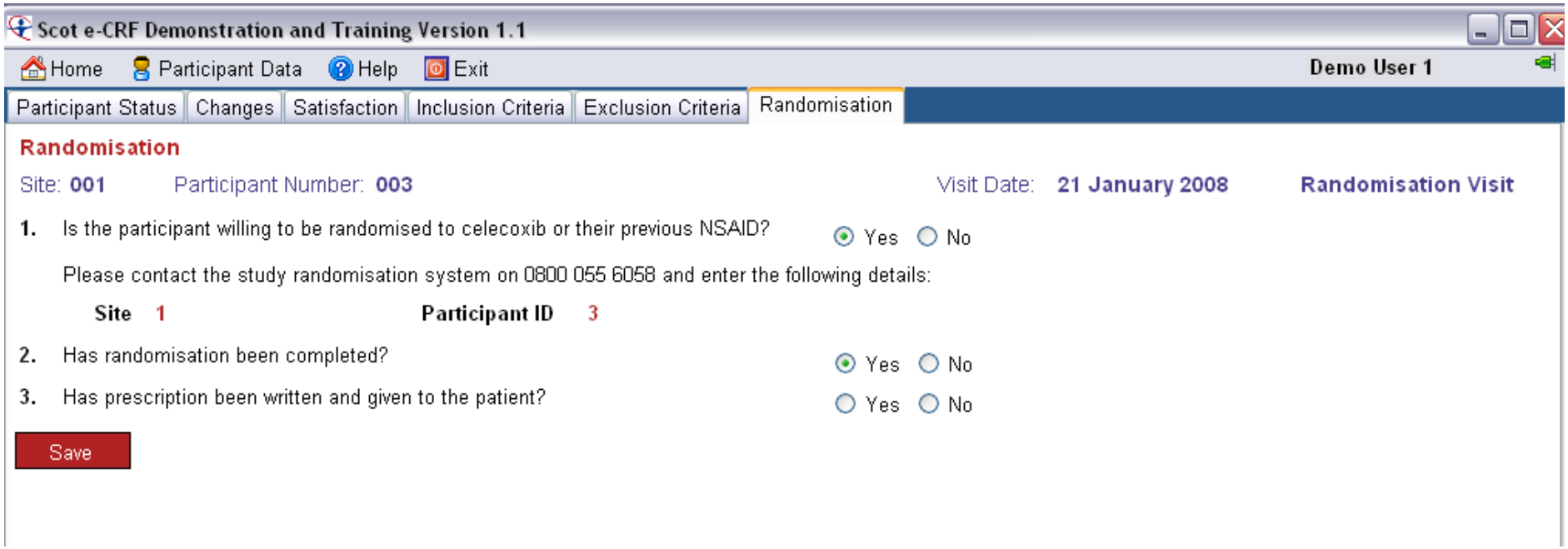
e-CRF – screening



Lab data in Scotland

- **Lab data in Scotland**
  - **Via hospital labs**
  - **SCI store(s)**
- **Issues:**
  - **Lots of negotiation!**

e-CRF – Randomisation



IVRS

Using SCOT IVRS

- Dial freephone number
- Enter study site and participant ID (screening number)
- Stratification by indication (RA or OA) and screening NSAID

Event follow-up

- **Information Services Division**

- **Electronic linkage to Scottish national linked datasets of hospital admissions, incident cancers and deaths**

