Quick user guide

Maps

1. **Type of statistic** (e.g. rate, proportion)
2. **Geographic boundaries**
3. **Year of data presented**
4. **Rate calculated per x number of people**
5. **Optimum values** Low indicates lower values are preferential (high indicates higher values are preferential). Local interpretation maybe required for some indicators.

Map 1a: Experimental statistic: Variation in rate of all vision outpatient attendances by clinical commissioning group (2019/20)

1 Directly standardised rate per 100,000 population 4
Optimum value: Requires local interpretation 5

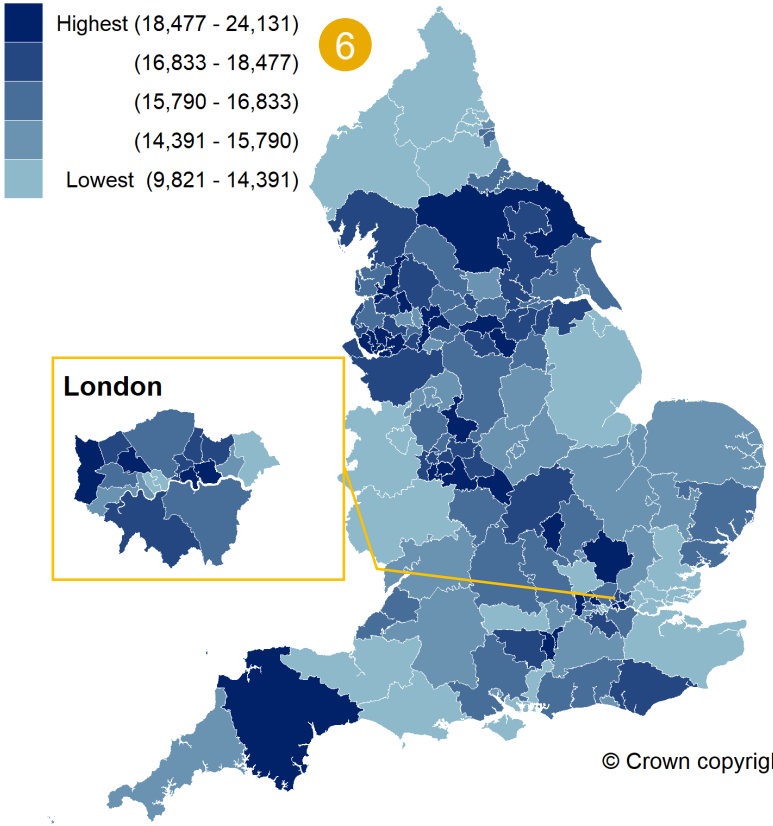
2

3

Equal-sized quintiles of geographies

Highest (18,477 - 24,131)
(16,833 - 18,477)
(15,790 - 16,833)
(14,391 - 15,790)
Lowest (9,821 - 14,391)

6

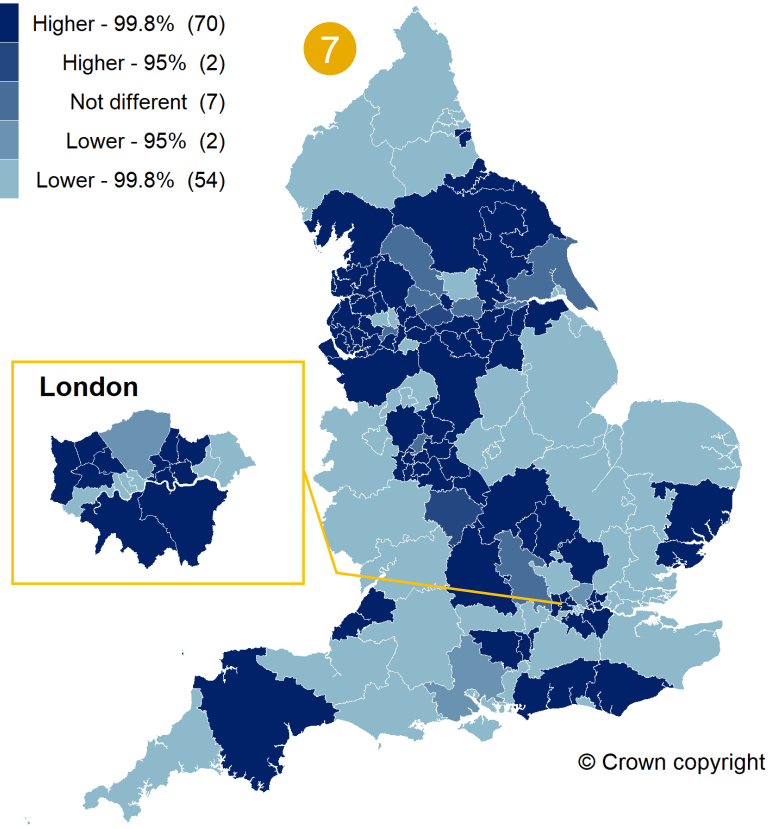


Significance level compared with England

Higher - 99.8% (70)
Higher - 95% (2)
Not different (7)
Lower - 95% (2)
Lower - 99.8% (54)

7

8



6. **Equal sized quintiles** The number of areas presented on the map are divided equally between the 5 categories with those with the highest values forming the 'Highest' group etc.

   For example, in 2020 there were 135 clinical commissioning groups (CCGs), so 27 CCGs are in each category. Darker areas have the highest values.

7. **Significance level compared with England** The darkest and lightest shading on map shows CCGs whose confidence intervals do not overlap with the England value.

   The second darkest and lightest colours show areas where the England value falls between the CCG's 95% and 99.8% CI.

   The number in brackets indicates the number of CCGs in each category.

8. **London** is presented as a separate zoomed in map for clarity.

Quick user guide

Chart, box plot and table

1. Title shows indicator details including: value type, geography and year.
2. The y-axis plots the value and gives details of the value type e.g. rate / proportion and the unit e.g. per 100,000 population.
3. The x-axis shows the geography and the number of areas on chart.
4. The line shows the England average.
5. Each bar represents an area (e.g. a CCG). The height of the bar is relative to the value for that area. Collectively, the bars show the spread of values across England.

   The colour of the bar represents how significant the area's value is in relation to England based on the area's confidence interval. Areas utilise the same colours and categories as the maps.

   Areas that are significantly higher than England at a 99.8% or 95% level are shown as darker bars whereas those with lower significance to England, at a 99.8% or 95% level, are lighter. The colour in the middle represents areas that are not significantly different from England.

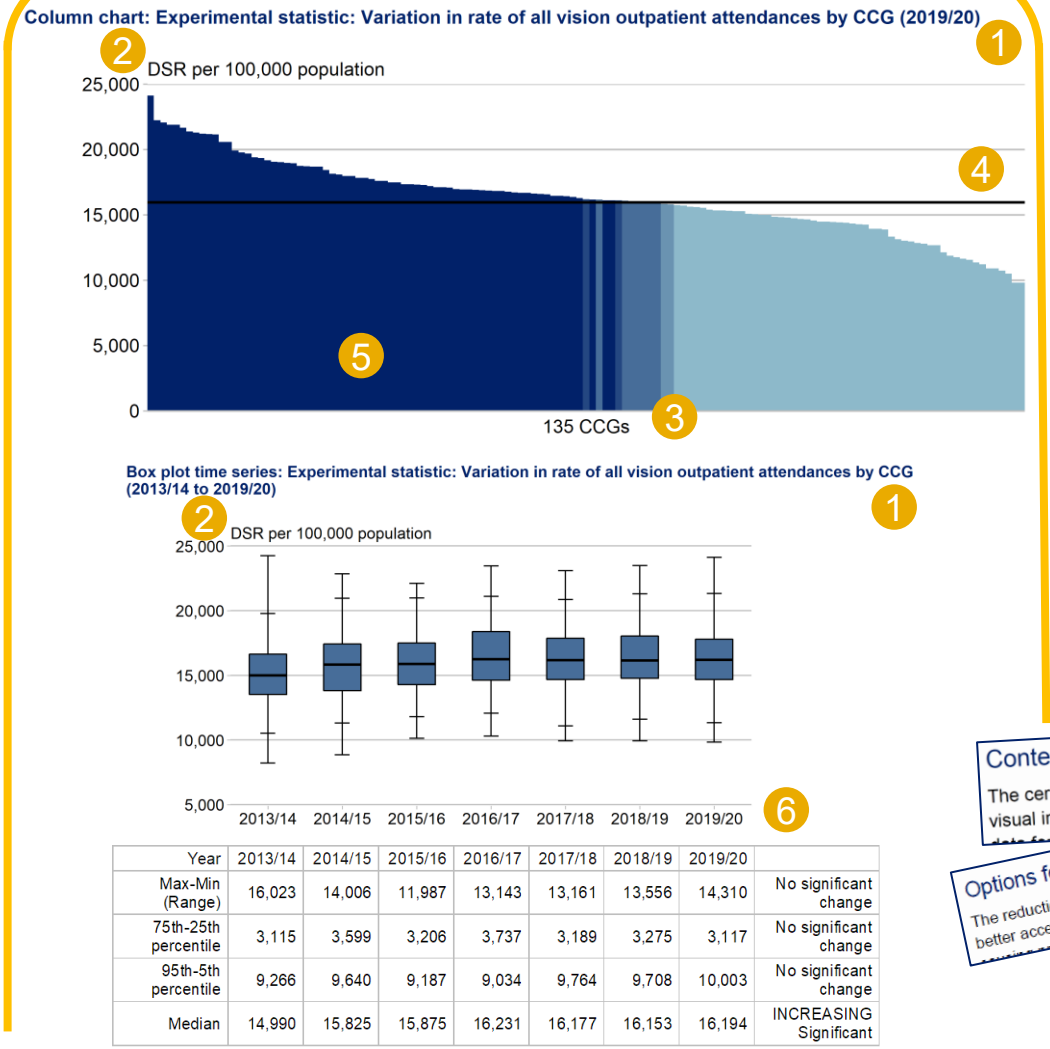
   Where the significance bar chart is unavailable, the equal interval map colours have been used.
6. For each indicator, data is presented visually in a time series of box and whisker plots. The box plots show the distribution of data.

