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Personal View

Community pharmacy: a crucial enabler in creating the effectiveness study environment in the Salford Lung Studies

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Abstract

Objective Creating an environment that supports conditions of routine clinical practice and enables an effectiveness trial design with a pre-licensed medicine is extremely challenging. Here, we summarise our experiences and achievements with engaging and mobilising community pharmacies in and around Salford, United Kingdom, in the Phase III effectiveness Salford Lung Studies (SLS).

Methods This article provides the authors' personal experiences and viewpoints on community pharmacy involvement in the SLS.

Key findings More than 130 community pharmacies were enabled, and >2500 pharmacy staff trained, for involvement in the SLS. Key to community pharmacy participation in the SLS was the formation of the SLS Pharmacy Steering Group (PSG), contributing to study oversight, and the development of a pharmacy standard operating procedure document, the major principle of which was to ensure minimum disruption to the normal medicine dispensing process while ensuring compliance with regulations, guidelines, good clinical practice and requirements for pharmacovigilance. The high level of commitment and collaboration of community pharmacy in the SLS demonstrated a willingness to work together and take on additional and novel roles beyond their everyday commercial functions for the benefit of patients, despite normally competing for prescription business.

Conclusions The involvement and integration of community pharmacy as a key partner in the SLS was pivotal in securing the delivery of these world-first clinical effectiveness studies. To our knowledge, this has not been previously achieved in a study of a pre-licensed maintenance therapy for a common disease in primary care.

The Salford Lung Studies (SLS) in chronic obstructive pulmonary disease (COPD) and asthma were world-first, open-label, pragmatic, phase III, randomised controlled effectiveness trials conducted in United Kingdom (UK) primary care, using electronic health records and through collaboratively engaging general practitioners (GPs) and community pharmacists in clinical research.[1,2] These studies were initiated with a pre-licensed inhaled medicine and have attracted global interest due to their novel design and execution. The study protocols and trial results have been published previously.[1–5]

In 1972, Archie Cochrane defined the concepts of efficacy and effectiveness and discussed the need to understand the risk/benefit of medicines when tested under conditions of normal practice (effectiveness) as well as under ideal conditions (efficacy).[6] The SLS examined the effectiveness of a new inhaled corticosteroid/long-acting beta$_2$-agonist combination (fluticasone furoate/vilanterol [RELVAR]) in a population of respiratory patients in and around the City of Salford, UK. The trials were designed to mimic routine clinical practice, with minimal disruption to patients' everyday lives (contrasting with the traditional efficacy trial setting, where trial management and dispensing occurs from a hospital 'clinical trial' environment). There were few mandated study visits and patient recruitment, day-to-day care, and medicines

supply were via patients' usual GP and community pharmacist. Key to the integrity of the effectiveness design was maintaining the normality of repeat prescribing and dispensing in a situation where a pre-licensed medicine was being evaluated. We therefore sought to fully involve and integrate community (high street) pharmacy as a key partner in the SLS. To the best of our knowledge, this has not been previously achieved in a study of a pre-licensed maintenance therapy for a common disease in primary care.

Box 1 summarises the achievements with community pharmacy in the SLS. Every community pharmacy in the City of Salford and areas surrounding the recruiting primary care practices were trained and involved in the trials. This article sets out the role of community pharmacy within the SLS and highlights how pharmacy became a key part of the trial operations.

The additional and novel roles of community pharmacy beyond their everyday business functions, in the conduct of the SLS are summarised in Box 2. The scope and solutions that underlie these roles are described herein.

In the UK, community pharmacies comprise private businesses that operate as part of large national or regional chains, or as small independent pharmacies. While often aligned to local GP practices geographically, these pharmacies are normally in competition with each other for prescription business. There was no prior experience of collaborating to deliver a large clinical research project with community pharmacies in and around Salford. Based on the template used in secondary care for similar studies, pharmacies were reimbursed for each dispensing and storage of the investigational product, as well as set-up and training costs.

One of the sponsor's SLS project team member's pharmacy experience and professional network were key in identifying a pathway to engage with community pharmacy in the set-up of the SLS. As one-fifth of the pharmacies in Salford belonged to a single regional pharmacy chain, it was essential to secure the support of this group. The pioneering, charismatic and pragmatic pharmacy superintendent of this group was instrumental in supporting and building our plan to engage community pharmacy in the SLS. First, the study design and goals were presented to the Company Chemists Association (CCA; an association representing eight of the major pharmacy chains in the UK), where superintendent pharmacists learned about the opportunities for pharmacy and personal development. Visits to individual superintendent pharmacists, smaller local chains and independent pharmacies followed, eventually leading to the formation of the SLS Pharmacy Steering Group (PSG). The PSG comprised 12 members representing all of the pharmacy contractors in the Salford area. All 60 community pharmacies in the Salford area were invited and agreed to take part in the study; thereafter, large multiple-partner pharmacies were targeted and those in the surrounding (three-mile) area were then approached. Transparent discussions were carried out with the PSG as to which pharmacies should be included. There was little difference in recruiting independent and chain pharmacies in the original Salford area.

