Impact of socioeconomic status on participation and outcomes in the Salford Lung Studies

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Take home message (max. 256 characters inc. spaces): Deprivation did not impact the main outcomes of the SLS, thus supporting recruitment of participants from all socioeconomic strata to randomised controlled trials for assessment of generalisability of study findings to routine clinical practice.

Abstract

COPD and asthma prevalence is associated with socioeconomic status (or 'deprivation'), yet deprivation is rarely considered in typical large-scale efficacy randomised controlled trials that recruit highly selected patient populations. In this *post hoc* analysis of the Salford Lung Studies in COPD and asthma — two 12-month, open-label, effectiveness randomised controlled trials conducted in UK primary care — we evaluated the impact of patient deprivation on clinical outcomes with initiating fluticasone furoate/vilanterol *versus* continuing usual care.

Patients were categorised into deprivation quintiles based on postcode and a countrywide database of indices of deprivation, and trial outcomes by quintile were assessed.

Fifty-two percent of patients in the COPD study were included in the most deprived quintile, contrasting with 20% in the asthma study. Greater deprivation was associated with higher rates of primary/secondary healthcare contacts and costs. However, the treatment effect of fluticasone furoate/vilanterol *versus* usual care for primary (COPD: moderate/severe exacerbations; asthma: Asthma Control Test responders at week 24) and secondary/other (healthcare consumption, adherence, treatment modifications, study withdrawals, exacerbations, serious adverse events) outcomes was similar across deprivation quintiles.

Our findings support the recruitment of participants from all socioeconomic strata to allow assessment of data generalisability to routine clinical practice.

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Introduction

Socioeconomic status is a key determinant of health outcomes [1]. The prevalence of chronic obstructive pulmonary disease (COPD), which is generally regarded as a disease of deprivation, and asthma tends to be higher in more deprived areas [2, 3]. Deprived patients may be under-represented in traditional randomised controlled trials (RCTs), which seldom, if ever, collect and report the socioeconomic status of their participants. Evidence suggests that only a limited proportion of patients with COPD or asthma are eligible for typical large efficacy RCTs [4–6]; thus, generalising trial findings to the broader population of patients seen in routine clinical practice (including deprived patients) is problematic.

The Salford Lung Studies (SLS) were pragmatic randomised trials in COPD and asthma set in routine clinical practice in the United Kingdom (UK) [7, 8]. The SLS provided a unique opportunity to explore the frequency of deprivation in pragmatic RCTs and whether deprivation impacts the trial outcomes.

Methods

Patients and study design

The SLS in COPD and asthma were concurrent, prospective, 12-month, open-label RCTs that evaluated the clinical effectiveness and safety of initiating fluticasone furoate/vilanterol (FF/VI) *versus* continuing usual care (UC) for the treatment of COPD and asthma, respectively (SLS COPD: NCT01551758 and SLS asthma: NCT01706198). The studies were conducted in primary care practices across Salford and South Manchester, UK. The trial designs and primary results have been reported previously [7, 8]. Recruitment for SLS COPD preceded that of SLS asthma.

Patient recruitment commenced in Salford, later extending to sites in more affluent areas of South Manchester.