   The line inside each box shows the median (the mid-point, so if the 135 CCGs were sorted in order of value, the value halfway between the CCGs in the 67th and 68th position would give the median). The bottom and top of the blue box represents the values which 25% and 75% of the areas fall below. 50% of the areas have a value within this range.

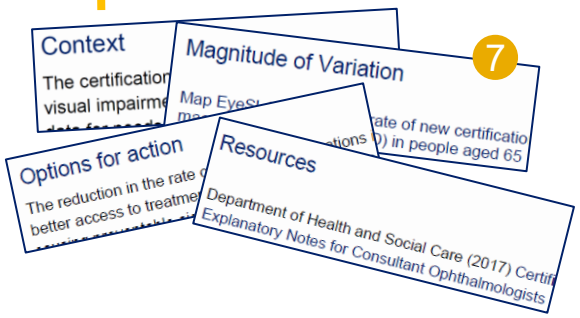
   The whiskers mark the values at which 5% and 95% of areas fall below. The median and maximum values are also shown.

   The time series allows us to see how the median has changed over time, but also whether the gap between the extreme values has changed.

   The table accompanying the box and whisker plots shows whether there has been any statistically significant change in the median, or in the degree of variation over time.



Year	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	
Max-Min (Range)	16,023	14,006	11,987	13,143	13,161	13,556	14,310	No significant change
75th-25th percentile	3,115	3,599	3,206	3,737	3,189	3,275	3,117	No significant change
95th-5th percentile	9,266	9,640	9,187	9,034	9,764	9,708	10,003	No significant change
Median	14,990	15,825	15,875	16,231	16,177	16,153	16,194	INCREASING Significant



7. **Sections in the chapter**

   Context – an overview of why the indicator is of public health interest

   Magnitude of variation – commentary in relation to the chart, box plot and table

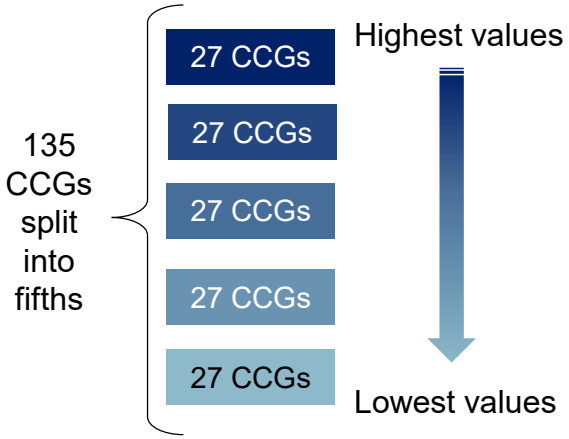
   Options for action – suggestions for best practice

   Resources – links to useful documents

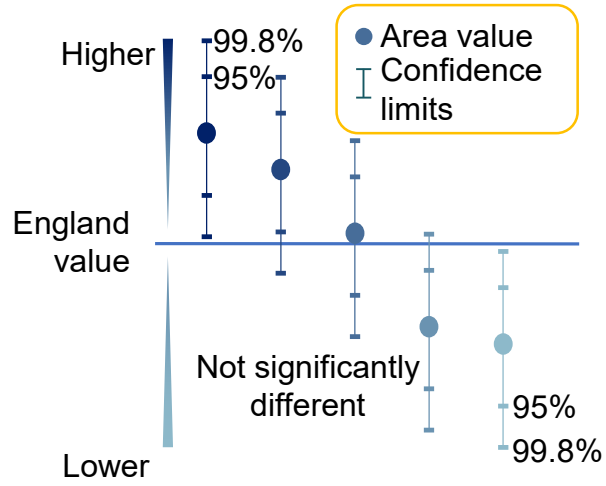
Quick user guide

How were the categories calculated?

Equal-sized quintiles



Significance to England



Confidence intervals give an estimated range in which the true CCG value lies.

Where the CCG's confidence interval does not overlap with the England value, the CCG is classed as being *significantly higher or lower than England at a 99.8% level*.

If the England value lies between the 99.8% and 95% CI, this value is classed as being *significantly higher or lower than England at a 95% level*.

Where the England value is between the upper and lower 95% CI, the CCG is classed as *not being significantly different from England*.

Box & whisker plot

Whiskers
Show the extreme values in the dataset.

Box
50% of the data values lie between the 25th and 75th percentile. The distance between these is known as the inter-quartile range (IQR).

Maximum The value of the area with the highest value.

95th percentile 95% of areas have values below this.

75th percentile 75% of areas have values below this.

Median (50th percentile) The median is the middle value of an ordered dataset. Half of the observations are below it and half above.

25th percentile 25% of areas have values below this.

5th percentile 5% of areas have a value below this.

Minimum The value of the area with the lowest value.

Box plot percentile	CCG rank position (135 CCGs in 2020)
Max	135
95%	Mid value between values of CCGs in ranks 128 and 129
75%	Mid value between values of CCGs in ranks 101 and 102
50% - Median	Mid value rank 68
25%	Mid value between values of CCGs in ranks 34 and 35
5%	Mid value between values of CCGs in ranks 7 and 8
Min	1

Intravitreal injections

Context

An intravitreal injection is an invasive procedure used to administer a drug or other therapeutic substance directly into the vitreous cavity of the eye to treat several conditions. This route of drug administration has been in use for many decades, predominantly to deliver antibiotic, antiviral or antifungal drugs to treat intraocular infection (endophthalmitis); and steroid drugs to manage intraocular inflammation (uveitis). Until the introduction of a class of drugs for ophthalmic uses known as the anti-vascular endothelial growth factor (anti-VEGF), annual health service activity associated with this procedure was relatively low.[1]

Intravitreal injection therapy with licensed anti-VEGF drugs for ophthalmic use was first introduced in the NHS in 2008.[2] Since then the drugs available in this class and their licensed indications for routine use have widened,[3, 4, 5, 6, 7, 8, 9, 10] making it possible to manage the common and previously untreatable retinal conditions associated with considerable visual morbidity in adults.[11] In addition, they are also used for the management of a variety of other less common retinal and ocular conditions.

Since 2013, Ranibizumab and Aflibercept have been the main licenced, NICE approved, anti-VEGF drugs for the routine management of wet age related macular degeneration (AMD), diabetic macular oedema (DMO) and macular oedema associated with retinal