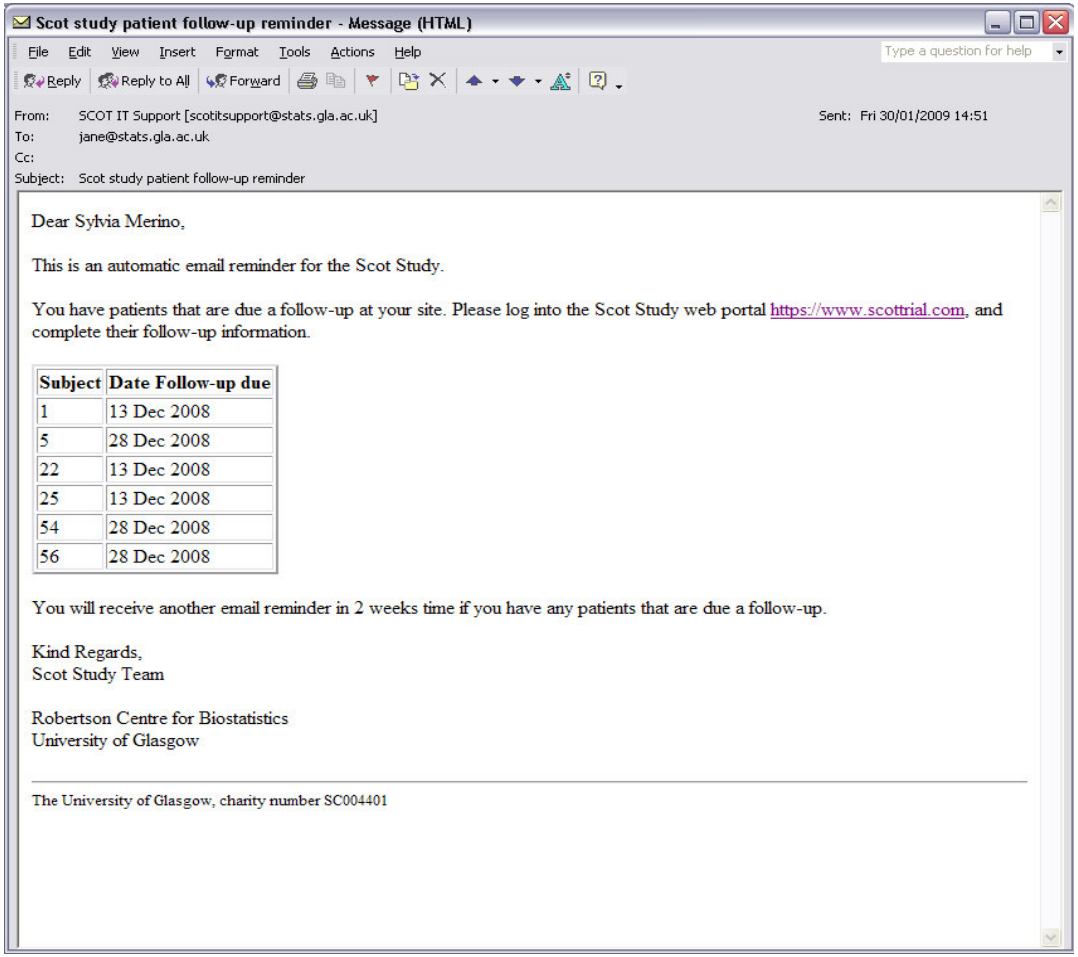
- **Historical approach**
  - Link on DOB, name, place of residence
  - probabilistic matching

- **Current/ Future**
  - Unique identifier matching (CHI)

Follow up datasets

- Datasets transferred routinely to the Data Centre from ISD:
  - **SMR 01** General acute inpatient and day case discharges
  - **SMR 04** Psychiatric and mental handicap hospitals and units: Admissions, residents and discharges
  - **SMR 06** Scottish cancer registrations
  - **GRO(S)** death registrations

GP Reminder - email



Scot study patient follow-up reminder - Message (HTML)

File Edit View Insert Format Tools Actions Help

Type a question for help

Reply | Reply to All | Forward

From: SCOT IT Support [scotitsupport@stats.gla.ac.uk] Sent: Fri 30/01/2009 14:51
To: jane@stats.gla.ac.uk
Cc:
Subject: Scot study patient follow-up reminder

Dear Sylvia Merino,

This is an automatic email reminder for the Scot Study.

You have patients that are due a follow-up at your site. Please log into the Scot Study web portal https://www.scottrial.com, and complete their follow-up information.