Briefly, patients in SLS COPD were aged ≥40 years, had a general practitioner's (GP's) diagnosis of COPD, had experienced ≥1 exacerbations of COPD in the prior 3 years and were receiving regular maintenance inhaler therapy [7]. Patients in SLS asthma were aged ≥18 years, had a documented GP's diagnosis of symptomatic asthma and were receiving regular maintenance inhaler therapy [8]. Both trials had minimal exclusion criteria. In both studies, patients were randomised 1:1 to initiate once-daily inhaled FF/VI 100 µg/25 µg (or 200 µg/25 µg for some patients in SLS asthma, according to GP assessment) or to continue with optimised UC as prescribed by their GP. Randomisation was stratified in SLS COPD by the presence/absence of a COPD exacerbation in the previous 12 months and baseline intended maintenance therapy (long-acting $beta_2$-agonist [LABA], long-acting muscarinic antagonist [LAMA] or LABA/LAMA; inhaled corticosteroid [ICS], ICS/LABA or ICS/LAMA; ICS/LAMA/LABA) and in SLS asthma by baseline Asthma Control Test (ACT) total score (≤15; 16–19; ≥20) and baseline intended maintenance therapy (ICS or ICS/LABA). Both studies had a 12-month follow-up period. Treatment modifications were permitted at GPs' discretion throughout the studies (patients could switch from FF/VI to UC but not *vice versa*). To minimise disruption to patients' everyday lives and preserve the real-world nature of the trials, there were few protocol-mandated visits (screening, randomisation and 12 months/end of study visit only); patients were additionally contacted by telephone at the 3-, 6- and 9-month time points for assessment of safety (both trials) and outcome questionnaire assessments, including ACT (SLS asthma only). Medications were dispensed as usual by local community pharmacies, and data were captured remotely and

continuously *via* patients' electronic health records using a primary/secondary care-linked database system [7, 8].

Assessment of patient deprivation

A deprivation score for each patient was calculated using patient-level postcodes and a countrywide database of indices of deprivation (version 2010) [9]. This database ranks all areas in England based on their relative level of deprivation, as measured using 38 separate indicators organised across seven distinct domains. Domains can be combined and weighted to produce a single overall Index of Multiple Deprivation, which is used to rank every small area in England according to the deprivation experienced by the people living there [9].

Deprivation scores were used to produce quintiles (quintile 1 being the most deprived and quintile 5 the least deprived).

Outcome measures

These *post hoc* analyses of patient deprivation focused on the primary effectiveness outcome measures analysed in the main trials, as reported in the primary SLS papers [7, 8]. For SLS COPD, the primary effectiveness outcome was the mean annual rate of moderate/severe exacerbations, defined as any worsening of respiratory symptoms necessitating treatment with antibiotics or systemic glucocorticoids (*i.e.* moderate exacerbations), or hospitalisation due to a COPD exacerbation (*i.e.* severe exacerbations). For SLS asthma, the primary effectiveness

outcome was the percentage of ACT responders (patients who achieved an ACT total score ≥20 and/or an increase from baseline ≥3) at week 24. The percentage of ACT responders was also assessed at weeks 12, 40 and 52.

Several secondary/other outcomes were also evaluated, including number of primary/secondary care contacts (PCCs/SCCs), total direct COPD-/asthma-related healthcare costs, treatment adherence (as estimated by the proportion of days covered [PDC] based on study medication prescribing data captured during the study), treatment modifications, patient withdrawals from study, rates of severe asthma exacerbations (SLS asthma only) and incidence of serious adverse events (SAEs; including the pre-specified pneumonia SAE of special interest). Details of outcome measures and their evaluation have been reported previously [7, 8].

Statistical analyses

Analyses of outcomes by deprivation quintile were performed as intent-to-treat (ITT; per randomised treatment group) in the total population, which comprised all randomised patients who received ≥1 prescription of study medication. The primary effectiveness outcome for each study was also examined in the primary effectiveness analysis (PEA) population, comprising all patients who had experienced ≥1 exacerbation of COPD in the year prior to randomisation (SLS COPD) or who had an ACT total score <20 at the randomisation visit (SLS asthma). For SLS asthma, outcomes by deprivation quintile were additionally analysed in the ICS/LABA therapy subset, which comprised patients whose baseline asthma maintenance therapy per randomisation stratification and pre-randomisation prescription was an ICS/LABA.