[1] Keenan TDL, Wotton CJ and Goldacre M (2012) Trends over time and geographical variation in rates of intravitreal injections in England Br J Ophthalmol 2012; 96(3):413-8 [Accessed 17 May 2021]
[2] National Institute for Health and Care Excellence (2008 updated 2012) Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (NICE technology appraisal guidance [TA155]) [Accessed 17 May 2021
[3] National Institute for Health and Care Excellence (2013) Ranibizumab for treating diabetic macular oedema (NICE technology appraisal guidance [TA274]) [Accessed 17 May 2021]
[4] National Institute for Health and Care Excellence (2013) Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion (NICE technology appraisal guidance [TA283]) [Accessed 17 May 2021]
[5] National Institute for Health and Care Excellence (2013) Ranibizumab for treating choroidal neovascularisation associated with pathological myopia (NICE technology appraisal guidance [TA298]) [Accessed 17 May 2021]
[6] National Institute for Health and Care Excellence (2013) Aflibercept solution for injection for treating wet age-related macular degeneration (NICE technology appraisal guidance [TA294]) [Accessed 17 May 2021]
[7] National Institute for Health and Care Excellence (2014) Aflibercept for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion (NICE technology appraisal guidance [TA305]) [Accessed 17 May 2021]
[8] National Institute for Health and Care Excellence (2015) Aflibercept for treating diabetic macular oedema (NICE technology appraisal guidance [TA346]) [Accessed 17 May 2021]
[9] National Institute for Health and Care Excellence (2016) Aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion (NICE technology appraisal guidance [TA409]) [Accessed 17 May 2021]
[10] National Institute for Health and Care Excellence (2017) Aflibercept for treating choroidal neovascularisation (NICE technology appraisal guidance [TA486]) [Accessed 17 May 2021]
[11] Quartilo A, Simkiss P, Zekite A and others (2016) Leading causes of certifiable visual loss in England and Wales during the year ending 31 March 2013 Eye (London) 2016 Apr; 30(4): 602–607 [Accessed 18 May 2021]

vein occlusion (RVO-MO), which are leading causes of certifiable sight impairment and sight loss in adults in England and Wales.[11] The aim of treatment is to stabilise visual acuity.[3, 4, 5, 6, 7, 8, 9, 10] Routine clinical management of these conditions involves multiple administrations, often over a number of years, and is the principal driver for current intravitreal injection therapy activity. Intravitreal injections are a high volume NHS activity performed mainly in adults aged 60 years and over.[12] Initially when first introduced it was delivered as an admitted episode of care often as a day-case procedure, but is now delivered primarily (over 80% of activity) in an outpatient setting,[12,13] in an enclosed, dedicated clean room (as defined by the local infection control team),[12, 13, 14] which may be in a hospital, community or mobile unit environment.

Since February 2021, Brolucizumab has been added to the list of licensed, NICE approved anti-VEGF drugs for wet AMD, but is not established as first line management.[15]

Unlike admitted episodes of care, there is no mandatory requirement for Hospital Episode Statistics outpatient episodes to be coded by diagnosis (ICD10) or by procedure (OPCS4). The indication for treatment given by diagnosis codes (ICD10) is often incomplete, particularly in outpatient settings.[16,17] However, given the volume of activity commissioned and generated and the cost to the NHS for service provision, these procedures are likely to be coded for outpatient and admitted episodes in most circumstances, covering predominantly anti-VEGF drugs, but also to a lesser extent a range of other drugs. Efforts to introduce more specific procedure codes for the ophthalmic use of anti-VEGF drugs (for example for high-cost drugs for subfoveal choroidal neovascularisation)[18] to distinguish these from other drugs used for intravitreal procedures, have not been sustainable and are hardly used.[12,13,18]

Despite these limitations, and for the purpose of this analysis, covering a period of established clinical practice, the OPCS procedure codes in both admitted care and outpatient settings, serve to cover intravitreal injection therapy primarily with the anti-VEGF agents Aflibercept and Ranibizumab for the management of wet AMD, DMO, RVO-MO, and to a much lesser extent for a range of other ocular conditions.

[12] NHS Digital Hospital Admitted Patient Care Activity [Accessed 18 May 2021]
[13] NHS Digital Hospital Outpatient Activity [Accessed 18 May 2021]
[14] Royal College of Ophthalmologists (2018) Ophthalmic Services Guidance: Intravitreal injection therapy [Accessed 18 May 2021]
[15] National Institute for Health and Care Excellence (2021) Brolucizumab for treating wet age-related macular degeneration [NICE technology appraisal guidance [TA672]) [Accessed 18 May 2021]
[16] NHS Digital Hospital Admitted Patient Care Activity 2019/20: Data Quality Statement [Accessed 13 July 2021]
[17] NHS Digital Hospital Outpatient Activity 2019/20: Data Quality Statement [Accessed 13 July 2021]
[18] Hollingworth W, Jones T, Reeves BC and others (2017) A longitudinal study to assess the frequency and cost of anti-vascular endothelial therapy, and inequalities in access in England between 2005 and 2015 BMJ Open 2017;7: e018289 [Accessed 21 May 2021]

Intravitreal injections during the COVID-19 pandemic

Since the onset of the coronavirus (COVID-19) pandemic in March 2020, clinical risk stratification has prioritised patients receiving treatment with anti-VEGF drugs (new and ongoing) for high risk conditions such as wet AMD, above all other indications. Patients classified as having medium and low risk clinical conditions had their management delayed or rescheduled for at least 3 to 6 months later. This is reflected in the significant reduction in activity for first and all episodes during the first wave of the pandemic (April to June 2020), which is followed by some recovery towards expected levels of activity by September 2020 (Figures 2.1 and 2.2).

Patients who need intravitreal injection therapy are more likely to have been classified as being clinically vulnerable to COVID-19 infection or shielding due to systemic comorbidities or their age. Patients may also have been reluctant to attend a hospital clinic especially during the first wave (and possibly subsequent waves). The more pronounced drop in first injection activity could also be attributed to the rescheduling of treatment for new patients presenting with medium and low risk retinal conditions for several months later.

Although there were signs of recovery of activity (first and all) by September 2020, the subsequent waves will have only added to the delays and backlog particularly in the management of retinal conditions other than AMD. New pathways developed to manage the backlogs should be reviewed for their impact on mitigating risk for irreversible disease progression; reducing delays and acceptability to patients.

Figure 2.1: Experimental statistic - Provisional data: All intravitreal injection therapy procedures in people aged 60 years and over for England (January 2018 to February 2021)