Subject	Date Follow-up due
1	13 Dec 2008
5	28 Dec 2008
22	13 Dec 2008
25	13 Dec 2008
54	28 Dec 2008
56	28 Dec 2008

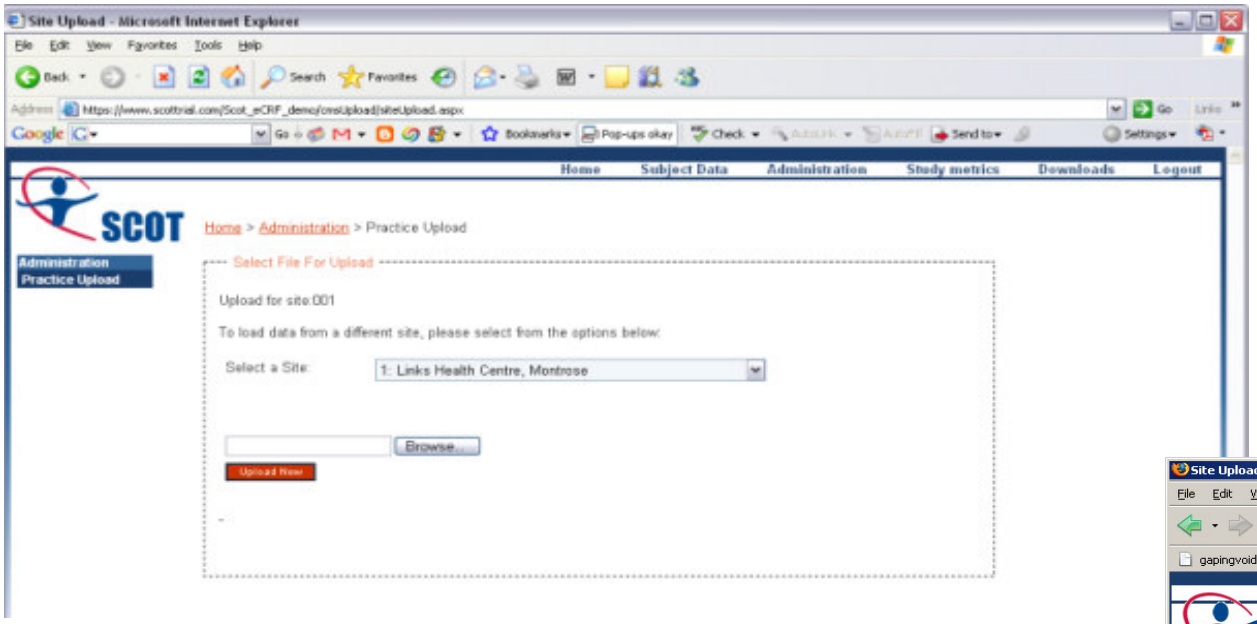
You will receive another email reminder in 2 weeks time if you have any patients that are due a follow-up.

