

# Appendices

## Living in limbo:

the scale of unmet  
need in difficult and  
severe asthma



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## Appendices

### Appendix A: Data used in the report

#### Data notes

##### **Clinical Practice Research Datalink (CPRD) data notes<sup>1</sup>**

This data extract covers those aged 18-54. It does not cover those who may display the symptoms of severe asthma who are either not registered with their GP, or who have not received either high-dose ICS or three or more courses of OCS. It covers activity in primary care, so will not cover those who are exclusively managed in secondary or tertiary care and may receive these courses of treatment, thus will be an underestimate of the total prevalence of these symptoms.

To estimate referrals, we used respiratory outpatient appointments as a proxy. The data does not specify whether the referral was to a general respiratory clinic in secondary care, or to tertiary care. As this data covers outpatient appointments, it could potentially include someone referred from accident and emergency (A&E) to an outpatient appointment. In most areas, patients have to be referred to their local (secondary) hospital respiratory service before being referred on to a tertiary severe asthma multi-disciplinary team (MDT). Although highly likely, we cannot be certain each referral was for the patient's asthma. It could be for a different respiratory condition, although patients with other respiratory diseases (such as chronic obstructive pulmonary disease (COPD)) were excluded from the data. It is also worth noting that the data for each year is discrete – it only accounts for new referrals, so does not include everyone in these categories who is under specialist care if they have been referred previously. Some outpatient appointments will have been referred in the previous year, and some referrals will be seen the following year. We have assumed these anomalies cancel each other out. Investigating the proportion of people never referred was investigated, but the sample size proved too small to be used.

##### **Quality and Outcomes Framework (QOF) data notes<sup>2,3,4,5</sup>**

QOF data does not cover those who are not registered with a GP, those who have not told their GP about their asthma and those who may have asthma, but are not currently being treated for it. For these reasons, QOF data provides an underestimate of the true prevalence of asthma. This dataset also does not provide a prevalence breakdown by age or sex.

To gain the number of people estimated to be on high-dose ICS or three or more courses of OCS, QOF data for the whole of the UK was used. Referral data only covers England, so only English data was used. To get an estimate of the numbers referred, the child/adult (ages 0-14 and 15+) split in the Health Survey prevalence data was applied to the overall QOF data for England.

##### **Health survey data notes**

We have used Health Survey data from the Health Survey for England, 2001; Scottish Health Survey, 2003; Welsh Health Survey, 2005/06; Northern Ireland Health and Wellbeing Survey, 2005/06.

### **IQVIA data notes**

The hospital prescribing data shows the number of ‘packs’ prescribed every month (it is different to that of an ‘item’, which is commonly used when analysing primary care data). We used the most recent data from April 2019 to show a snapshot of the numbers receiving a mAb currently. Since mepolizumab is one injection administered every four weeks, we can make the reasonable assumption that the number of packs (each pack contains one 100mg vial of mepolizumab and therefore one injection) prescribed in a month equates to the number of people receiving mepolizumab. For reslizumab and omalizumab, we used the same assumption as the World Health Organisation (WHO) Collaborating Centre for Drug Statistics Methodology (WHO CC) uses for the ATC/DDD Index 2019 (measuring drug utilisation) to estimate the number of people receiving each mAb.

### **IDEAL study data notes**

We used the IDEAL study to estimate the percentage of people eligible for mepolizumab and omalizumab in England, Wales, Northern Ireland and Scotland<sup>2 3 4 5</sup>. The IDEAL Study included 670 people with severe asthma who were aged 12 years or over and were on high-dose ICS with a controller. We applied the 3.6% estimation of people with severe asthma (those who are on high-dose ICS with a controller and who are adherent) to the QOF prevalence<sup>6</sup>. QOF prevalence includes all ages and the IDEAL study excludes those aged under 12. Since there is not an age breakdown for QOF prevalence, we have applied the eligibility estimates to the whole population. We then applied the relevant percentage from the IDEAL study (see table 8) to give us an estimated number eligible for each mAb.

### **Differences between the previous difficult asthma estimate and our data**

The figures presented in the report present a considerably lower figure for those with suspected difficult asthma than the Hekking et al study<sup>6</sup> mentioned. Their figure is 17.4%, compared to only 3.4%-5.7% of people with asthma in the UK meeting certain referral criteria. This may be due to the data source used – it does not cover those managed in secondary care and those who are not registered with a GP. The data presented here covers those aged 18-54, while the Hekking et al estimation covered an older population (with a mean age of 62.5). Although smoking status was used in the study criteria, this older age group may still contain some who have COPD or other lung conditions. Using an anonymous survey meant that there was no objective test of lung function for respondents. Although there are demographic similarities between the Netherlands and the UK, differing prescribing practices may also give different results. As this report’s authors recognise, this 17.4% may be an overestimation of the difficult asthma population, while the figure presented here may be an underestimation. Given the importance of accurate epidemiological data to effective commissioning, we recommend research to provide robust, UK-based estimates of difficult and severe asthma prevalence.