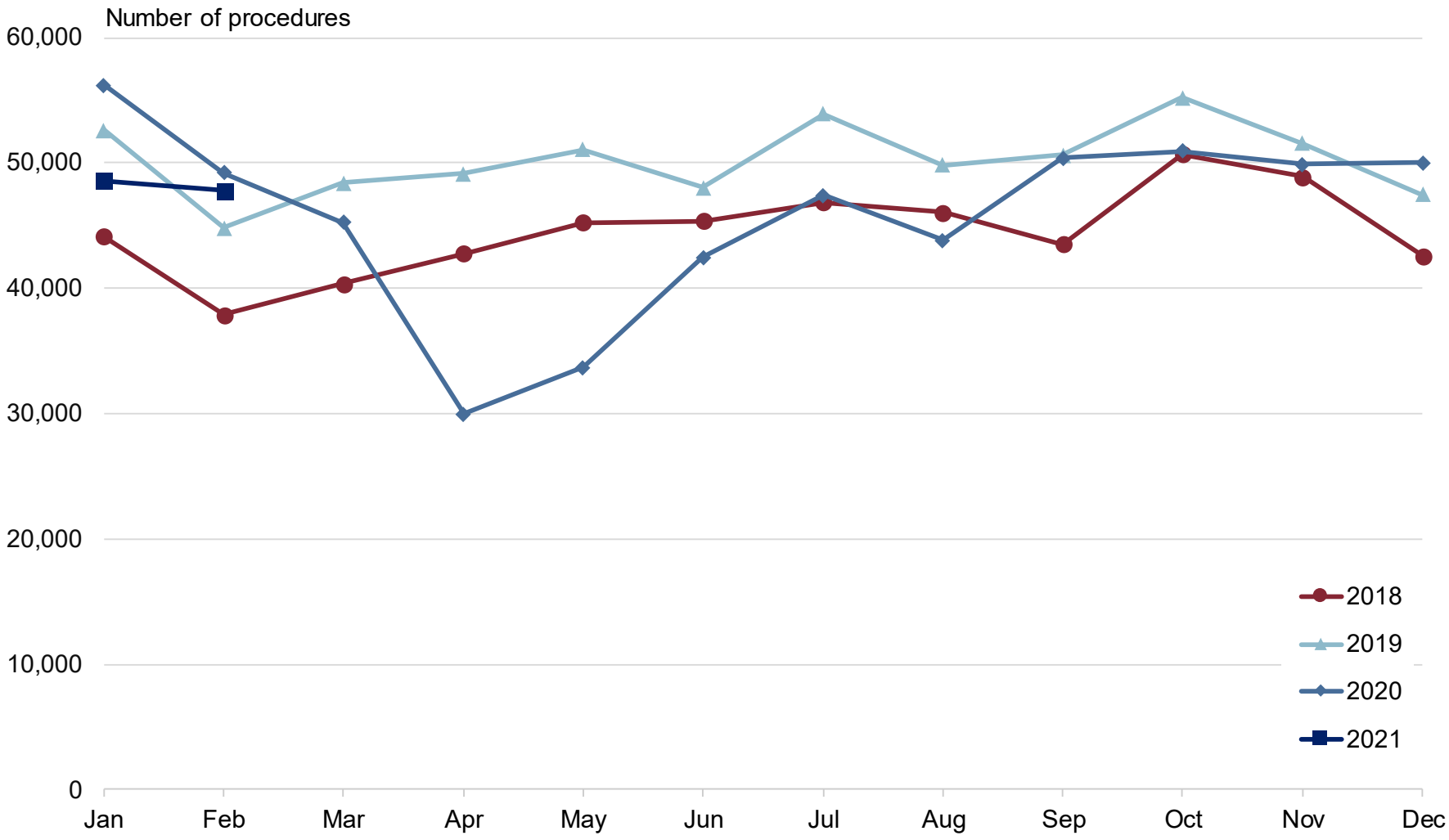
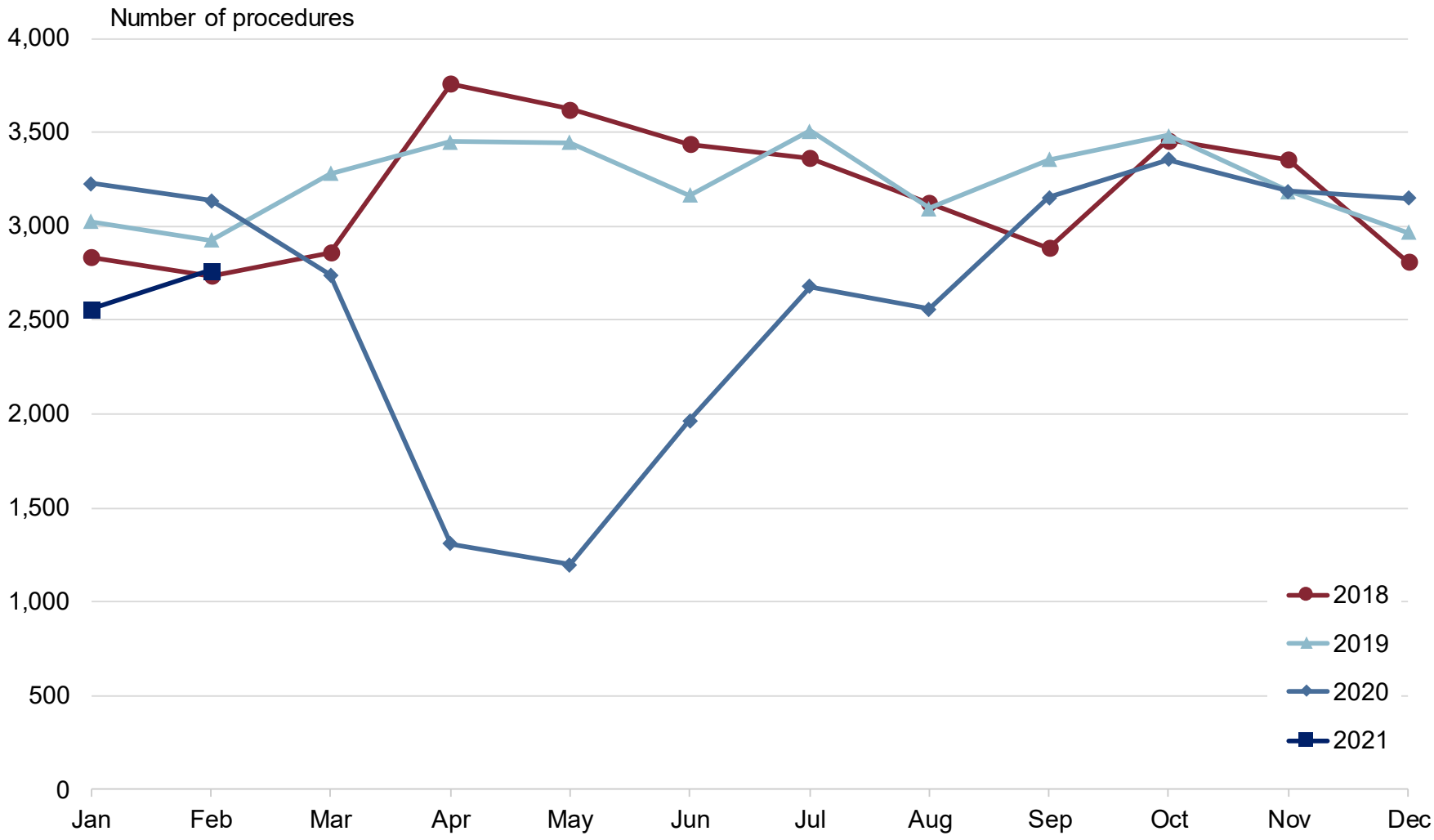
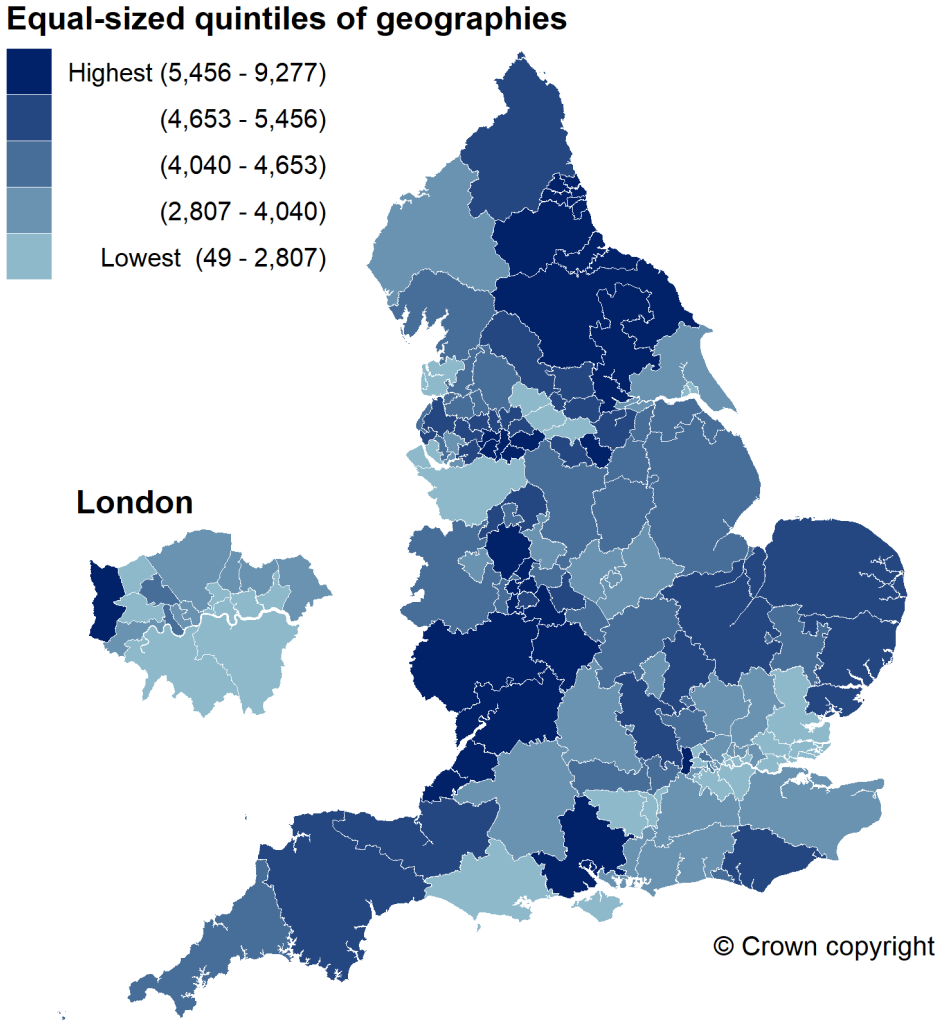