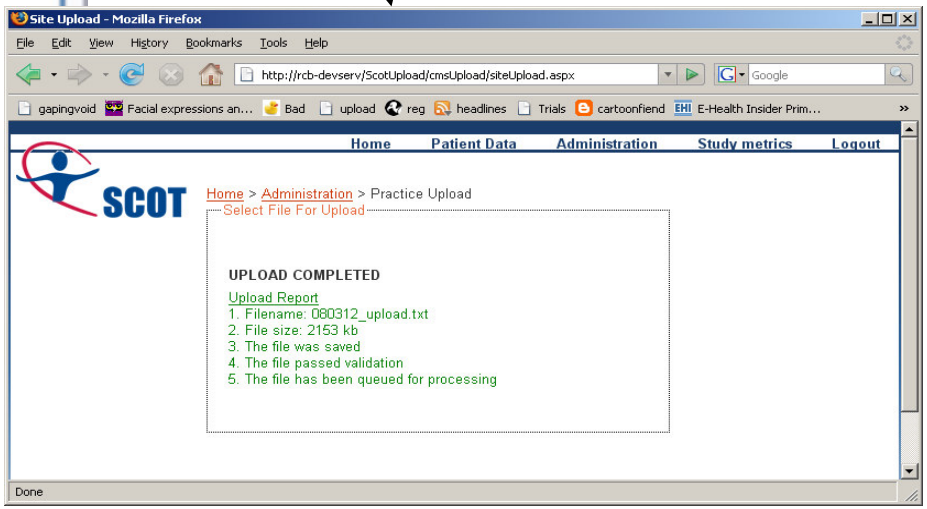
Kind Regards,
Scot Study Team

Robertson Centre for Biostatistics
University of Glasgow

The University of Glasgow, charity number SC004401

GP: Upload Prescribing Data

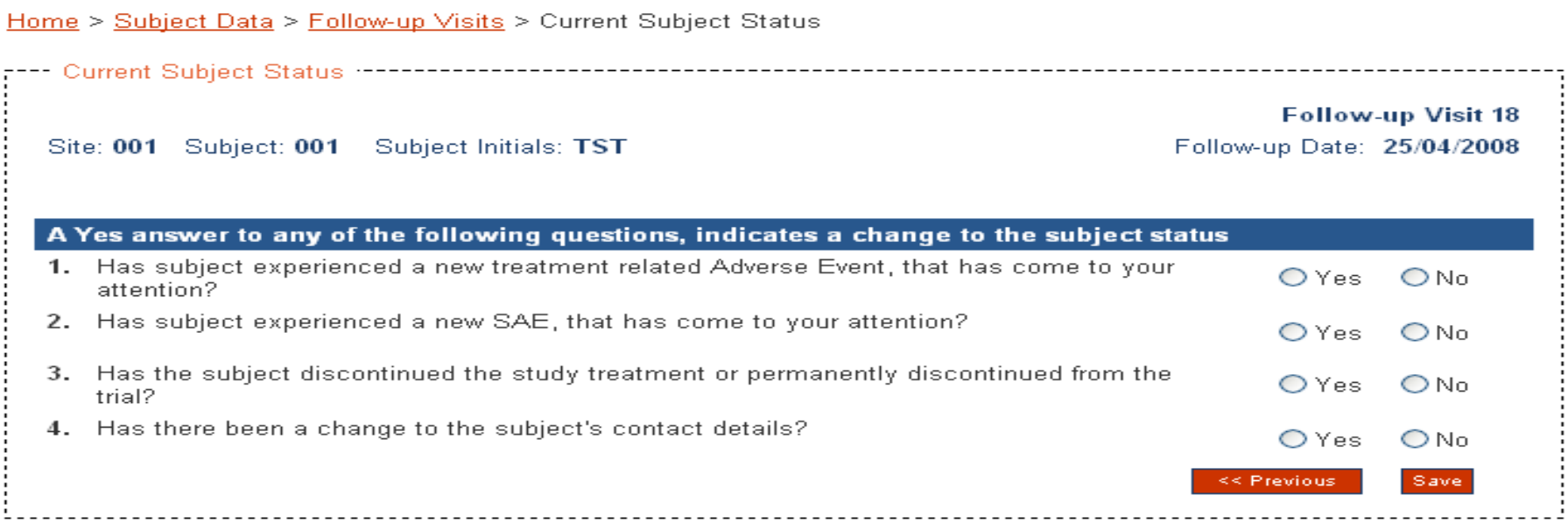




