



The Salford Lung Study

Challenges and Complexities with the Reporting of
Electronic Medical Record Data in a Pioneering and Novel
Approach to Clinical Trials

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- **Background**
 - The Salford Lung Study (**SLS**) Asthma Study
 - **How** Data was Captured
 - **Challenges** with the Data with **Examples**
 - **Conclusion**

Traditional Phase III Trials

- Double-blind randomised trials – “GOLD” standard
 - Highly controlled
 - Patient population with strict inclusion and exclusion criteria
 - Frequent scheduled visits
 - Comprehensive CRF specifically designed

Statistical basis very robust

Demand for Real World Data

- Complement pivotal Phase III studies
- Evaluate drug effectiveness, safety and benefit/risk in the real world
- Contribute to reimbursement and policy decisions

Challenges

- Set-up / Data Collection / Programming
- Taking the data and transforming into interpretable summaries for analyses

Salford Lung Study (SLS) Asthma Study

The SLS Asthma Study

Set in Salford and Southern Manchester districts, UK



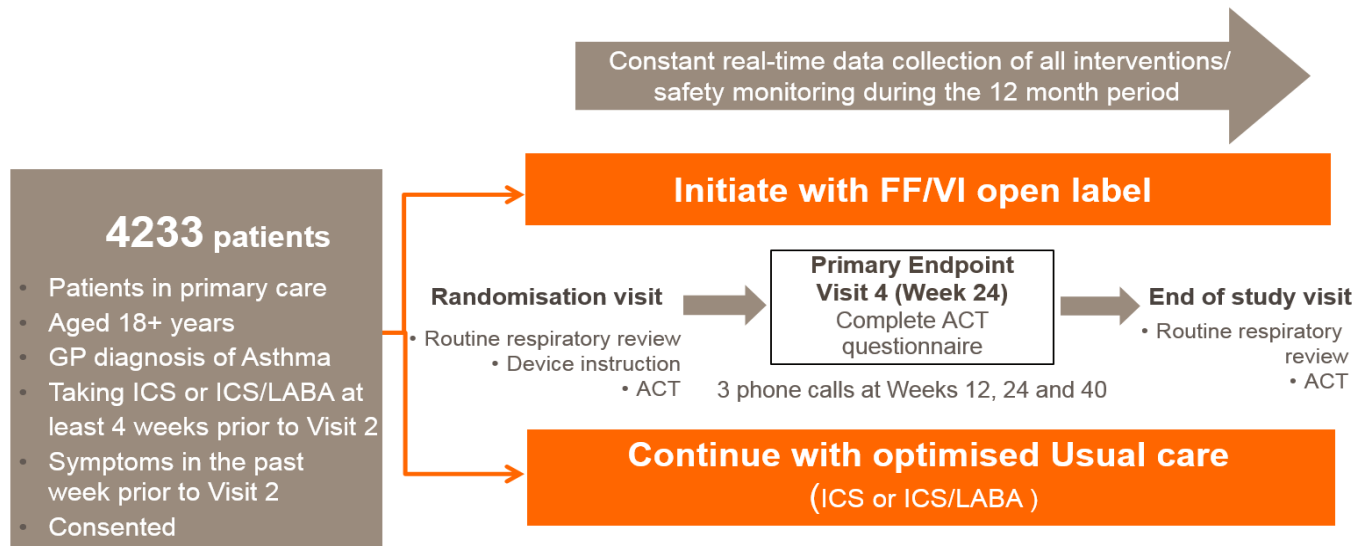
- Randomised open-label, parallel group design
- 12 month study
- Evaluate effectiveness of initiating Relvar® Ellipta® (FF/VI) compared to continuing treatment with 'Usual Care' (UC)



The SLS Asthma Study



Study Design



Intention: Maintain scientific rigour of a traditional RCT, but aim to keep as near to everyday clinical practice as possible

The SLS Asthma Study



Comparison of RCTs and SLS/Effectiveness Studies

Efficacy (Randomised Controlled Trials)

- Double blind
- Double dummy
- Strict inclusion/exclusion criteria
- Adherence encouraged
- Frequent reviews
- Drugs provided
- Treatment pathways defined

Effectiveness (SLS Study)

- Open label
- Broad population
- All comers
- Co-morbid included
- Set in normal care
- No extra review
- Drugs prescribed and collected in usual way for each individual patient
- “Usual care”
- Modification of treatment is permitted