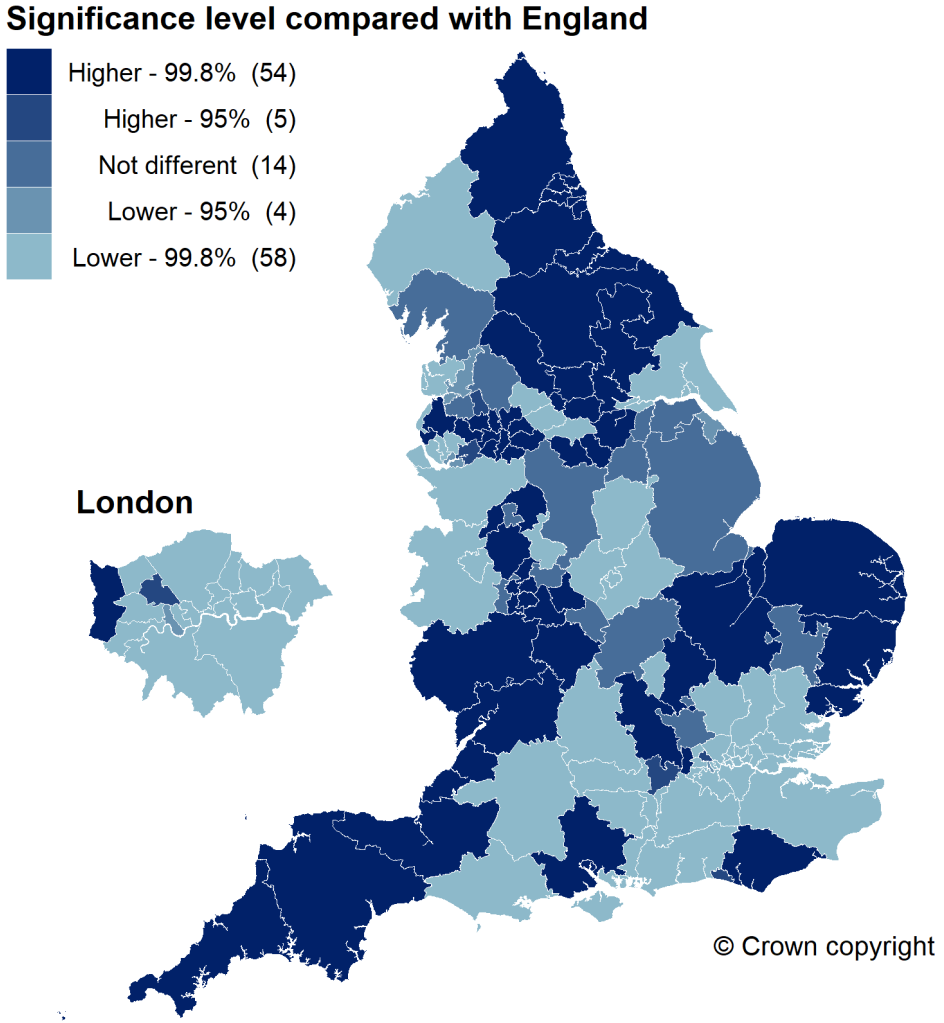
Figure 2.2: Experimental statistic - Provisional data: First intravitreal injection therapy procedures in people aged 60 years and over for England (January 2018 to February 2021)



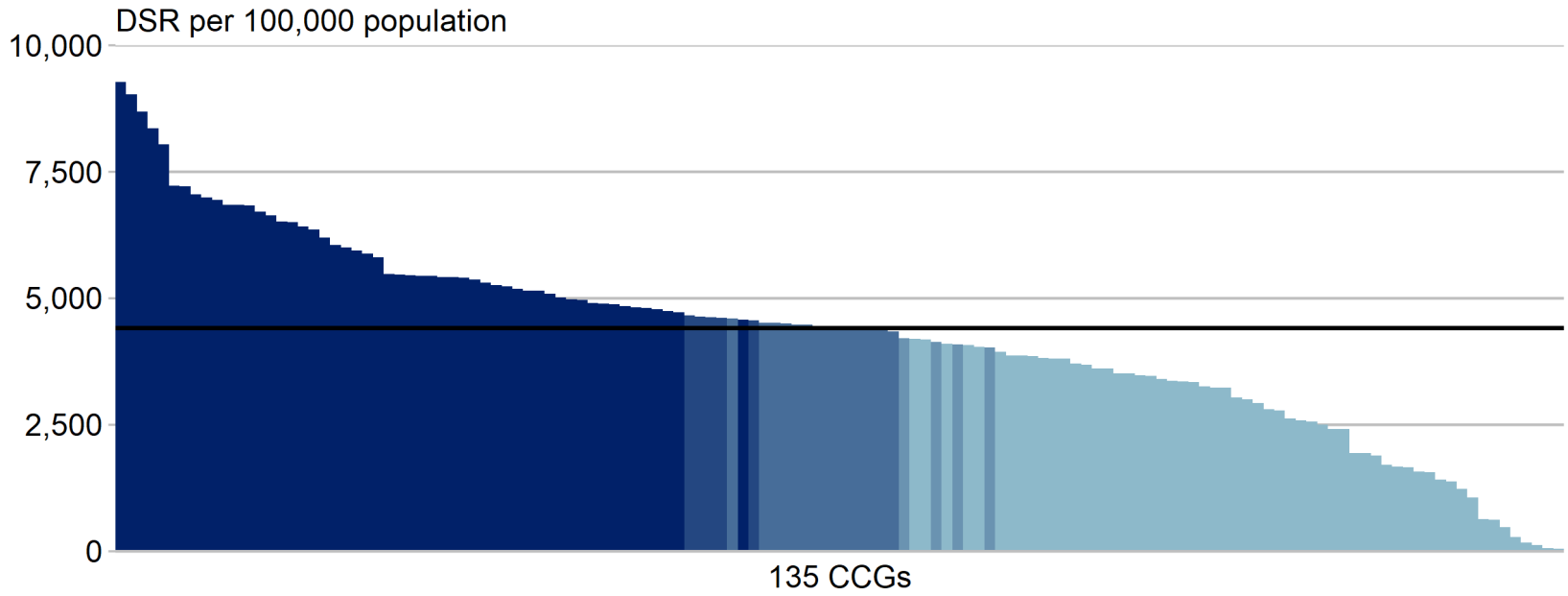
Map 2a: Experimental statistic: Variation in rate of all intravitreal injection therapy procedures in people aged 60 years and over by clinical commissioning group (2019/20)

Directly standardised rate per 100,000 population
Optimum value: Requires local interpretation

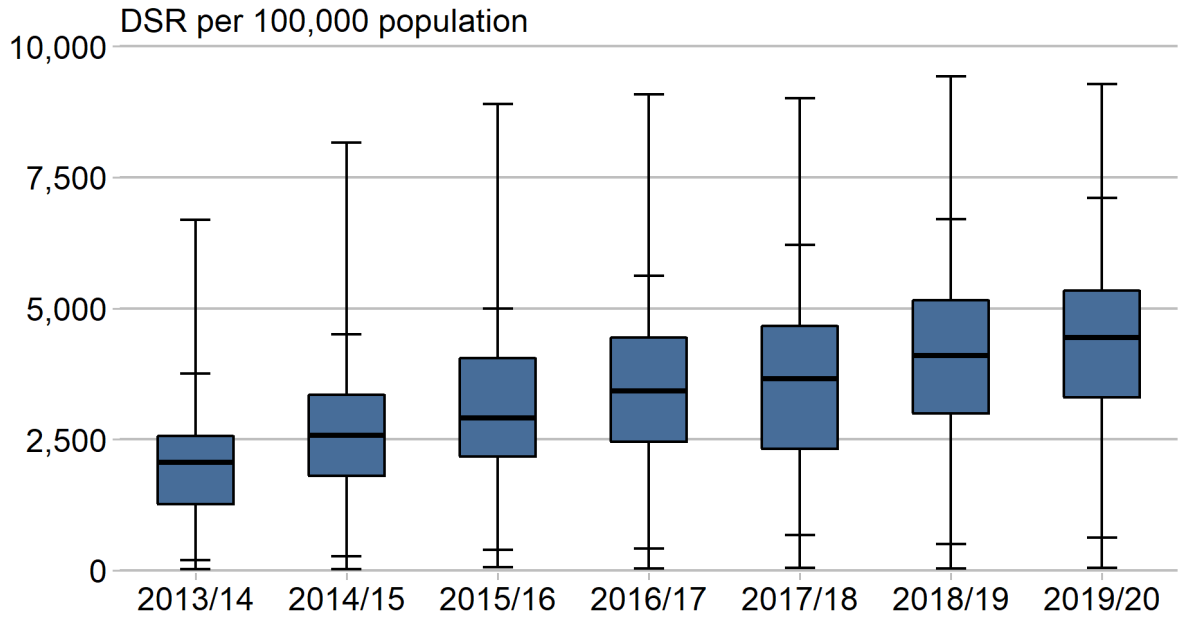




Column chart: Experimental statistic: Variation in rate of all intravitreal injection therapy procedures in people aged 60 years and over by CCG (2019/20)