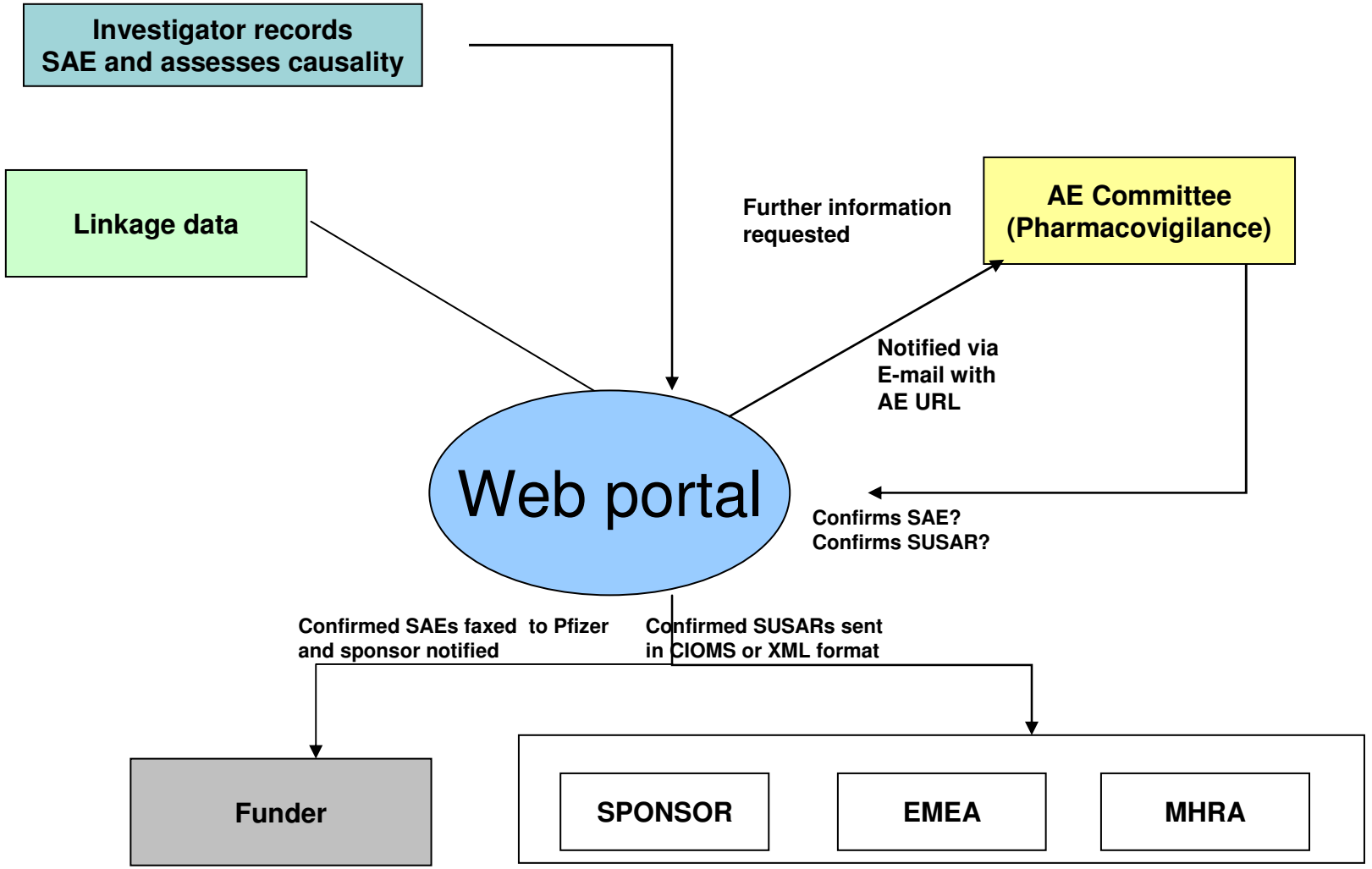
GP Follow up- Via web portal

- **Every 2 months**
  - **Adverse Events leading to discontinuation of randomised study treatment**
  - **Serious Adverse Events**
    - **Regulatory requirement**