In these *post hoc* analyses, the primary effectiveness endpoint for each study was analysed according to the method reported in the respective primary publication [7, 8], but with the inclusion of deprivation quintile and its interaction with randomised treatment group in each statistical model. For SLS COPD, the primary effectiveness endpoint (mean annual rate of moderate/severe COPD exacerbations) was analysed using a general linear model assuming a negative binomial distribution. Least squares (LS) mean annual rates, treatment ratios and 95% confidence intervals (CIs) by deprivation quintile are presented. For SLS asthma, the primary effectiveness endpoint (percentage of ACT responders at week 24) was analysed using logistic regression. Adjusted odds ratios and 95% CIs for FF/VI *versus* UC are presented by deprivation quintile. ACT responder analyses were additionally conducted at weeks 12, 40 and 52.

Healthcare resource utilisation data are described as the mean combined annual rates of PCCs/SCCs for FF/VI and UC by deprivation quintile. The interaction of deprivation with treatment effect on PCC/SCC rates was evaluated using a general linear model. Geometric mean total COPD/asthma care costs (costs for COPD-/asthma-related healthcare, rescue medication and study drugs) are presented by deprivation quintile and randomised treatment group.

Data for treatment modifications, treatment adherence (PDC) and study withdrawals are summarised by deprivation quintile and randomised treatment group.

The statistical analysis of rates of on-treatment severe asthma exacerbations by randomised treatment group and deprivation quintile was conducted using a general linear model. LS mean annual rates, treatment ratios and 95% CIs are presented.

The treatment effect of FF/VI *versus* UC on pneumonia SAE rates by deprivation

quintile was analysed using a negative binomial regression model. LS mean annual rates, treatment ratios and 95% CIs are presented.

The overall aim of this *post hoc* exploratory work was to establish trends and/or consistency across deprivation quintiles on the outcomes of interest. As such, no adjustments for multiplicity were performed.

Results

In SLS COPD, 52% of patients (1453/2791) were in the most deprived quintile by postcode, whereas in SLS asthma, deprivation was more equally distributed with only 20% of patients (855/4218) in the most deprived quintile (figure 1). When analysed according to investigators who recruited to both SLS COPD and SLS asthma, patient distribution across the deprivation quintiles was similar to that observed in the overall studies (data not shown).

In SLS COPD, there was a numerical trend toward patients being younger and for higher proportions of females and current smokers in the more deprived quintiles relative to the least deprived quintiles (table 1). There was also a trend for higher body mass index (BMI) in more deprived patients, but the absolute difference across quintiles may be too small to be clinically relevant. No notable difference in COPD exacerbation history was observed across the deprivation quintiles. Similar trends were observed in SLS asthma, where patients in the more deprived quintiles were numerically more likely to be younger, to smoke, to have a higher BMI, and to have uncontrolled asthma (ACT total score ≤15) and recent asthma symptoms (rescue medication use, activity limitations, night-time symptoms/awakenings) relative to

patients in the less deprived quintiles (table 1). There was no notable difference in asthma exacerbation history across the deprivation quintiles. Characteristics of patients in the SLS asthma ICS/LABA therapy subset were generally similar to the total study population (supplementary table S1).

In SLS COPD, the treatment effect of initiating FF/VI *versus* continuing UC on the mean annual rate of moderate/severe exacerbations across deprivation quintiles was broadly similar to the overall PEA population (figure 2a). In SLS asthma, there was a consistent benefit for FF/VI over UC for the percentage of ACT responders at week 24 across the deprivation quintiles in the PEA population (figure 2b); a similar benefit for FF/VI *versus* UC was also observed at weeks 12, 40 and 52 in each deprivation quintile in the PEA population (figure 3) and at weeks 12, 24, 40 and 52 in the ICS/LABA therapy subset of the PEA population (supplementary figure S1).