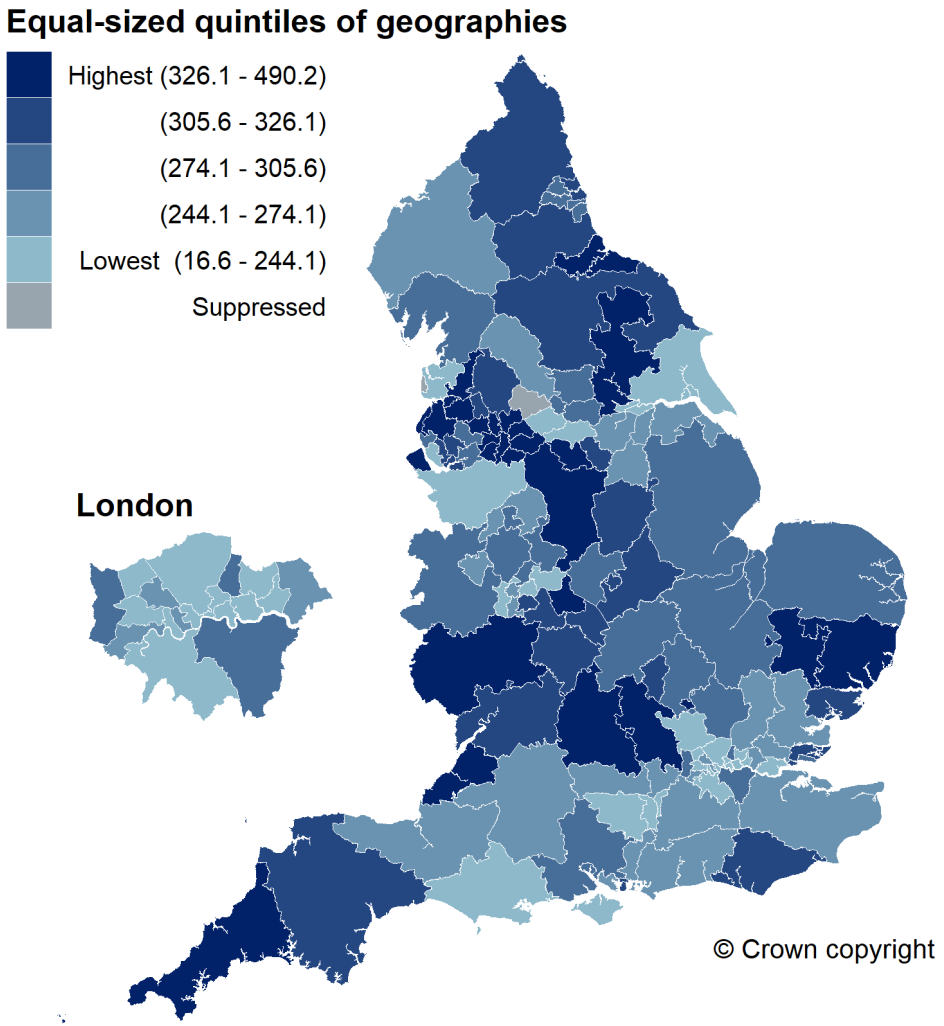
Box plot time series: Experimental statistic: Variation in rate of all intravitreal injection therapy procedures in people aged 60 years and over by CCG (2013/14 to 2019/20)

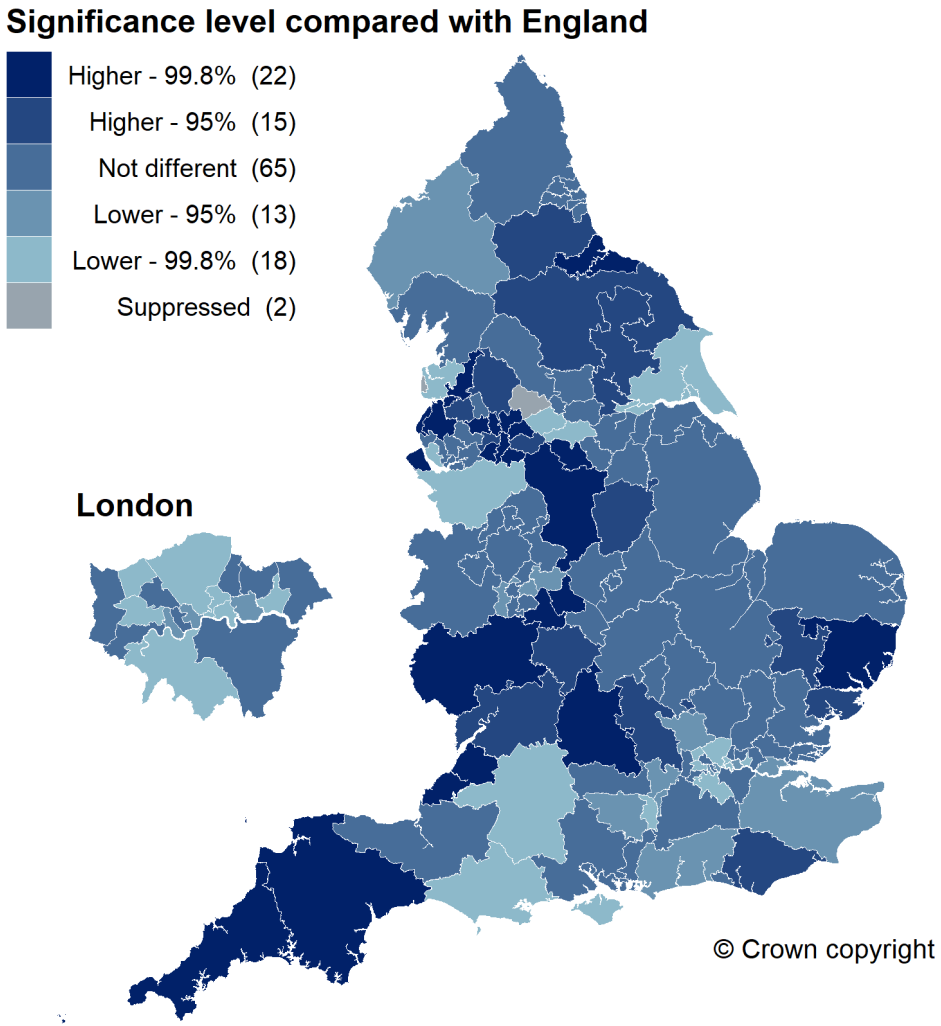


Year	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	
Max-Min (Range)	6,657	8,143	8,840	9,047	8,959	9,388	9,228	WIDENING Significant
75th-25th percentile	1,307	1,548	1,868	1,991	2,340	2,157	2,033	WIDENING Significant
95th-5th percentile	3,556	4,236	4,599	5,203	5,536	6,199	6,479	WIDENING Significant
Median	2,063	2,579	2,910	3,427	3,662	4,099	4,436	INCREASING Significant

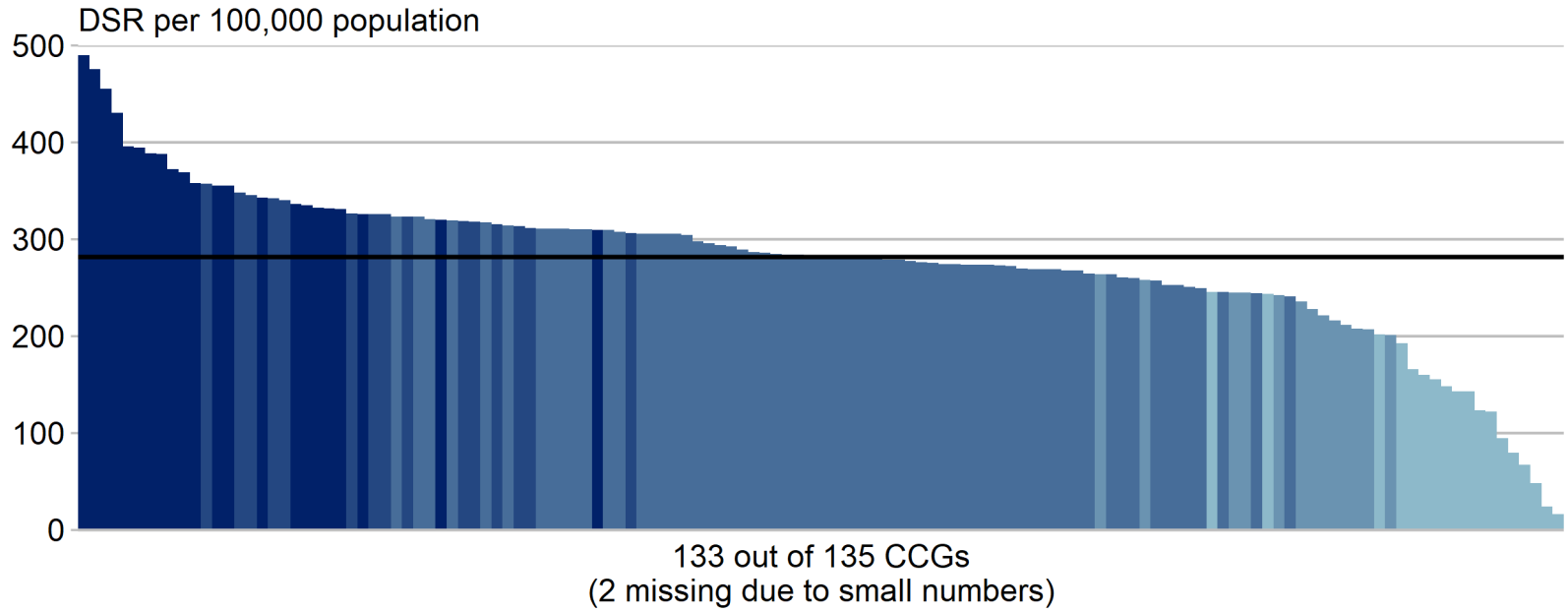
Map 2b: Experimental statistic: Variation in rate of first intravitreal injection therapy procedures in people aged 60 years and over by clinical commissioning group (2019/20)

