

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

3

4 **Authors:** Rupert Jones¹, Andy Nicholls², Dominy Browning³, Nawar Diar Bakerly^{4,5},
5 Ashley Woodcock^{5,6}, Jørgen Vestbo^{5,6}, David A. Leather⁷, Loretta Jacques⁸, James
6 Lay-Flurrie², Henrik Svedsater⁹ and Susan Collier¹⁰

7

8 **Affiliations:** ¹Community and Primary Health Care, Faculty of Health, Plymouth
9 University, Plymouth, UK. ²Clinical Statistics, GlaxoSmithKline plc., Uxbridge, UK.
10 ³Respiratory Research and Development, GlaxoSmithKline plc., Brentford, UK.
11 ⁴Salford Royal NHS Foundation Trust, Salford, UK. ⁵Division of Infection, Immunity
12 and Respiratory Medicine, Manchester Academic Health Sciences Centre, The
13 University of Manchester, Manchester, UK. ⁶Manchester University NHS Foundation
14 Trust, Manchester, UK. ⁷Global Respiratory Franchise, GlaxoSmithKline plc.,
15 Brentford, UK. ⁸Clinical Sciences, GlaxoSmithKline plc., Uxbridge, UK. ⁹Value
16 Evidence and Outcomes, GlaxoSmithKline plc., Brentford, UK. ¹⁰UK Medical,
17 GlaxoSmithKline plc., Uxbridge, UK.

18

19 **Corresponding author:**

20 Dr Rupert Jones

21 Community and Primary Health Care, Faculty of Health, Plymouth University, ITTC

22 Building (N14), Plymouth PL6 8BX, UK

23 Tel: +44 1752 764258

24 Email: rupert.jones@plymouth.ac.uk

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36 figure)

37

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

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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.

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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68 **Introduction**

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

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

82

83 **Methods**

84 **Patients and study design**

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

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

94 Briefly, patients in SLS COPD were aged ≥ 40 years, had a general practitioner's
95 (GP's) diagnosis of COPD, had experienced ≥ 1 exacerbations of COPD in the prior 3
96 years and were receiving regular maintenance inhaler therapy [7]. Patients in SLS
97 asthma were aged ≥ 18 years, had a documented GP's diagnosis of symptomatic
98 asthma and were receiving regular maintenance inhaler therapy [8]. Both trials had
99 minimal exclusion criteria. In both studies, patients were randomised 1:1 to initiate
100 once-daily inhaled FF/VI 100 $\mu\text{g}/25$ μg (or 200 $\mu\text{g}/25$ μg for some patients in SLS
101 asthma, according to GP assessment) or to continue with optimised UC as
102 prescribed by their GP. Randomisation was stratified in SLS COPD by the
103 presence/absence of a COPD exacerbation in the previous 12 months and baseline
104 intended maintenance therapy (long-acting beta₂-agonist [LABA], long-acting
105 muscarinic antagonist [LAMA] or LABA/LAMA; inhaled corticosteroid [ICS],
106 ICS/LABA or ICS/LAMA; ICS/LAMA/LABA) and in SLS asthma by baseline Asthma
107 Control Test (ACT) total score (≤ 15 ; 16–19; ≥ 20) and baseline intended maintenance
108 therapy (ICS or ICS/LABA). Both studies had a 12-month follow-up period.

109 Treatment modifications were permitted at GPs' discretion throughout the studies
110 (patients could switch from FF/VI to UC but not *vice versa*). To minimise disruption to
111 patients' everyday lives and preserve the real-world nature of the trials, there were
112 few protocol-mandated visits (screening, randomisation and 12 months/end of study
113 visit only); patients were additionally contacted by telephone at the 3-, 6- and 9-
114 month time points for assessment of safety (both trials) and outcome questionnaire
115 assessments, including ACT (SLS asthma only). Medications were dispensed as
116 usual by local community pharmacies, and data were captured remotely and

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

119

120 **Assessment of patient deprivation**

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

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

130

131 **Outcome measures**

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

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

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

150

151 **Statistical analyses**

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

163 In these *post hoc* analyses, the primary effectiveness endpoint for each study was
164 analysed according to the method reported in the respective primary publication [7,
165 8], but with the inclusion of deprivation quintile and its interaction with randomised
166 treatment group in each statistical model. For SLS COPD, the primary effectiveness
167 endpoint (mean annual rate of moderate/severe COPD exacerbations) was analysed
168 using a general linear model assuming a negative binomial distribution. Least
169 squares (LS) mean annual rates, treatment ratios and 95% confidence intervals (CIs)
170 by deprivation quintile are presented. For SLS asthma, the primary effectiveness
171 endpoint (percentage of ACT responders at week 24) was analysed using logistic
172 regression. Adjusted odds ratios and 95% CIs for FF/VI *versus* UC are presented by
173 deprivation quintile. ACT responder analyses were additionally conducted at weeks
174 12, 40 and 52.