Table 1: Rate of high-dose ICS and three or more OCS use in the UK, 2006-2016

## Data tables

All data refers to adults only.

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
High-dose ICS	5.5%	5.8%	6.0%	6.3%	6.4%	6.4%	6.3%	5.9%	5.6%	5.7%	5.7%
Three or more OCS	1.9%	2.1%	2.2%	2.2%	2.3%	2.7%	2.7%	2.7%	2.9%	2.9%	3.4%

Table 2: Estimated number of people on high-dose ICS and three or more OCS in the UK, using QOF and Health Survey estimates

		2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
QOF estimate	High-dose ICS	171,628	178,443	191,325	199,784	199,416	196,483	188,495	177,143	184,892	187,504
	Three or more OCS	61,928	65,587	66,918	70,731	83,686	84,566	85,417	92,242	95,386	109,758
Health Survey estimate	High-dose ICS	249,853	259,297	270,030	276,469	275,181	268,313	251,999	238,262	242,984	246,418
	Three or more OCS	90,153	95,305	94,446	97,880	115,482	115,482	114,194	124,068	125,356	144,245

Table 3: Annual incidence of referral to specialist clinic in England

	2008	2009	2010	2011	2012	2013	2014	2015	2016
High-dose ICS	11.4%	12.7%	12.9%	13.9%	12.2%	15.5%	15.7%	17.4%	18.0%
Three or more OCS	15.5%	17.1%	14.7%	16.7%	18.1%	18.5%	19.2%	18.1%	23.4%

Table 4: Number of people in England with suspected difficult and severe asthma referred each year to secondary or tertiary care, using QOF numbers

	2008	2009	2010	2011	2012	2013	2014	2015	2016
High-dose ICS	16,936	20,207	21,490	23,145	20,009	24,228	23,102	26,582	27,858
Three or more OCS	8,492	9,571	8,663	11,692	12,766	13,115	14,706	14,242	21,271

Table 5: Use of high-dose ICS and three or more OCS by age group, aggregated across study period in the UK (2006 - 2016)

	18-24	25-34	35-44	45-54
All asthma	28.4%	25.5%	25.8%	20.3%
High-dose ICS	15.2%	25.1%	36.2%	23.5%
Three or more OCS	14.1%	23.8%	39.4%	22.8%

Table 6: Percentage of women with asthma, using high-dose ICS and on three or more OCS, aggregated across study period in the UK (2006 - 2016)

	Percentage women
All asthma	57.4%
High-dose ICS	62.6%
Three or more OCS	70.6%

Table 7: Percentage of people with asthma on high-dose ICS or three or more OCS, aggregated across study period in the UK (2006 - 2016)

	England	Scotland	Wales	N Ireland	UK
High-dose ICS	5.1%	5.9%	7.1%	5.5%	5.7%
Three or more OCS	2.9%	4.3%	3.8%	3.0%	3.4%

### Biologic estimation methodology notes

Table 8: Estimated numbers eligible for each mAb<sup>7,8,9</sup>.

	Severe asthma		Omalizumab		Mepolizumab	
	Percentage with severe asthma <sup>10</sup>	Number with severe asthma (using QOF)	Percentage eligible (IDEAL study)	Number eligible	Percentage eligible (IDEAL study)	Number eligible
England, Wales & Northern Ireland	3.6%	134,672	27%	36,361	13%	17,507
Scotland	3.6%	12,955	27%	3,498	12%	1,555
UK	3.6%	147,627	27%	39,859	13%	19,062

Table 9: Numbers receiving each mAb and the percentage of those eligible receiving each mAb

Monoclonal Antibody (mAb)	Numbers receiving in April 2019	Percentage of those eligible
Omalizumab	8,667	21.7%
Mepolizumab	3,258	17.1%
Reslizumab	68	-
Total	11,993	20.4%