In both trials, higher rates of PCCs/SCCs were observed in the more deprived relative to less deprived quintiles (table 2), but there was no apparent interaction of deprivation quintile with treatment effect for FF/VI *versus* UC. Care costs were higher for more deprived patients with COPD, but not for those with asthma. There was no consistent impact of deprivation on treatment adherence, treatment modification rates, patient withdrawals from study (tables 3–5) or on-treatment severe asthma exacerbations (supplementary table S2). There were small differences in the incidence of on-treatment SAEs between the most and least deprived patients in both the COPD and asthma studies, but no difference in SAE incidence between randomised treatment groups in each of the deprivation quintiles. There was no difference in pneumonia SAE incidence between randomised treatment groups in each of the deprivation quintiles in SLS COPD (supplementary table S3). In SLS

asthma, the on-treatment pneumonia SAE incidence was <1% of all patients [10] and analysis by deprivation quintile was not conducted.

Discussion

Salford is a typical urban area in North West England and a substantial proportion of the population live in socioeconomically deprived areas. Over one half of SLS COPD patients were categorised in the most deprived quintile, compared to 20% of SLS asthma patients. Higher healthcare resource utilisation and care costs in more deprived patients could be linked to the observed differences in baseline patient characteristics (*i.e*. higher proportions of current smokers, trend for higher BMI in the more deprived quintiles). Indeed, deprivation has previously been identified as a risk factor for COPD hospital admissions [11]. The level of deprivation did not influence any of the main clinical effectiveness and safety outcomes in the SLS, indicating that the overall trial results are relevant to all patients with asthma and COPD in routine care.

The major strengths of this study relate to the pragmatic trial design of the SLS, successful recruitment of patients from all socioeconomic strata and the richness of the dataset. We were able to access deprivation data for almost all randomised patients (n>7000) and capture healthcare contacts data using a primary/secondary care-linked electronic database. Weaknesses include the *post hoc* nature of these analyses, which were conducted without multiplicity adjustment. Furthermore, the high proportion of deprived patients in SLS COPD (in contrast to SLS asthma) resulted in small sample sizes for some deprivation quintiles, limiting results interpretation. Another limitation is that patients were allocated into deprivation quintiles based on ranking of deprivation scores derived by postcode, rather than

based on individual characteristics. It could be argued, therefore, that patients allocated to the most deprived quintiles in this study may not necessarily themselves be truly socioeconomically deprived. Such detailed socioeconomic information was not available on an individual patient basis in this study. It is noteworthy, however, that Salford is listed as one of the top 20 local authorities in England with the highest proportions of areas that are amongst the 10% most deprived [9]; it follows, therefore, that the SLS likely did include patients who were genuinely of lower socioeconomic status.

Overall, our data support the view that patients' socioeconomic status should not be a barrier to participation in RCTs, and that enrolment of a broad patient population should be actively encouraged. Routine reporting of data on patients' baseline socioeconomic status will allow for assessment of generalisability of trial results in comparison to patients in routine clinical practice.

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Contributions: R. Jones: Study concept, data analysis/interpretation, manuscript writing/review and approval of the final version to be submitted. A. Nicholls: Statistical analysis planning and review (accountability) for the *ad hoc* work, and manuscript writing/review and approval of the final version to be submitted. D. Browning: Data analysis/interpretation, manuscript writing/review and approval of the final version to be submitted. N. Diar Bakerly: Study conception/design, data acquisition, data analysis/interpretation, and manuscript writing/review and approval of the final version to be submitted. A. Woodcock: Study conception/design, data analysis/interpretation, and manuscript writing/review and approval of the final version to be submitted. J. Vestbo: Contributed to the overall study design and analysis, the interpretation of the data presented in this manuscript and revision of the primary manuscript, manuscript writing/review and approval of the final version to be submitted. D.A. Leather: Conceived the original study concept, contributed to protocol development, analysis plan, data interpretation, study operations, manuscript writing/review and approval of the final version to be submitted. L. Jacques: Data analysis/interpretation, manuscript writing/review and approval of the final version to be submitted. J. Lay-Flurrie: Data analysis/interpretation, manuscript writing/review and approval of the final version to be submitted. H. Svedsater: Study conception/design, data analysis/interpretation, manuscript writing/review and

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Data sharing statement: Anonymised individual participant data from this study plus the annotated case report form, protocol, reporting and analysis plan, dataset specifications, raw dataset, analysis-ready dataset and clinical study report are available for research proposals approved by an independent review committee. Proposals should be submitted to www.clinicalstudydatarequest.com. A data access agreement will be required.