Directly standardised rate per 100,000 population
Optimum value: Requires local interpretation

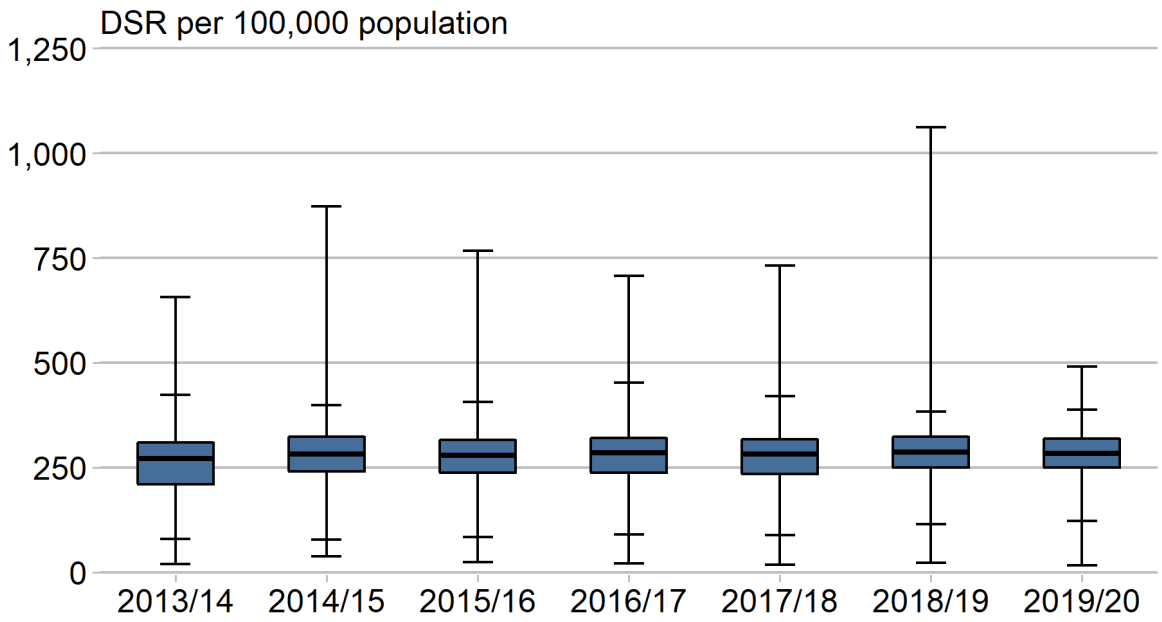




Column chart: Experimental statistic: Variation in rate of first intravitreal injection therapy procedures in people aged 60 years and over by CCG (2019/20)



Box plot time series: Experimental statistic: Variation in rate of first intravitreal injection therapy procedures in people aged 60 years and over by CCG (2013/14 to 2019/20)



Year	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	
Max-Min (Range)	637.6	833.9	743.2	685.3	712.6	1,038.2	473.7	No significant change
75th-25th percentile	100.3	82.5	77.9	82.5	83.9	73.3	68.6	NARROWING Significant
95th-5th percentile	344.2	319.4	321.3	361.6	331.9	268.4	265.3	No significant change
Median	271.8	281.6	278.3	284.7	281.5	286.6	283.2	No significant change

Magnitude of Variation

Map 2a: Experimental statistic: Variation in rate of all intravitreal injection therapy procedures in people aged 60 years and over by clinical commissioning group

The maps and column chart display the latest period (2019/20), during which clinical commissioning group (CCG) values ranged from 49 per 100,000 population to 9,277 per 100,000 population, which is a 188.6-fold difference between CCGs.

The England value for 2019/20 was 4,411 per 100,000 population.

The box plot shows the distribution of CCG values for the period 2013/14 to 2019/20.

There has been significant widening of all three measures of variation.

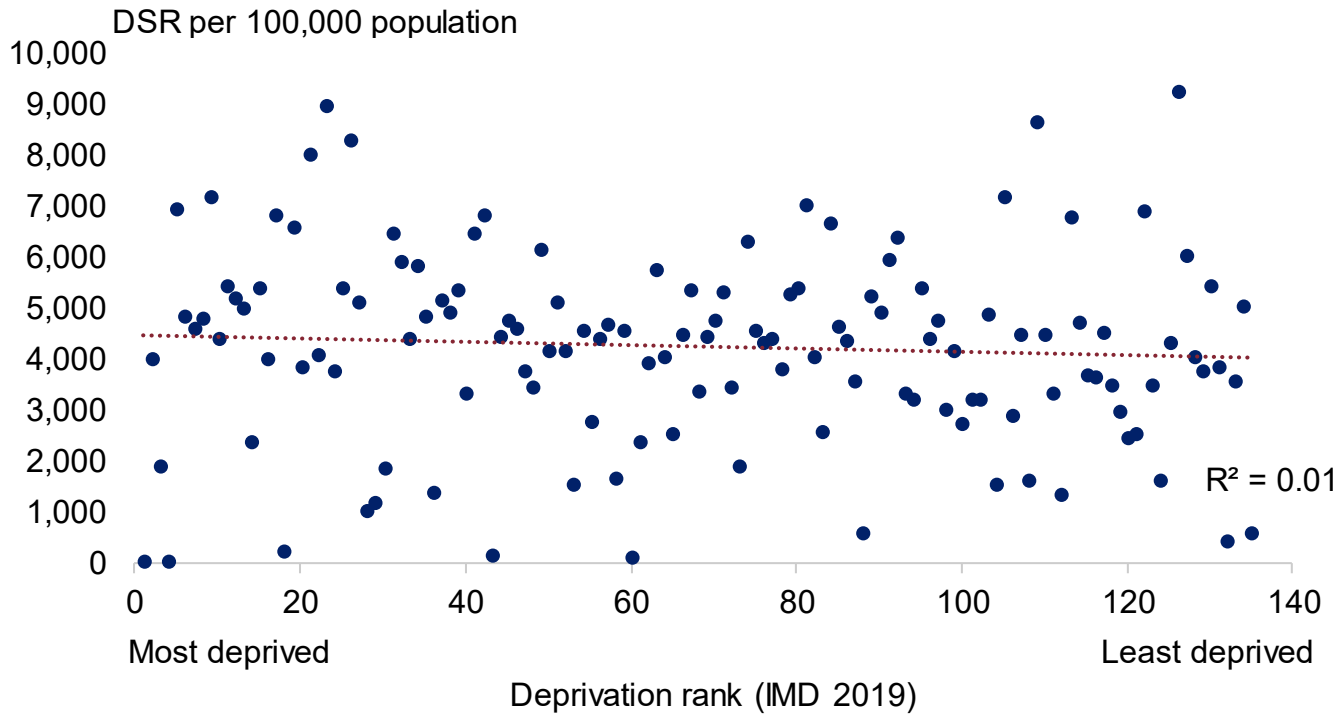
The median increased significantly from 2,063 per 100,000 population in 2013/14 to 4,436 per 100,000 population in 2019/20.

During 2019/20 a total of 608,000 intravitreal injection procedures were performed for 143,000 persons of 60 years of age and over i.e. the population at risk of eye conditions that may need intravitreal injection therapy with anti-VEGF class of drugs.

Over the 7 year period of established practice (2013/14 to 2019/20), the rates for all intravitreal injection procedures rose steadily in the presence of significant and widening variation in activity. Most of the variation lies at the extremes of the distribution of activity. Eighty-three per cent (112/135) of CCGs had procedure rates which were significantly different to the national rate at the 99.8% level.

The deprivation chart (Index of Multiple Deprivation rank) Figure 2.3 shows there is no strong association with the variation of rates for all intravitreal injection procedures at a CCG level, indicating that services currently meet known demand but should be checked locally as this could be compounded by access to services.

Figure 2.3: Scatterplot of all intravitreal injection therapy procedures in people aged 60 years and over by index of multiple deprivation by clinical commissioning group (2019/20)



Despite this limitation, the data currently available from over 600,000 procedures performed on a population at risk may additionally reflect the following:

Differences in the distribution of underlying conditions:

Underlying eye conditions, that are treated by intravitreal injection therapy, are known to vary across different ethnic groups.[19, 20, 21]

Differences in clinical protocols:

Care plans for the licenced indications all involve multiple episodes of care at varying intervals and duration.