The SLS PSG was established in April 2011 and its members shared a common vision for the studies and had a shared purpose to collaborate for the long-term benefit of patients. The PSG had a charter and met at monthly intervals, with pre-set agendas and action minutes. A standard operating procedure (SOP) to be used by all pharmacies participating in the SLS was developed by the PSG. A major principle of the document was to ensure minimum disruption to the normal medicine dispensing process while ensuring compliance with regulations, guidelines, good clinical practice (GCP) and requirements for pharmacovigilance. GCP training began in September 2011.

Box 1 Achievements with Community Pharmacy in the SLS

- >130 community pharmacies enabled to take part in the study.
- >60 training sessions for community pharmacy on good clinical practice and the bespoke standard operating procedure written and ratified by the SLS Pharmacy Steering Group.
- >2500 pharmacy staff trained in good clinical practice.
- One standard operating procedure written and implemented; the only changes were as a result of changes to the study design.

Box 2 The Role of Pharmacy in the SLS

- Maintain normal repeat prescribing conditions for all patients recruited to both usual care and investigational product arms of the study
- Assist in the recruitment of patients from primary care
- Meet statutory requirements for the ordering, handling, storage and dispensing of the investigational products and maintenance of study protocol records
- Act as part of the pharmacovigilance system operating within the SLS
- Develop processes, good practice and standard operating procedures to support the above

The SOP was the detailed guide to be followed when any study prescription was dispensed in any of the participating pharmacies; however, from the patient's perspective, it was 'collection as usual' for all of their prescriptions. The SOP included directions for:

- ordering and transportation
- receipt
- handling and storage of the investigational product
- quarantine procedure for the investigational product
- labelling of study medications to comply with additional Medicines and Healthcare products Regulatory Agency (MHRA) regulations
- dispensing procedures for all study medication
- study initiation
- presentation of repeat prescriptions
- dispensing and record keeping for the 'private prescription' for the investigational product
- prescription collection and delivery
- ensuring functionality within the Electronic Prescription Service
- requests for emergency supply
- reporting of study data to NorthWest eHealth (NWEH).

Of note, the pharmacy training covered the issue of creating bias by discussing the study medicines with patients. Pharmacists and store staff were trained not to directly question patients on their experiences with the investigational product, but to record if patients self-reported their experiences.

Each pharmacy had a lead pharmacist (with a principal investigator [PI] role) who was responsible for patient safety and implementing procedures to the required standards. A 'pharmacy safety alert' form was used for notifying NWEH and the clinical safety team of serious adverse events, non-serious adverse drug reactions, pregnancy and medical device malfunction. On the few occasions (eight in total) when a breach of the SOP was notified to the PSG, the group initiated a post-action review and implemented educational alerts to all the participating pharmacies.

Regarding educating pharmacy staff on GCP and study conduct for the SLS, the PSG ran intensive training over a 3-week period involving >1000 pharmacy team members. Every PSG member was involved in this training, which included GCP; recognition of adverse events; and familiarisation with the complexities of the SOP which would sit above their own pharmacy dispensing procedure and be followed by all participating pharmacies. Two hard-to-reach groups were locums and independent pharmacies. Locum recruiting agencies were engaged and pharmacist locums who had been trained on SLS were more likely to be employed for cover. For both of these hard-to-reach groups, the PSG set up evening training programmes. The Chairman of the Local Pharmaceutical Committee, who was also an SLS PSG member, was instrumental in keeping the independent pharmacies up to date and aiding compliance. One unexpected finding was the magnitude of the turnover of pharmacy staff. This necessitated monthly training sessions. Eventually, >2500 pharmacy staff were trained. The duration of the two SLS studies also required the PSG to conduct refresher training sessions for pharmacy staff (either face-to-face or by e-learning).

Community pharmacy played an important role in the recruitment of primary care patients in the SLS. The eligibility criteria for the SLS COPD and SLS asthma trials required that patients were receiving regular inhaled maintenance therapy. The community pharmacy is inevitably the place where patients must visit to collect their usual prescription medication. As such, the pharmacist and their staff represent a frequent point of contact in primary care for respiratory patients on maintenance therapy. To increase awareness of the SLS and to encourage patients to enrol in the study we:

- placed appropriate advertising in pharmacies; all adverts (small handouts describing the study) were approved by the PSG, the pharmacies, the study sponsor and the local ethics committee
- talked to regular pharmacy customers with COPD and asthma about why they might want to take part in the trials.

It was important in the SLS to maintain normal repeat prescribing conditions for patients recruited to both the usual care and investigational product arms of the study. Repeat prescriptions are generated either on request by patients, or by the pharmacy doing so on their behalf after first having checked that there is a requirement for further medication. It was important for the conduct of the SLS that these procedures remained in place.

In the SLS, we had to ensure that statutory requirements for the handling and dispensing of the investigational product were met. Most patients in the SLS were prescribed both study medication and non-study medication and the requirements of the usual dispensing procedures plus those outlined in the SOP created a degree of additional complexity in community pharmacy practice. The presence of pharmacy superintendents in the PSG ensured that all requirements complied with pharmacy regulations and governance. PSG members kept in regular contact with bodies such as the National Pharmacy Association and the General Pharmaceutical Council to

confirm compliance with professional standards, good practice and issues related to indemnity insurance.