Patient consent and ethical approval: All patients provided written informed consent. 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).

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TABLE 1 Patient demographics and baseline characteristics by deprivation quintile for SLS COPD and SLS asthma (total study populations)

	SLS COPD				
	Deprivation quintile[#] (N=2791)				
Characteristic	**1 (n=1453)**	**2 (n=601)**	**3 (n=391)**	**4 (n=209)**	**5 (n=137)**
Age, years, mean (SD)	65.0 (9.8)	67.2 (10.1)	68.8 (9.5)	70.4 (8.4)	70.1 (9.5)
Male, n (%)	733 (50)	305 (51)	197 (50)	111 (53)	78 (57)
BMI, kg/m^2, mean (SD)[¶]	28.0 (7.1)	27.9 (6.1)	27.6 (5.4)	27.6 (5.4)	27.1 (5.0)
Current smoker, n (%)	763 (53)	247 (41)	156 (40)	70 (33)	48 (35)
Duration of COPD ≥5 years, n (%)	764 (53)	305 (51)	204 (52)	127 (61)	75 (55)
COPD exacerbations in the year prior to randomisation, mean (SD)	2.1 (2.1)	1.9 (1.8)	2.0 (1.8)	2.0 (1.9)	1.5 (1.4)
	SLS asthma				
	Deprivation quintile[#] (N=4218)				
Characteristic	**1 (n=855)**	**2 (n=834)**	**3 (n=856)**	**4 (n=831)**	**5 (n=842)**
Age, years, mean (SD)	47.1 (15.8)	47.9 (16.0)	49.9 (16.2)	50.0 (16.9)	54.1 (16.0)
Male, n (%)	346 (40)	330 (40)	359 (42)	344 (41)	353 (42)
BMI, kg/m^2, mean (SD)[¶]	31.0 (7.6)	30.6 (7.1)	30.4 (7.1)	29.1 (6.2)	28.5 (5.8)
Current smoker, n (%)[¶]	276 (33)	218 (26)	179 (21)	108 (13)	65 (8)
Duration of asthma ≥10 years, n (%)	627 (73)	624 (75)	634 (74)	611 (74)[¶]	638 (76)
Severe asthma exacerbations in the year prior to randomisation, mean (SD)	0.7 (1.2)	0.7 (1.2)	0.7 (1.3)	0.6 (1.0)	0.5 (0.9)
Uncontrolled asthma (ACT ≤15), n (%)	462 (54)[¶]	384 (46)	354 (41)	282 (34)	231 (27)
Daytime symptoms more than twice a week, n (%)[+]	772 (90)	760 (91)	781 (91)	750 (90)	755 (90)
SABA use more than twice a week, n (%)[+]	689 (81)	648 (78)	640 (75)	552 (66)	504 (60)
Activity limitations in the past week, n (%)[+]	501 (59)	474 (57)	454 (53)	374 (45)	351 (42)
Nocturnal symptoms/awakenings in the past week, n (%)[+]	504 (59)	446 (53)	409 (48)	383 (46)	365 (43)

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; SD: standard deviation; BMI: body mass index; ACT: Asthma Control Test; SABA: short-acting beta$_2$-agonist. [#]: where 1 = most deprived, 5 = least deprived; [¶]: based on patients with available data; [+]: based on patients' recall of asthma symptoms in the past week, as assessed at the baseline (randomisation) visit.

