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

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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.

52% 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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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 <http://bit.ly/34qk9EH>

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The Salford Lung Studies are registered at www.clinicaltrials.gov with identifier numbers NCT01551758 and NCT01706198. 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.

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Introduction

Socioeconomic status is a key determinant of health outcomes [1]. The prevalence of 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 ClinicalTrials.gov identifier: NCT01551758; and SLS asthma ClinicalTrials.gov identifier: 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 (GP) diagnosis of COPD, had experienced ≥ 1 exacerbation of COPD in the previous 3 years and were receiving regular maintenance inhaler therapy [7]. Patients in SLS asthma were aged ≥ 18 years, had a documented GP 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 $\mu\text{g}/25 \mu\text{g}$ (or 200 $\mu\text{g}/25 \mu\text{g}$ 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 β_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 the GP's 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); 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].

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).

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 being 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 and other outcomes were also evaluated, including number of primary care contacts (PCCs), secondary care contacts (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 the *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 a deprivation quintile and its interaction with the 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.

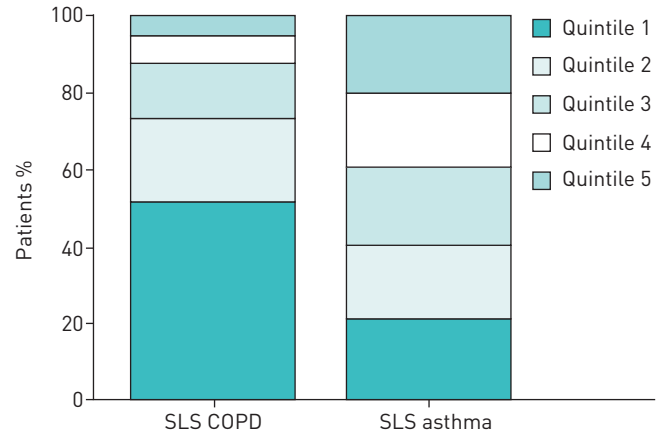
The treatment effect of FF/VI *versus* UC on pneumonia SAE rates by deprivation quintile was analysed using a negative binomial regression model. LS mean annual rates, treatment ratios and 95% CIs are presented.

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 of 2791) were in the most deprived quintile by postcode, whereas in SLS asthma, deprivation was more equally distributed, with only 20% of patients (855 of 4218) in the most deprived quintile (figure 1). When analysed according to investigators who recruited to both SLS COPD

FIGURE 1 Patient distribution by deprivation quintile in the Salford Lung Study (SLS) of COPD and the SLS of asthma (total study populations). 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 is the most deprived and 5 is the least deprived.



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 a higher proportion 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,

TABLE 1 Patient demographics and baseline characteristics by deprivation quintile for the Salford Lung Study (SLS) of COPD and SLS asthma (total study populations)

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

Data are presented as n/N, mean±SD or n (%). BMI: body mass index; SABA: short-acting β₂-agonist. [#]: where 1 is the most deprived and 5 is the least deprived; [¶]: based on patients with available data; ⁺: Asthma Control Test score ≤15; [§]: based on patients' recall of asthma symptoms in the past week, as assessed at the baseline (randomisation) visit.

to smoke, to have a higher BMI, to have uncontrolled asthma (ACT total score ≤ 15) and to have recent asthma symptoms (rescue medication use, activity limitations and 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

