Appendix 1 - Multi-morbidities project

<u>Data that the gout committee requested to inform decision making</u>

General points which could be useful for all review questions for context and for questions 3.1 – 5.3:

1. Prevalence of gout and age of diagnosis
2. Top 5 comorbidities of gout patients and percentages of patients with each respective comorbidity, percentages of gout patients with multiple comorbidities (of these top 5) and percentage of gout patients without any other comorbidity
3. Percentage of patients with gout who are treated with allopurinol or febuxostat
4. For patients taking ULT, when was their urate level last checked and what was it?
5. Data on co-prescribing of drugs for gout (stratified by CKD stage 3-5 and non-CKD population stage 1-2)
    o *diuretics*
    o *fenofibrate*
    o *statins*
    o *fibrates*
    o *verapamil*
    o *diltiazem*
    o *digoxin*
    o *amiodarone*
    o *ketoconazole (oral)*
    o *macrolides*
    o *low dose aspirin*
    o *Beta-Blockers*
    o *ACEi (all ACEi combined (or the commonly used ones)*
    o *non-losartan ARBs (or the commonly used ones)*
    o *losartan*
    o *Tacrolimus*
    o *Ciclosporin*

1. Gout Overview

1.1 Background

The data set is from the Gold Dataset in the Clinical Practice Research Datalink (CPRD). The data was analysed with the approval of the Medicines and Healthcare products Regulatory Agency Independent Scientific Advisory Committee (ISAC 20_018). To minimise disclosure, small cell sizes are suppressed (cells with absolute numbers between 1 and 4). This dataset contains records on 5,085,577 patients in 530 primary care practices. We apply additional eligibility criteria for inclusion in this analysis:

- Practices were eligible if:

    o   they contributed up to standard data on the index date (30/11/2015) and
    o   had linkage to Hospital Episode Statistics and death registration data.
- Individual patients were included if:

    o   their data was categorised by CPRD as acceptable for research,
    o   if they were alive and registered with an eligible GP practice on the index date, and
    o   had been registered with the practice for at least two years prior to the index date.

The underlying total patient population used in this analysis consists of 1,169,077 patients from 380 general practices.

1.2 Identifying patients diagnosed with gout in CPRD

We restrict the cohort of patients with gout to those with a Read coded diagnosis of gout in the primary care record.

Analysis is provided for two cohorts:

1. Prevalent (all people diagnosed with gout): This cohort contains everyone with a GP-recorded diagnosis of gout before 30/11/2015, as defined above.

2. Recently diagnosed people with gout. This is the subset of the prevalent cohort who were diagnosed with gout for the first time in the year before 30/11/2015. An additional check that this first diagnosis is not a record of a 'History of gout' code is also made.

1.3 Prevalent clinical population: all patients diagnosed with gout

The prevalent clinical population comprises 32,828 patients diagnosed with gout identified in our subset, which is 2.81% of the total eligible cohort.

The age/sex breakdown of this cohort is:

Table 1: Prevalence of gout by sex (all people with gout)

Sex	Number of patients	%	Age at Diagnosis		Age at Index	
			Mean ± SD	Range	Mean ± SD	Range
Male	26,044	79.3	54.7 ± 14.3	0 - 98	64.5 ± 13.9	11 - 107
Female	6,784	20.7	64.7 ± 14.1	0 - 98	72.2 ± 13.4	21 - 104

Table 2: Age at diagnosis of gout by sex (all people with gout)

Age group	Male		Female		Total	
	N	% of age group	N	% of age group	N	% of cohort
<=24	205	80.1	51	19.9	256	0.8
25-34	1,753	92.6	141	7.4	1,894	5.8
35-44	4,810	92.2	407	7.8	5,217	15.9
45-54	6,427	87.3	938	12.7	7,365	22.4
55-64	5,964	79.6	1,524	20.4	7,488	22.8
65-74	4,441	69.9	1,913	30.1	6,354	19.4
75-84	2,083	59.0	1,450	41.0	3,533	10.8
85-94	354	50.4	349	49.6	703	2.1
>=95	7	38.9	11	61.1	18	0.1