TABLE 2 Healthcare contacts[#] and care costs by deprivation quintile in SLS COPD and SLS asthma (total study populations)

	SLS COPD (N=2791)				SLS asthma (N=4218)			
	Mean (SD) annual number of healthcare contacts[+]		Geometric mean (geometric SD) total COPD care costs per patient, £[§]		Mean (SD) annual number of healthcare contacts[+]		Geometric mean (geometric SD) total asthma care costs per patient, £[§]	
Deprivation quintile[¶]	**FF/VI (n=1396)**	**UC (n=1395)**	**FF/VI (n=1396)**	**UC (n=1395)**	**FF/VI (n=2105)**	**UC (n=2113)**	**FF/VI (n=2105)**	**UC (n=2113)**
1	n=731	n=722	n=731	n=722	n=412	n=443	n=412	n=443
	32.0 (23.4)	29.4 (22.2)	842.1 (2.3)	981.4 (2.1)	20.0 (19.0)	18.8 (17.0)	417.3 (1.8)	453.7 (1.9)
2	n=307	n=294	n=307	n=294	n=434	n=400	n=434	n=400
	29.7 (21.8)	28.4 (21.8)	742.5 (2.1)	984.1 (2.1)	18.1 (15.0)	18.5 (17.6)	412.9 (1.8)	433.3 (1.9)
3	n=189	n=202	n=189	n=202	n=401	n=455	n=401	n=455
	29.9 (19.0)	28.4 (20.3)	819.0 (2.0)	955.2 (2.1)	17.0 (14.8)	17.0 (14.6)	411.0 (1.6)	479.7 (1.9)
4	n=104	n=105	n=104	n=105	n=425	n=406	n=425	n=406
	29.2 (19.3)	27.4 (18.6)	730.7 (1.9)	894.8 (2.0)	16.0 (13.7)	13.2 (11.6)	431.3 (1.8)	431.6 (1.9)
5	n=65	n=72	n=65	n=72	n=433	n=409	n=433	n=409
	27.5 (22.4)	21.3 (14.9)	743.4 (2.0)	823.6 (1.8)	14.2 (12.6)	13.2 (11.4)	419.7 (1.8)	427.8 (1.8)

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; SD: standard deviation; FF/VI: fluticasone furoate/vilanterol; UC: usual care. [#]: on-treatment, all-cause healthcare contacts; [¶]: where 1 = most deprived, 5 = least deprived; [+]: composite analysis of all primary and secondary healthcare contacts; [§]: including total direct costs for COPD-/asthma-related healthcare resource utilisation, rescue medication and study drugs.

TABLE 3 Treatment adherence (PDC) by deprivation quintile in SLS COPD and SLS asthma (total study populations and SLS asthma ICS/LABA therapy subset[#])

	Mean (SD) PDC, %[¶]							
	SLS COPD (N=2791)			**SLS asthma (N=4218)**			**ICS/LABA therapy subset (N=2642)**	
Deprivation quintile[+]	**FF/VI (n=1396)**	**UC (n=1395)**	**Deprivation quintile[+]**	**FF/VI (n=2105)**	**UC (n=2113)**	**Deprivation quintile[+]**	**FF/VI (n=1319)**	**UC (n=1323)**
1 (n=1423)	n=722 83.8 (23.3)	n=701 82.6 (23.0)	1 (n=848)	n=410 78.2 (24.3)	n=438 78.9 (25.4)	1 (n=546)	n=266 78.7 (23.5)	n=280 76.6 (25.4)
2 (n=587)	n=303 85.4 (21.7)	n=284 83.1 (22.9)	2 (n=829)	n=432 79.4 (24.3)	n=397 79.0 (25.5)	2 (n=522)	n=274 81.1 (22.9)	n=248 78.2 (25.5)
3 (n=386)	n=187 87.5 (20.3)	n=199 81.1 (22.3)	3 (n=849)	n=399 82.4 (23.2)	n=450 79.9 (24.6)	3 (n=545)	n=250 81.7 (23.7)	n=295 77.8 (25.0)
4 (n=206)	n=101 86.8 (21.9)	n=105 80.4 (24.7)	4 (n=823)	n=422 85.4 (21.2)	n=401 77.2 (25.7)	4 (n=505)	n=262 85.3 (21.6)	n=243 76.1 (25.5)
5 (n=131)	n=65 86.1 (19.8)	n=66 84.6 (25.3)	5 (n=833)	n=426 85.9 (20.6)	n=407 75.8 (27.6)	5 (n=497)	n=254 86.8 (18.9)	n=243 73.7 (28.1)