None of the pharmacies involved in the study had any experience of handling an investigational product as part of a pre-licensed clinical trial. To be compliant with GCP, we had to ensure that all pharmacy teams were aware of and utilised the SOP. This was achieved with the continued support of PSG members, through their lines of pharmacy management, and bringing together other members of their teams with the clinical research associates (CRAs) who were 'on the ground' visiting the pharmacy PIs. The length and frequency of CRA visits were dependent on the number of prescriptions a site was taking as part of the study, a site's training needs and any local issues requiring support.

NWEH created a bespoke IT infrastructure for the SLS, based on patients' electronic heath records and a primary/secondary care-linked database system to capture comprehensive safety data that were collated and analysed daily. A considerable amount of work went into achieving an electronic solution for data capture from participating pharmacies, although the process was eventually quite straightforward for the pharmacy team (tagging patients and running monthly reports), and meant that patients could collect their medication from any of the participating sites. As chain pharmacies had centrally managed IT systems, some additional time was required to implement the solution at these sites compared with independent pharmacies. Data could be extracted from several different dispensing platforms into a useable format. It is a process that could be replicated for other studies. System suppliers should take note that this valuable store of information should be available within their software in a more user-friendly manner.

Pharmacy also played an important role in the unique safety reporting for the SLS, full details of which have been published previously.[7] Safety monitoring and reporting were conducted by a clinical safety team comprising three safety reporting units; this included the pharmacy investigator site team, in which lead pharmacists recorded patient self-reported safety events during routine consultations and reported these to the specialist safety team using the Pharmacy Safety Alert form.

In summary, supporting routine clinical practice while enabling an effectiveness trial design with a pre-licensed medicine is extremely challenging. To the best of our knowledge, pharmacy involvement in such a study design has never been secured in this way, with complete commitment and collaboration. Motivation to become involved in the study covered the full range of pharmacy providers – members of the CCA saw the value of conducting the SLS, large-chain pharmacy managers through to small independent pharmacists engaged with the SLS study team – and this enabled the successful execution of the study. In SLS, pharmacists willingly worked with each other and with colleagues in participating GP practices in a collaborative and supportive manner for the benefits of patients. The PSG was instrumental in the design of study procedures and SOPs suitable for use in community pharmacy, and adopted a solution-orientated 'can do' approach to their involvement in the study. Medicines supply was secured within the SLS (compliant with regulations) and highly audited by CRAs, yet patient and GP practice experiences with pharmacy during the study remained normal, with repeat prescribing and dispensing maintained as usual. The enormity of this task at first seemed overwhelming, but through the work of key, innovative pharmacists, we successfully executed the delivery of this world-first clinical effectiveness study.

Declarations

Conflict of interest

DAL: Employment and stock/share ownership in GlaxoSmithKline plc. SH: No conflicts to disclose. GH: No conflicts to disclose. LS: Employment and stock/share ownership in GlaxoSmithKline plc. at the time of manuscript drafting (now retired from GlaxoSmithKline plc.).

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Authors' contributions

SH and GH were involved in data acquisition. All authors were involved in the study conception or design, writing/critical review of the manuscript, and all approved the final version of the manuscript for submission for publication.

Ethical approval

Not applicable; this article does not report an original research study involving animals or human volunteers. This article is based on the previously reported Salford Lung Studies in chronic obstructive pulmonary disease and asthma. All patients provided written informed consent for participation, and the trials were conducted in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines and the provisions of the 2008 Declaration of Helsinki. The trial protocols were approved by the National Research Ethics Service Committee North West, Greater Manchester South (approval numbers 11/NW/0798 and 12/NW/0455).

References

1. Vestbo J *et al*. Effectiveness of fluticasone furoate-vilanterol for COPD in clinical practice. *N Eng J Med* 2016; 375: 1253–1260.
2. Woodcock A *et al*. Effectiveness of fluticasone furoate plus vilanterol on asthma control in clinical practice: an open-label, parallel group, randomised controlled trial. *Lancet* 2017; 390: 2247–2255.
3. New JP *et al*. Obtaining real-world evidence: the Salford Lung Study. *Thorax* 2014; 69: 1152–1154.
4. Bakerly ND *et al*. The Salford Lung Study protocol: a pragmatic, randomised phase III real-world effectiveness trial in chronic obstructive pulmonary disease. *Respir Res* 2015; 16: 101.
5. Woodcock A *et al*. The Salford Lung Study protocol: a pragmatic, randomised phase III real-world effectiveness trial in asthma. *BMC Pulm Med* 2015; 15: 160.
6. Cochrane AL. *Effectiveness and Efficiency: Random reflections on Health Services*. London, UK: Nuffield Provincial Hospitals Trust, 1972.
7. Collier S *et al*. Monitoring safety in a phase III real-world effectiveness trial: use of novel methodology in the Salford Lung Study. *Pharmacoepidemiol Drug Saf* 2017; 26: 344–352.