[19] Wong WL, Su X, Li X and others (2014) Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis Lancet Glob Health 2014; 2: 106-16 [Accessed 24 May 2021]

[20] Sivaprasad S, Gupta B, Gulliford MC and others (2012) Ethnic Variations in the Prevalence of Diabetic Retinopathy in People with Diabetes Attending Screening in the United Kingdom (DRIVE UK) PLoS One 2012;7:e32182 [Accessed 24 May 2021]

[21] Rogers S, McIntosh RL, Cheung N and others (2010) The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia Ophthalmology 2010; 117: 313–9.e1 [Accessed 20 May 2021]

Capacity pressure:

Capacity pressures to deliver services and manage the rising clinical activity so generated

Map 2b: Experimental statistic: Variation in rate of first intravitreal injection therapy procedures in people aged 60 years and over by clinical commissioning group

The maps and column chart display the latest period (2019/20), during which CCG values ranged from 16.6 per 100,000 population to 490.2 per 100,000 population, which is a 29.5-fold difference between CCGs.

The England value for 2019/20 was 281.7 per 100,000 population.

The box plot shows the distribution of CCG values for the period 2013/14 to 2019/20.

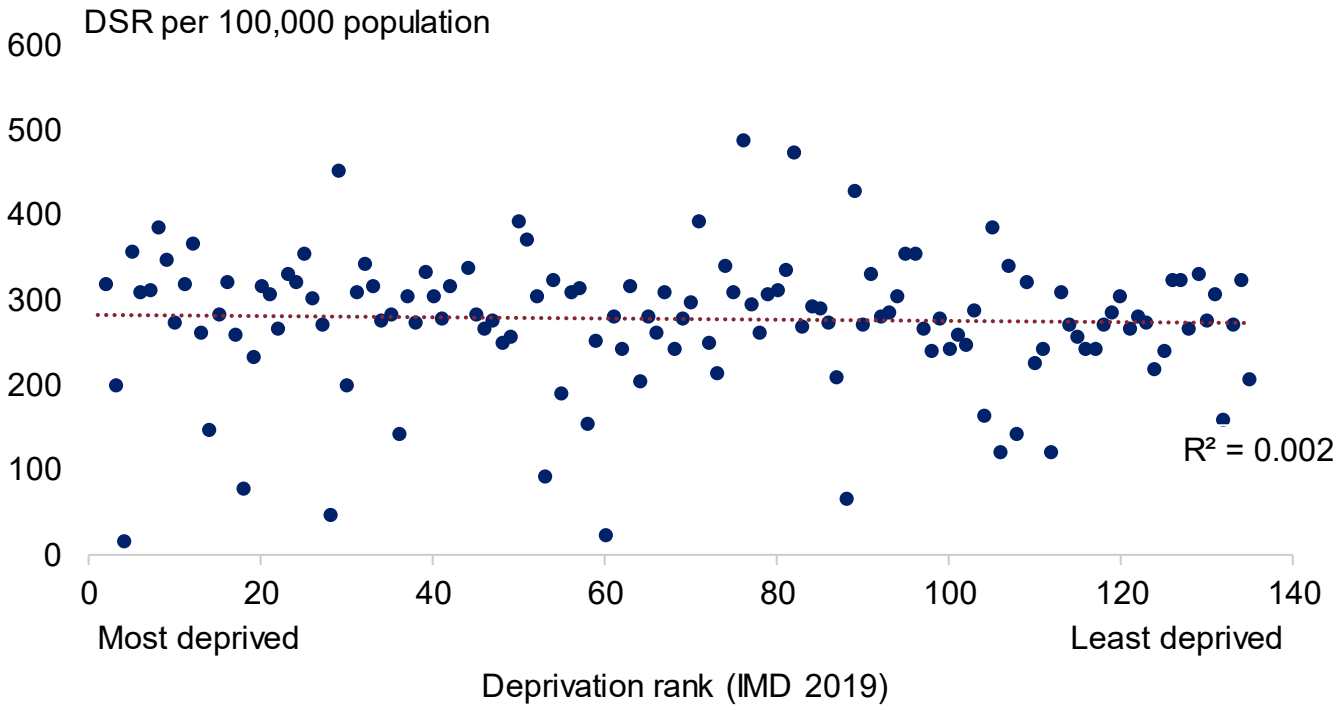
The 75th to 25th percentile gap narrowed significantly.

During 2019/20, almost 39,000 first procedures were performed on persons aged 60 years and over. In 2019/20, the ratio of first to ongoing injection procedures is approximately 1:15, broadly reflecting anecdotal clinical experience.

Over the 7 year period of established practice (2013/14 to 2019/20) there was no significant change in the rate of first injections for the population at risk, but there was a significant decrease in variation as indicated by the narrowing of the difference between the 75th and 25th percentile. Thirty per cent (40/133) of CCGs having rates which were significantly different to the national rate at the 99.8% level.

The deprivation chart (Index of Multiple Deprivation rank) Figure 2.4 shows there to be no strong association with the variation in the rates for first intravitreal injection procedures at a CCG level, indicating that services currently meet known demand but should be checked locally as this could be compounded by access to services.

Figure 2.4: Scatterplot of all first intravitreal injection therapy procedures in people aged 60 years and over by index of multiple deprivation by clinical commissioning group (2019/20)



Differences in organisational practice and priorities for OPCS coding data of their activity are the most likely to be the major, systematic factor contributing to the variations, potentially underestimating rates of first injection and masking the existence of true variations.

However, despite this limitation, from the data currently available the variations may also be influenced by:

Levels of need and demand in local populations:

Differences in the risk and distribution of the underlying conditions which are licenced indications for intravitreal injection therapy (health needs), are known to be associated with ethnicity.[19, 20, 21]

Timely access to NHS services:

Although rates for first injection procedures (the new demand) remained unchanged over a period of established practice, the underlying number of people in the population at risk may have changed with subsequent change in the number of episodes of care required to be delivered. New or first episodes of care in ophthalmology are generally prioritised for outpatient settings and rapid access and treatment pathways for wet AMD are recommended and increasingly available,[22] but local circumstances for managing

[22] National Institute for Health and Care Excellence (2018) Age-related macular degeneration (NICE guideline [NG 82]) [Accessed 13 May 2021]

capacity and demand are likely to influence whether these are sufficiently operational or not.

Options for action

Data quality: improve coding of routine NHS activity for Hospital Episode Statistics

It is unlikely that OPCS and ICD coding for all NHS outpatient attendances will be mandated soon. However, given the high volume of NHS activity generated and the total resources consumed (from clinical, patient and health service perspectives), all providers of these NHS commissioned services should be required to code all their intravitreal injection procedures from all settings of service delivery, for their returns to HES.

This information is essential to ensure equitable use of health resources to meet health needs, and to reliably inform capacity and demand management; at local level (place), Integrated Care System (ICS) and national level.

Review clinical protocols: ensure consistent, effective, evidence-based clinical management

The protocols for the licensed indications all require multiple procedures, often over several years. Variations are more likely to arise around interpretation of treat and extend regimes from clinical trials for application into routine practice for ongoing management, rather than around loading courses on starting therapy.

Clinical protocols should be reviewed to ensure provision of effective, evidence-based services, with clear guidance on monitoring of response to active treatment, criteria for stopping therapy, the processes (including duration) for monitoring of stable patients following treatment; and for managing recurrence. In addition, as new anti-VEGF agents are introduced, criteria for potential treatment switches should be agreed for defined and demonstrable clinical need for example Brolucizumab for wet AMD.[15] These should all be applicable at place and ICS level.

Report outcomes of treatment for quality assurance of services

Whilst these are likely to be the subject of departmental audit and discussion, wider reporting and review locally (place) and at ICS level would provide assurance on the quality of services delivered for the population at risk. The following outcomes proposed in the Portfolio of Indicators for Eye Health and Care (Indicator 7),[23] based on data collected during routine clinical care, are a useful starting point and should not incur additional burden for data collection:

[23] Clinical Council for Eye Health Commissioning (2018) SAFE: Portfolio of Indicators for Eye Health and Care [Accessed 09 Aug 2021]

- visual acuity outcomes of anti-VEGF therapy at baseline and at one year after starting treatment for: wet AMD, diabetic macular oedema, and macula oedema complicating retinal vein occlusions

Review service activity by demographic factors such as ethnicity and gender to:

- ensure equity in meeting need and demand within overall service provision
- monitor for unintended consequences of clinical risk stratification
- identify potential health seeking behaviours

The risk of developing wet AMD, diabetic macular oedema and macular oedema associated with retinal vein occlusion, will vary by age and ethnicity.[19, 20, 21] Patients are now risk stratified to prioritise their care as a means to manage backlogs, capacity and demand, which have all been further intensified since the onset of the COVID-19 pandemic. In doing so, some patient groups may be placed at particular risk of ongoing limited or delayed access to care, especially in the context of multiple morbidities (ocular and systemic).

Resources

National Institute for Health and Care Excellence (2018) Age-related macular degeneration (NICE guideline [NG 82]) [Accessed 13 May 2021]

Moorfields Eye Hospital NHS Foundation Trust (2018) Patient Information: Anti-VEGF Intravitreal Injection Treatment [Accessed 18 May 2021]

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