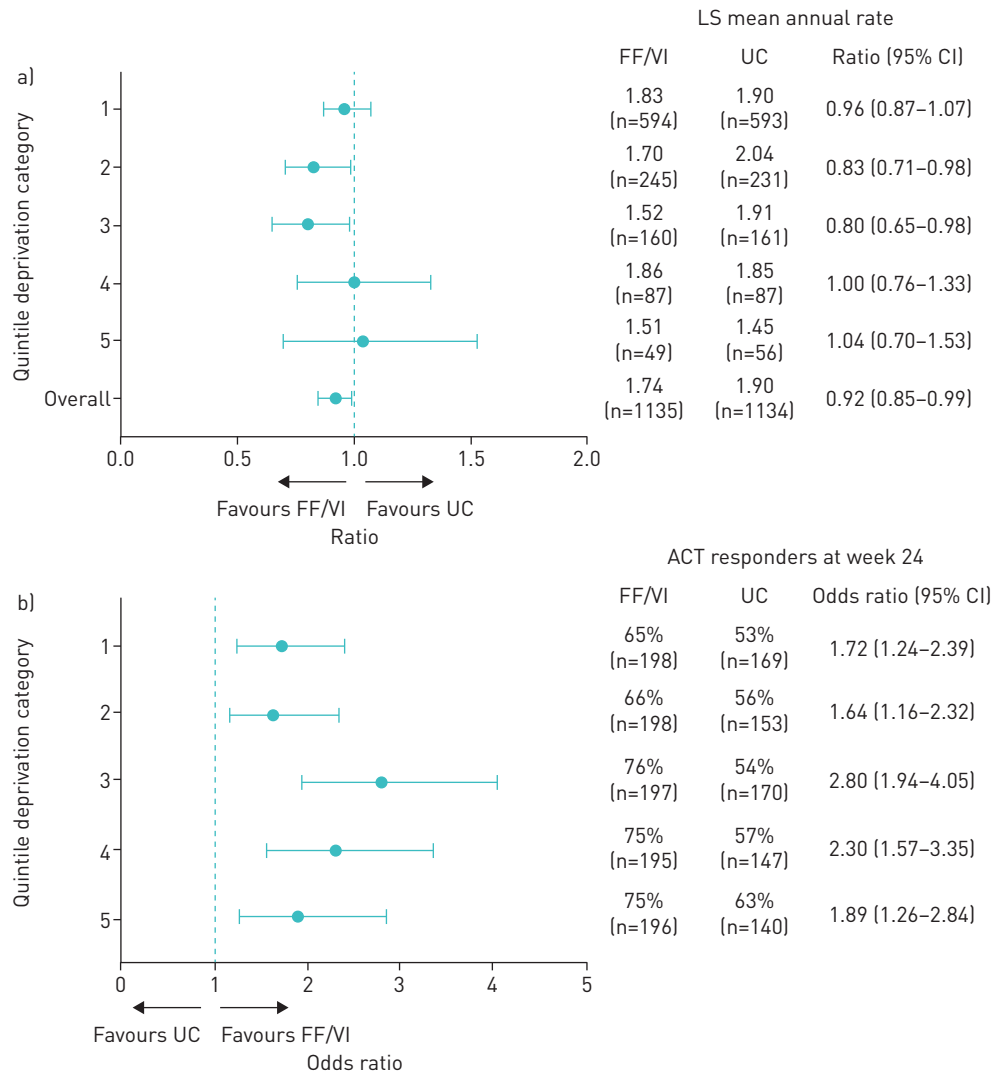


FIGURE 2 Primary effectiveness outcomes by treatment group and deprivation quintile. a) Salford Lung Study (SLS) of COPD: mean annual rate of moderate/severe exacerbations [primary effectiveness analysis (PEA) population, n=2269]. Moderate/severe exacerbations are defined as reported previously [7]. 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 is the most deprived and 5 is the least deprived. b) SLS asthma: percentage of Asthma Control Test (ACT) responders at week 24 (PEA population; n=3015). 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, sex, baseline smoking status, deprivation quintile and a randomised treatment-by-deprivation quintile interaction term. FF/VI: fluticasone furoate/vilanterol; UC: usual care; LS: least squares.