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

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

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

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

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

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

192

193 **Results**

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

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

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

214 In SLS COPD, the treatment effect of initiating FF/VI *versus* continuing UC on the
215 mean annual rate of moderate/severe exacerbations across deprivation quintiles was
216 broadly similar to the overall PEA population (figure 2a). In SLS asthma, there was a
217 consistent benefit for FF/VI over UC for the percentage of ACT responders at week
218 24 across the deprivation quintiles in the PEA population (figure 2b); a similar benefit
219 for FF/VI *versus* UC was also observed at weeks 12, 40 and 52 in each deprivation
220 quintile in the PEA population (figure 3) and at weeks 12, 24, 40 and 52 in the
221 ICS/LABA therapy subset of the PEA population (supplementary figure S1).

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

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

236

237 **Discussion**

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

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

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

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

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278 Contributions: R. Jones: Study concept, data analysis/interpretation, manuscript
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280 Statistical analysis planning and review (accountability) for the *ad hoc* work, and
281 manuscript writing/review and approval of the final version to be submitted. D.
282 Browning: Data analysis/interpretation, manuscript writing/review and approval of the
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300

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322

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

329

330 Patient consent and ethical approval: All patients provided written informed consent.
331 The trials were conducted in accordance with the International Conference on
332 Harmonisation Good Clinical Practice guidelines and the provisions of the 2008
333 Declaration of Helsinki. The trial protocols were approved by the National Research
334 Ethics Service Committee North West, Greater Manchester South (approval
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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					
Characteristic	Deprivation quintile# (N=2791)				
	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/m², 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					
Characteristic	Deprivation quintile# (N=4218)				
	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/m², 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 beta₂-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)

Deprivation quintile [¶]	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, £ [§]	
	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)

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 beta₂-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 (%)								
Deprivation quintile [¶]	SLS COPD (N=2791)		Deprivation quintile [¶]	SLS asthma (N=4218)		Deprivation quintile [¶]	ICS/LABA therapy subset (N=2642)	
	FF/VI (n=1396)	UC (n=1395)		FF/VI (n=2105)	UC (n=2113)		FF/VI (n=1319)	UC (n=1323)
1 (n=1453)	n=731 181 (25)	n=722 78 (11)	1 (n=855)	n=412 82 (20)	n=443 113 (26)	1 (n=551)	n=268 62 (23)	n=283 80 (28)
2 (n=601)	n=307 69 (22)	n=294 37 (13)	2 (n=834)	n=434 94 (22)	n=400 65 (16)	2 (n=526)	n=276 59 (21)	n=250 40 (16)
3 (n=391)	n=189 40 (21)	n=202 19 (9)	3 (n=856)	n=401 89 (22)	n=455 80 (18)	3 (n=551)	n=252 54 (21)	n=299 50 (17)
4 (n=209)	n=104 26 (25)	n=105 16 (15)	4 (n=831)	n=425 94 (22)	n=406 64 (16)	4 (n=511)	n=265 61 (23)	n=246 44 (18)
5 (n=137)	n=65 26 (40)	n=72 10 (14)	5 (n=842)	n=433 103 (24)	n=409 53 (13)	5 (n=503)	n=258 73 (28)	n=245 37 (15)

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta₂-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 (%)								
Deprivation quintile [¶]	SLS COPD (N=2791)		Deprivation quintile [¶]	SLS asthma (N=4218)		Deprivation quintile [¶]	ICS/LABA therapy subset (N=2642)	
	FF/VI (n=1396)	UC (n=1395)		FF/VI (n=2105)	UC (n=2113)		FF/VI (n=1319)	UC (n=1323)
1 (n=1453)	n=731 54 (7)	n=722 53 (7)	1 (n=855)	n=412 40 (10)	n=443 37 (8)	1 (n=551)	n=268 23 (9)	n=283 18 (6)
2 (n=601)	n=307 26 (8)	n=294 14 (5)	2 (n=834)	n=434 47 (11)	n=400 43 (11)	2 (n=526)	n=276 26 (9)	n=250 29 (12)
3 (n=391)	n=189 12 (6)	n=202 15 (7)	3 (n=856)	n=401 32 (8)	n=455 38 (8)	3 (n=551)	n=252 20 (8)	n=299 26 (9)
4 (n=209)	n=104 9 (9)	n=105 7 (7)	4 (n=831)	n=425 37 (9)	n=406 30 (7)	4 (n=511)	n=265 23 (9)	n=246 18 (7)
5 (n=137)	n=65 4 (6)	n=72 3 (4)	5 (n=842)	n=433 37 (9)	n=409 24 (6)	5 (n=503)	n=258 20 (8)	n=245 14 (6)

SLS: Salford Lung Study; COPD: chronic obstructive pulmonary disease; ICS: inhaled corticosteroid; LABA: long-acting beta₂-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.