PDC: proportion of days covered; SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta$_2$-agonist; SD: standard deviation; FF/VI: fluticasone furoate/vilanterol; UC: usual care; eCRF: electronic case report form. [#]: the SLS asthma ICS/LABA therapy subset comprised patients whose baseline maintenance therapy per randomisation stratification and pre-randomisation prescription was an ICS/LABA; [¶]: values are mean (SD) PDC based on eCRF study medication prescribing data captured during the study. Based on patients with available PDC data (N=2733 for SLS COPD; N=4182 for SLS asthma; N=2615 for SLS asthma ICS/LABA therapy subset); [+]: where 1 = most deprived, 5 = least deprived.

TABLE 4 Treatment modifications by deprivation quintile in SLS COPD and SLS asthma (total study populations and SLS asthma ICS/LABA therapy subset[#])

Patients with ≥1 treatment modification during study, n (%)								
	SLS COPD (N=2791)			SLS asthma (N=4218)			ICS/LABA therapy subset (N=2642)	
Deprivation quintile[¶]	FF/VI (n=1396)	UC (n=1395)	Deprivation quintile[¶]	FF/VI (n=2105)	UC (n=2113)	Deprivation quintile[¶]	FF/VI (n=1319)	UC (n=1323)
1 (n=1453)	n=731	n=722	1 (n=855)	n=412	n=443	1 (n=551)	n=268	n=283
	181 (25)	78 (11)		82 (20)	113 (26)		62 (23)	80 (28)
2 (n=601)	n=307	n=294	2 (n=834)	n=434	n=400	2 (n=526)	n=276	n=250
	69 (22)	37 (13)		94 (22)	65 (16)		59 (21)	40 (16)
3 (n=391)	n=189	n=202	3 (n=856)	n=401	n=455	3 (n=551)	n=252	n=299
	40 (21)	19 (9)		89 (22)	80 (18)		54 (21)	50 (17)
4 (n=209)	n=104	n=105	4 (n=831)	n=425	n=406	4 (n=511)	n=265	n=246
	26 (25)	16 (15)		94 (22)	64 (16)		61 (23)	44 (18)
5 (n=137)	n=65	n=72	5 (n=842)	n=433	n=409	5 (n=503)	n=258	n=245
	26 (40)	10 (14)		103 (24)	53 (13)		73 (28)	37 (15)

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta$_2$-agonist; FF/VI: fluticasone furoate/vilanterol; UC: usual care. [#]: the SLS asthma ICS/LABA therapy subset comprised patients whose baseline maintenance therapy per randomisation stratification and pre-randomisation prescription was an ICS/LABA; [¶]: where 1 = most deprived, 5 = least deprived.

TABLE 5 Rates of patient withdrawals from study by deprivation quintile in SLS COPD and SLS asthma (total study populations and SLS asthma ICS/LABA therapy subset[#])