Web Portal - GP Follow-up

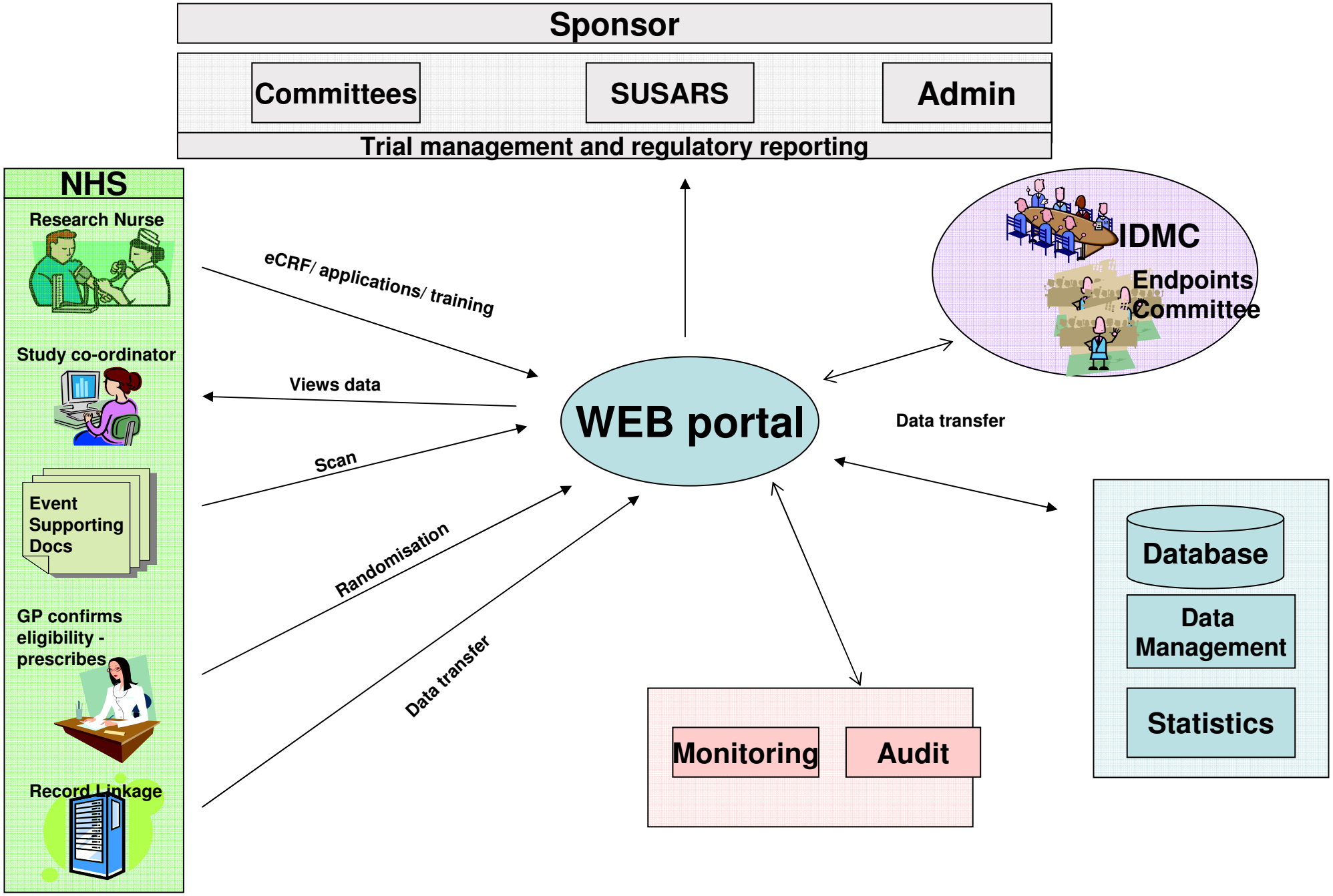


Pharmacovigilance



SAE Reporting

- Report to Sponsor and Pfizer
  - Pfizer insist on communicating by fax!!
- Report to Ethics and Regulatory authorities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Data Management
Statistics
Monitoring
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Web portal

- **Secure controlled-access**
- **Demonstration version for training**
- **Components:**
  - Electronic data capture (e-CRF)
  - Source document scan/ upload
  - Endpoint Committee Review and Adjudication
  - Reports
  - Documentation library
  - Data upload interface for primary care datasets
  - Automated e-mail reminders to GPs
  - Live study metrics

Challenges…

- Heterogeneity of primary care and lab systems
- Requirements for SAE reporting
  - primary care investigator reporting
  - duplicate reporting resolution
  - reporting of relatedness etc
    - Do we need this in Phase IV??
- Potential need for adjudication of events
  - non-inferiority studies subject to greater event quality scrutiny
  - uncertainty about quality of event coding in routinely collected health records