How Data was Captured

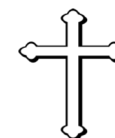


Electronic Medical Records



Linked Database System (LDS)

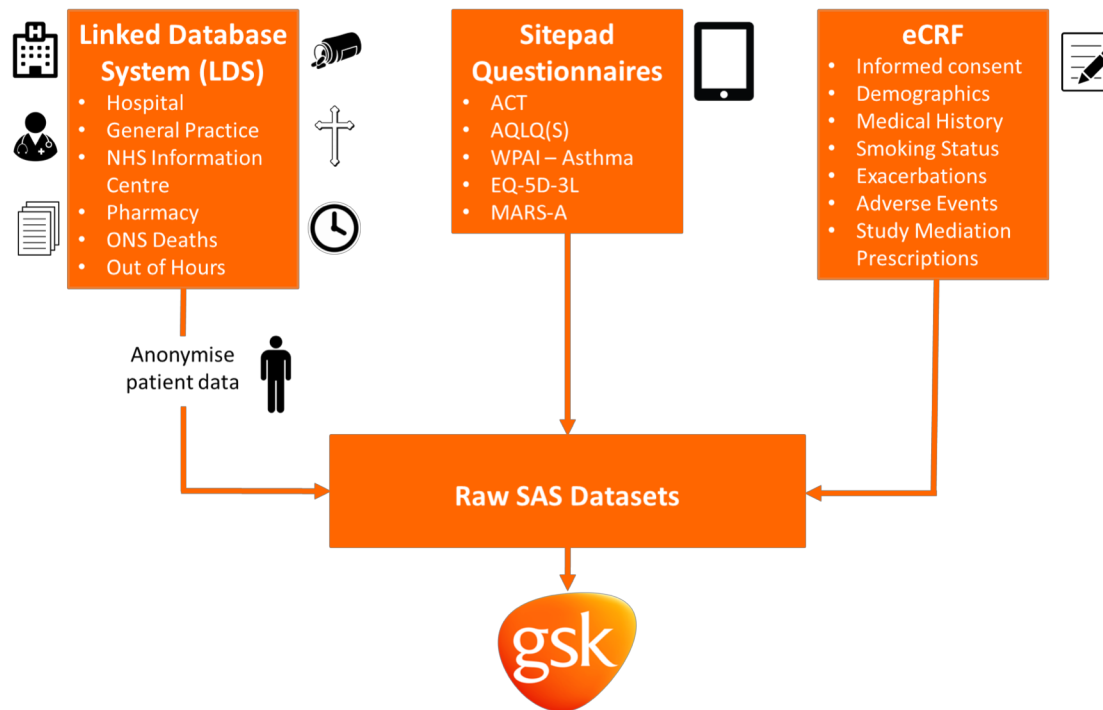
- Hospital
- General Practice
- NHS Information Centre
- Pharmacy
- ONS Deaths
- Out of Hours



How Data was Captured



Data to GSK



Electronic Medical Records (EMR) data such as primary and secondary care cannot be queried

- Data is not collected primarily for clinical trial research
- Potentially duplicate data (true and false duplicates)
- Missing data
- Free-text fields
- Gigabits of data
- Filtering out information required
- Data extracted to multiple datasets
- Lots of different coding systems used

All the following examples are for illustrative purposes and do not contain real data

Example 1: Scrambling Treatment Data



The Situation

- Open-label
- Modification any time
- Single inhalers vs multiple
- Maintain the blind
- Exposure based on Investigator's prescriptions captured in CRF
- Scrambled by independent unblinded programmer

Subject ID	Exposure Start Date	Exposure End Date	Drug Name	Dose	Frequency of dosing code	# of puffs per dose
1001	05-Jan-15	05-Jan-16	FF/VI	100/25	OD	1
1002	11-Feb-15	20-Sep-15	UC Drug A	100	BID	2
1002	11-Feb-15	20-Sep-15	UC Drug B	25	BID	2
1003	19-Oct-16	02-Nov-16	UC Drug A	50	BID	1
1003	03-Nov-16	03-Feb-17	UC Drug B	100	BID	4
1003	04-Feb-17	10-Feb-17	UC Drug B	100	BID	2
1003	11-Feb-17	20-Oct-17	UC Drug C	50	BID	1