	Patient withdrawal rate, n (%)							
	SLS COPD (N=2791)			SLS asthma (N=4218)			ICS/LABA therapy subset (N=2642)	
Deprivation quintile[¶]	FF/VI (n=1396)	UC (n=1395)	Deprivation quintile[¶]	FF/VI (n=2105)	UC (n=2113)	Deprivation quintile[¶]	FF/VI (n=1319)	UC (n=1323)
1 (n=1453)	n=731	n=722	1 (n=855)	n=412	n=443	1 (n=551)	n=268	n=283
	54 (7)	53 (7)		40 (10)	37 (8)		23 (9)	18 (6)
2 (n=601)	n=307	n=294	2 (n=834)	n=434	n=400	2 (n=526)	n=276	n=250
	26 (8)	14 (5)		47 (11)	43 (11)		26 (9)	29 (12)
3 (n=391)	n=189	n=202	3 (n=856)	n=401	n=455	3 (n=551)	n=252	n=299
	12 (6)	15 (7)		32 (8)	38 (8)		20 (8)	26 (9)
4 (n=209)	n=104	n=105	4 (n=831)	n=425	n=406	4 (n=511)	n=265	n=246
	9 (9)	7 (7)		37 (9)	30 (7)		23 (9)	18 (7)
5 (n=137)	n=65	n=72	5 (n=842)	n=433	n=409	5 (n=503)	n=258	n=245
	4 (6)	3 (4)		37 (9)	24 (6)		20 (8)	14 (6)

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta$_2$-agonist; FF/VI: fluticasone furoate/vilanterol; UC: usual care. [#]: the SLS asthma ICS/LABA therapy subset comprised patients whose baseline maintenance therapy per randomisation stratification and pre-randomisation prescription was an ICS/LABA; [¶]: where 1 = most deprived, 5 = least deprived.

Figure legends

FIGURE 1

Patient distribution by deprivation quintile in SLS COPD and SLS asthma (total study populations).[#¶]

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease. [#]: N=2791 and N=4218 patients with available deprivation data for SLS COPD and SLS asthma, respectively. Percentages are based on a denominator of the number of patients with available deprivation data; [¶]: for deprivation quintile, 1 = most deprived, 5 = least deprived.

FIGURE 2

Primary effectiveness outcomes by treatment group and deprivation quintile. a) SLS COPD: mean annual rate of moderate/severe exacerbations (PEA population; N=2269).[#¶+] b) SLS asthma: percentage of ACT responders at week 24 (PEA population; N=3015).[+§‖]

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; PEA: primary effectiveness analysis; ACT: Asthma Control Test; FF/VI: fluticasone furoate/vilanterol; UC: usual care; CI: confidence interval; LS: least squares. [#]: moderate/severe exacerbations are defined as reported previously [7]; [¶]: analysis using a general linear model assuming a negative binomial distribution, with the logarithm of time on treatment as an offset variable and adjusting for randomised treatment, baseline COPD maintenance therapy per randomisation stratification,

number of prior moderate/severe COPD exacerbations in the previous year, baseline smoking status, deprivation quintile and a randomised treatment-by-deprivation quintile interaction term; [+]: for deprivation quintile, 1 = most deprived, 5 = least deprived; [§]: ACT responders were defined as patients who achieved an ACT total score ≥20 and/or increase from baseline ≥3; [‖]: analysis by logistic regression with adjustment for randomised treatment, baseline ACT total score, baseline ACT total score squared, asthma maintenance therapy at baseline per randomisation stratification, age, gender, baseline smoking status, deprivation quintile and a randomised treatment-by-deprivation quintile interaction term.

FIGURE 3

Percentage of ACT responders at weeks 12, 40 and 52 by treatment group stratified by deprivation quintile in SLS asthma (PEA population; N=3015).[#¶+]

ACT: Asthma Control Test; SLS: Salford Lung Study; PEA: primary effectiveness analysis; UC: usual care; FF/VI: fluticasone furoate/vilanterol; CI: confidence interval. [#]: ACT responders were defined as patients who achieved an ACT total score ≥20 and/or increase from baseline ≥3; [¶]: analysis by logistic regression with adjustment for randomised treatment, baseline ACT total score, baseline ACT total score squared, asthma maintenance therapy at baseline per randomisation stratification, age, gender, baseline smoking status, deprivation quintile and a randomised treatment-by-deprivation quintile interaction term; [+]: for deprivation quintile, 1 = most deprived, 5 = least deprived.