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 quintiles 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 half of patients in SLS COPD were categorised in the most deprived quintile, compared to 20% of patients in SLS asthma. 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 and a 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

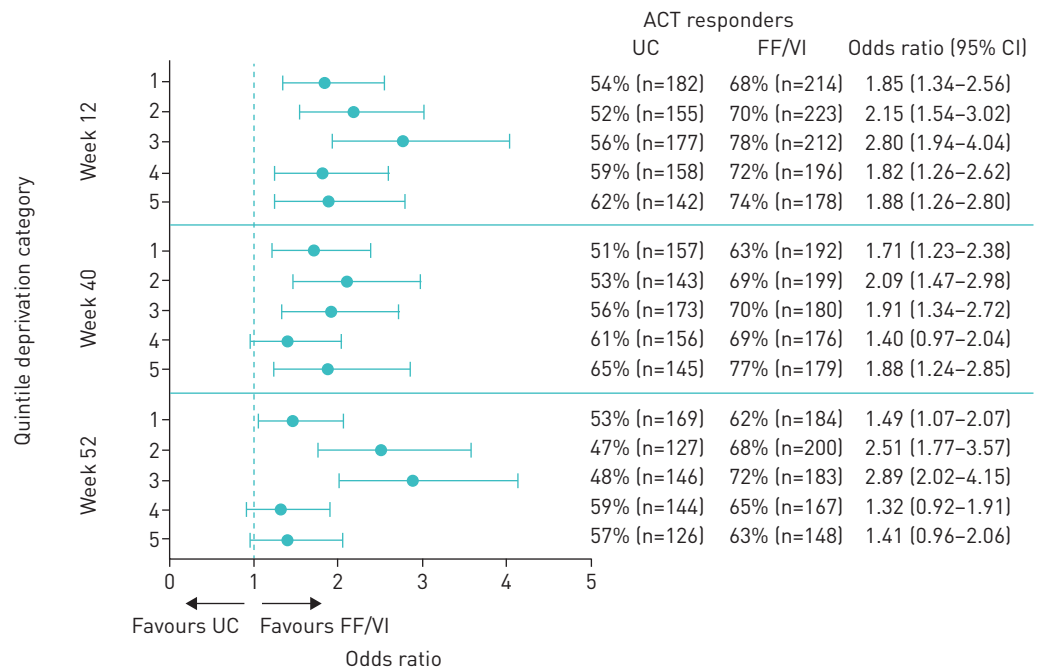


FIGURE 3 Percentage of Asthma Control Test (ACT) responders at weeks 12, 40 and 52 by treatment group stratified by deprivation quintile in the Salford Lung Study of asthma [primary effectiveness analysis population; n=3015]. ACT responders were defined as patients who achieved an ACT total score ≥20 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, sex, baseline smoking status, deprivation quintile and a randomised treatment-by-deprivation quintile interaction term. For deprivation quintile, 1 is the most deprived and 5 is the least deprived. UC: usual care; FF/VI: fluticasone furoate/vilanterol

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

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

FF/VI: fluticasone furoate/vilanterol; UC: usual care. [#]: on-treatment, all-cause healthcare contacts; [¶]: where 1 is the most deprived and 5 is the 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.

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 among the

TABLE 3 Treatment adherence (proportion of days covered) by deprivation quintile in the Salford Lung Study (SLS) of COPD and SLS asthma (total study populations and SLS asthma inhaled corticosteroid (ICS)/long-acting β₂-agonist (LABA) therapy subset[#])

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

Data are presented as mean±SD proportion of days covered (PDC) based on electronic case report form 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). 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 is the most deprived and 5 is the least deprived.

TABLE 4 Treatment modifications by deprivation quintile in the Salford Lung Study (SLS) of COPD and SLS asthma (total study populations and SLS asthma inhaled corticosteroid (ICS)/long-acting β_2 -agonist (LABA) therapy subset[#])

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

Data area presented as the n (%) patients with one or more treatment modification during the study. 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 is the most deprived and 5 is the least deprived.

TABLE 5 Rates of patient withdrawals from study by deprivation quintile in the Salford Lung Study (SLS) of COPD and SLS asthma (total study populations and SLS asthma inhaled corticosteroid (ICS)/long-acting β_2 -agonist (LABA) therapy subset[#])

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

Data are presented as n (%) who withdrew from the study. 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 is the most deprived and 5 is the least deprived.

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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