Example 1: Scrambling Treatment Data



Simple Scramble of three subjects

Subject ID	Exposure Start Date	Exposure End Date	Drug Name	Dose	Frequency of dosing code	# of puffs per dose
1001	19-Oct-16	02-Nov-16	UC Drug A	50	BID	1
	03-Nov-16	03-Feb-17	UC Drug B	100	BID	4
	04-Feb-17	10-Feb-17	UC Drug B	100	BID	2
	11-Feb-17	20-Oct-17	UC Drug C	50	BID	1
1002	05-Jan-15	05-Jan-16	FF/VI	100/25	OD	1
1003	11-Feb-15	20-Sep-15	UC Drug A	100	BID	2
	11-Feb-15	20-Sep-15	UC Drug B	25	BID	2

- Pre-programming issues: derivations falling outside of treatment phase
- Solution used: Keep the subjects real start date and take away from scrambled start date to get the “constant”

Example 1: Scrambling Treatment Data



The Outcome

Subj. ID	Subject's Date of First Exposure	Constant	Initial Scrambled Exposure Start Date	Initial Scrambled Exposure End Date	Final Scrambled Exposure Start Date	Final Scrambled Exposure End Date	Drug Name	Dose	Freq. of dosing	# of puffs per dose
1001	05-Jan-15	653	19-Oct-16	02-Nov-16	05-Jan-15	19-Jan-15	UC Drug A	50	BID	1
1001	05-Jan-15	653	03-Nov-16	03-Feb-17	20-Jan-15	22-Apr-15	UC Drug B	100	BID	4
1001	05-Jan-15	653	04-Feb-17	10-Feb-17	23-Apr-15	29-Apr-15	UC Drug B	100	BID	2
1001	05-Jan-15	653	11-Feb-17	20-Oct-17	30-Apr-15	06-Jan-16	UC Drug C	50	BID	1
1002	11-Feb-15	-37	05-Jan-15	05-Jan-16	11-Feb-15	11-Feb-16	FF/VI	100/25	OD	1
1003	19-Oct-16	-616	11-Feb-15	20-Sep-15	19-Oct-16	28-May-17	UC Drug A	100	BID	2
1003	19-Oct-16	-616	11-Feb-15	20-Sep-15	19-Oct-16	28-May-17	UC Drug B	25	BID	2

- Each extraction: Took 40% of exposure data, scrambled it and applied it back onto 100% of the subjects

Example 2: Primary Care Contacts



The Situation

Endpoint: Number of Primary Care Contacts

Also: Number of Asthma-related Primary Care Contacts

- **Primary Care:** GPs/doctors; services which are the first point of contact for healthcare advice or treatment
- How much **resource** a patient may consume from the NHS
- Data into **two** datasets: PC1HRU / PC2HRU

Example 2: Primary Care Contacts



The Data: PC1HRU

- PC1HRU: **When** primary care occurred and **who** they were Seen By
- List of Staff categorised into **GPs, Nurse, Other, Admin**
- Staff categorisation based on discussions with wider team **prior to unblinding**

Subj. ID	Date of Primary Care	Seen By
1001	03-Jul-15	System Administrator
1001	08-Jul-15	Receptionist
1001	19-Jul-15	General Medical Practitioner
1001	27-Jul-15	System Administrator
1001	30-Jul-15	Receptionist

GP	Nurse	Other	Admin
Associate Practitioner	Associate Practitioner - Nurse	Acupuncturist	Administrator
Associate Practitioner - General Practitioner	Community Nurse	Chiroprapist/Podiatrist	Appointments Clerk
GP Registrar	Community Psychiatric Nurse	Health Care Support Worker	Assistant
General Medical Practitioner	Contact Tracing Nurse	Health Professional Access Role	Audit Manager
House Officer - Pre Registration	Enrolled Nurse	Healthcare Assistant	Community Administrator
Locum	Midwife	Other Allied Health Professionals	Computer Manager
Partner	Nurse Consultant	Other Health Care Professional	Health Records Administrator
Senior Partner	Other Nursing & Midwifery	Other Students	Other Admin & Clerical
Sessional GP	Practice Nurse	Pharmacist	Receptionist
Sole Practitioner	Specialist Nurse Practitioner	Physiotherapist	System Administrator