Table 10: Biologic eligibility criteria

Monoclonal Antibody	Diagnosis	Age	Blood eosinophil count	Number of exacerbations
<b>England, Wales and Northern Ireland</b>				
Omalizumab	Severe persistent confirmed allergic IgE mediated asthma	6 years and over	N/A	Continuous OCS or four or more courses of OCS in the previous year
Mepolizumab	Severe eosinophilic asthma	18 years and over	300 cells/microlitre or more in the previous 12 months	Continuous OCS previous six months or four or more courses of OCS in the previous year
Reslizumab	Severe eosinophilic asthma	18 years and over	400 cells/microlitre or more in the previous 12 months	Three or more courses of OCS in the previous year
Benralizumab	Severe eosinophilic asthma	18 years and over	Same eligibility criteria as mepolizumab and reslizumab (specifies use of LABA)	
<b>Scotland</b>				
Omalizumab	Same eligibility criteria as England, Wales and Northern Ireland			
Mepolizumab	Severe eosinophilic asthma	18 years and over	At least 150 cells/microlitre at initiation of treatment	Continuous OCS or four or more courses of OCS in the previous year
Benralizumab	Severe eosinophilic asthma	18 years and over	Same eligibility as mepolizumab (specifies use of LABA)	

## Appendix B: Asthma referral criteria

Referral criteria for adults with asthma is a key part of this report, and the differing criteria used across healthcare in the UK is outlined below. The points below relate to referral from primary care.

### BTS/SIGN

**For adults with asthma, the criteria for referral in the BTS/SIGN guidelines are:**

- High-dose ICS use and/or
- Continuous or frequent oral steroid use
- Symptoms of acute severe or life-threatening asthma
- Signs of occupational asthma

This report has used the 2016 BTS/SIGN guidelines. On 24 July 2019, a new set of guidelines were published. The main revisions for criteria for referral was revised to recommend that ‘all patients whose asthma is not adequately controlled on recommended initial or additional controller therapies should be referred for specialist care’ – thus broadening the criteria. There was a further declaration that BTS/SIGN will work with NICE to produce a joint ‘Guideline on Chronic Asthma’, which Asthma UK welcomes.<sup>11</sup>

### NICE

**The National Institute for Health and Care Excellence (NICE) introduced asthma guidelines in 2017, so after the period the CPRD data was collect. There are no explicit referral criteria in the guideline, but it includes in its definition that severe asthma is asthma that remains uncontrolled after:**

- Use of high-dose ICS with long-acting beta2 agonist (LABA) or leukotriene modifier or theophylline
- Six months or more on OCS.

NICE have also published a quality standard on the referral of people with suspected severe asthma to a specialist. Quality standards are statements designed to help drive quality improvement in a particular area of care<sup>12</sup>. Asthma quality standard 5 covers ‘suspected severe asthma’:

- People with suspected severe asthma are referred to a specialist multidisciplinary severe asthma service.

NICE use the GINA definition of severe asthma, and ask for evidence that the team in secondary or tertiary care is multidisciplinary, the proportion of people referred, and for the outcome, the rate of emergency admissions for asthma attacks and the proportion on two or more courses of OCS in a year<sup>13</sup>. However, without clear referral criteria, this standard is not measurable. NICE should address this gap in the guideline and quality standard.

**GINA**

**In the Global Initiative for Asthma (GINA) Difficult-to-treat & Severe asthma in adolescent & adult patients: Diagnosis and Management pocket guide<sup>14</sup>, referral to a specialist or severe asthma clinic should be considered if:**

- There is difficulty confirming the diagnosis of asthma
- Patient has frequent healthcare utilisation
- Patient needs frequent or maintenance OCS
- Occupational asthma is suspected
- Food allergy or anaphylaxis is present, as this increases the risk of death
- Symptoms are suggestive of infective or cardiac cause
- Symptoms are suggestive of complications such as bronchiectasis
- Presence of multiple co-morbidities

There is no specific referral criteria from primary care to secondary care, reflecting differences in global health systems (for example, some countries do not have GPs as gatekeepers to specialist care).

**NRAD**

**Although the National Review of Asthma Deaths (NRAD)<sup>15</sup> is not a clinical guideline, it is an important report that has proved influential in the care and management of people with asthma. NRAD recommends the following:**

- Patients with asthma must be referred to a specialist asthma service if they have required more than two courses of systemic corticosteroids, oral or injected, in the previous 12 months or require management using British Thoracic Society (BTS) stepwise treatment 4 or 5 to achieve control, i.e. high-dose ICS as above.

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Every ten seconds someone in the UK has a potentially life-threatening asthma attack and three people die every day. Tragically two thirds of these deaths could be prevented, whilst others still suffer with asthma so severe current treatments don't work.

This has to change. That's why Asthma UK exists. We work to stop asthma attacks and, ultimately, cure asthma by funding world leading research and scientists, campaigning for change and supporting people with asthma to reduce their risk of a potentially life-threatening asthma attack.

### We fight asthma in three ways:

- We fund world class asthma research.
- We campaign to improve the quality of care received by people with asthma.
- We help hundreds of thousands of people a year with our expert advice and support.

### To find out more about Asthma UK's work:



**Asthma UK Helpline:**  
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