Primary Care Contacts

Example 2: Primary Care Contacts



The Data: PC2HRU

- PC2HRU: **Read codes** and **terms**
 - Standard coding system used by GPs in the UK to code diagnoses, clinical signs, administrative items, tests and findings etc.
 - Similar to Adverse Events and coding

Subj. ID	Date of Primary Care	Read Term	Read Code
1001	03-Jul-15	Letter from consultant	9N36-1
1001	17-Jul-15	SMS text message sent to patient	9N3G
1001	19-Jul-15	Medication review with patient	8B3x
1001	19-Jul-15	Acute exacerbation of asthma	H333
1001	19-Jul-15	SMS text message sent to patient	9N3G
1001	26-Jul-15	Bowel cancer screening programme: faecal occult blood result	6866
1001	26-Jul-15	Bowel cancer screening programme: administration	90w
1001	26-Jul-15	No response to bowel cancer screening programme invitation	90w2
1001	30-Jul-15	Letter encounter to patient	9N35

Example 2: Primary Care Contacts



The Outcome

Merge of PC1HRU and PC2HRU

- By Subject ID and Date of Primary Care
- Some records in one dataset not the other
- Counted Primary Care by unique date
- Asthma-related Primary Care denoted by Read code

Subj. ID	Date of Primary Care	Seen By	Read Term	Read Code
1001	03-Jul-15	System Administrator	Letter from consultant	9N36-1
1001	08-Jul-15	Receptionist		
1001	17-Jul-15		SMS text message sent to patient	9N3G
1001	19-Jul-15	General Medical Practitioner	Medication review with patient	8B3x
1001	19-Jul-15	General Medical Practitioner	Acute exacerbation of asthma	H333
1001	19-Jul-15	General Medical Practitioner	SMS text message sent to patient	9N3G
1001	26-Jul-15		Bowel cancer screening programme: faecal occult blood result	6866
1001	26-Jul-15		Bowel cancer screening programme: administration	90w
1001	26-Jul-15		No response to bowel cancer screening programme invitation	90w2
1001	27-Jul-15	System Administrator		
1001	30-Jul-15	Receptionist	Letter encounter to patient	9N35

In this example:

- Number of Primary Care Contacts = 1
- Number of Asthma-related Primary Care Contacts = 1

‘Ground-Breaking’ study

**Insight into challenges
encountered in
programming**

**Trials in Real-world: Inform
Healthcare Professionals**

**Imperative that
programmers involved at
early stage along with
Statistician**

- See first-hand what and how data is collected**
- Understand data format and structure**

Effectiveness of Fluticasone Furoate– Vilanterol for COPD in Clinical Practice

Jørgen Vestbo, D.M.Sc., David Leather, M.B., Ch.B., Nawar Diar Bakerly, M.D.,
John New, M.B., B.S., J. Martin Gibson, Ph.D., Sheila McCorkindale, M.B., Ch.B.,
Susan Collier, M.B., Ch.B., Jodie Crawford, M.Sc., Lucy Frith, M.Sc.,
Catherine Harvey, D.Phil., Henrik Svedsater, Ph.D., and Ashley Woodcock, M.D.,
for the Salford Lung Study Investigators*

NEJM Sept 2016

Effectiveness of fluticasone furoate plus vilanterol on asthma control in clinical practice: an open-label, parallel group, randomised controlled trial

Ashley Woodcock, Jørgen Vestbo*, Nawar Diar Bakerly, John New, J Martin Gibson, Sheila McCorkindale, Rupert Jones, Susan Collier,
James Lay-Flurrie, Lucy Frith, Loretta Jacques, Joanne I. Fletcher, Catherine Harvey, Henrik Svedsater, David Leather, on behalf of the Salford Lung
Study Investigators†*

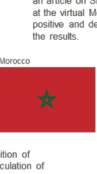
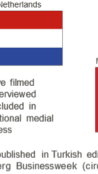
Lancet 2017

Coverage Highlights

Communicating SLS Asthma results



Local press conference held covering:
 • Results of a quality of life survey
 • Introduce the Salford Lung Study
 Resulted in over 100 references on printed media and websites, with a further 180 local private TVs and 80 private radios





do more
feel better
live longer

Thank You
and
Questions

Jacky
Community research nurse
Salford, UK