Figure 1: Distribution of age at diagnosis by sex (all people with Gout)
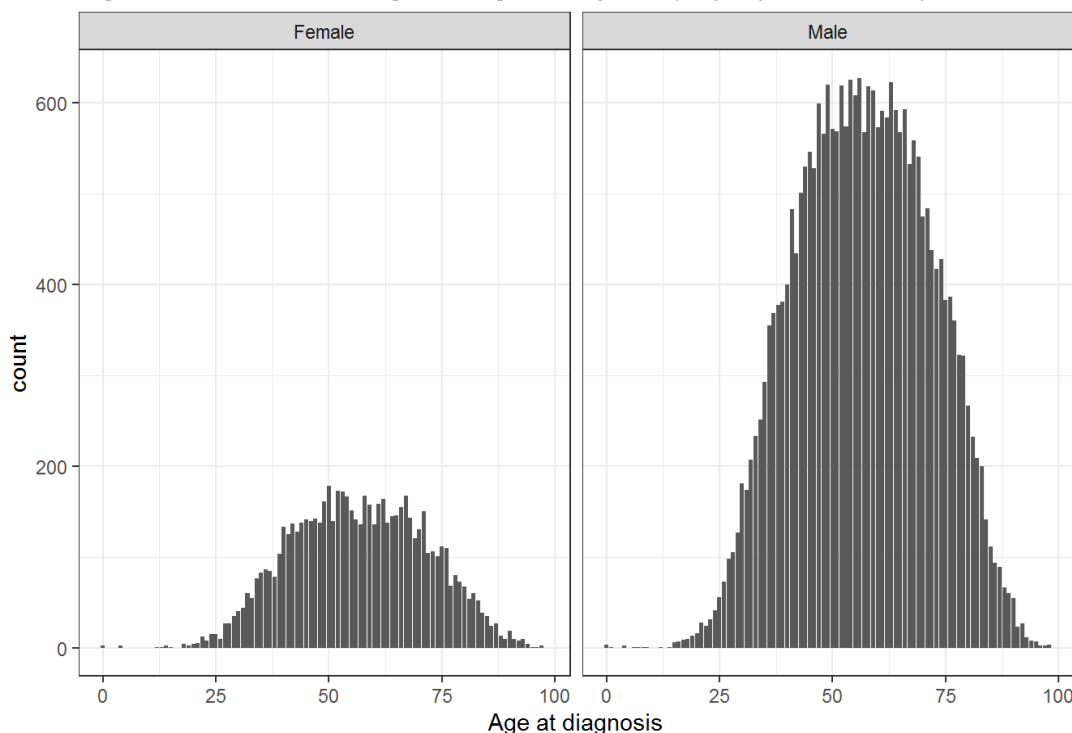
1.4 Comorbidities

These comorbidities are currently defined based on their Primary Care readcode defined conditions (+ biomedically defined CKD), as defined by the CALIBER project (https://github.com/spiros/chronological-map-phenotypes/tree/master/primary_care). Comorbidities are presented as individual conditions, and groups of conditions (e.g. Diabetes mellitus incorporates Type 1, Type 2 and uncertain diabetes)

Table 3: Individual comorbidities: Overall number (%) in prevalent clinical population with gout, and percentage of each age group with each comorbidity (all people with gout)

Condition	N	%	Under	45-	55-	65-	75-	Over

			45	54	64	74	84	85
Hypertension	18,057	55.0	12.0	28.9	48.8	63.5	73.5	78.1
Osteoarthritis	9,595	29.2	2.4	8.4	21.2	33.4	45.5	52.6
Dermatitis	9,573	29.2	23.0	22.4	26.0	30.5	34.3	36.5
Chronic kidney disease	7,901	24.1	3.7	5.4	9.2	21.3	44.4	64.6
Depression	6,587	20.1	20.8	21.7	23.1	20.1	17.3	16.5
Type 2 diabetes mellitus	6,303	19.2	3.9	9.7	16.7	23.4	26.9	22.4
Erectile dysfunction	5,945	18.1	4.3	10.7	20.3	25.6	19.8	11.0
Anxiety	4,898	14.9	15.3	15.1	17.0	15.6	13.0	12.2
Gastro-oesophageal reflux disease	4,872	14.8	9.0	10.9	14.4	15.7	18.0	17.0
Asthma	4,676	14.2	17.8	14.9	13.8	13.8	14.2	12.7

Table 4 shows the percentage of patients diagnosed with gout, who have none (0), or multiple of the above 10 most common comorbidities (individual conditions).

Table 4: Percentage of patients with multiple of the Top 10 individual comorbidities: (all people with gout)

Number of comorbidities	Percentage
0	13.1
1	20.5
2	22.9
3	19.3
4	12.8
5	7.0
6	3.2
7	1.0
8	0.3
9	0.0
10	0.0

Table 5: Grouped comorbidities: Overall number (%) in prevalent clinical population with gout, and percentage of each age group with each comorbidity (all people with gout)

Condition	N	%	Under 45	45-54	55-64	65-74	75-84	Over 85
Hypertension	18,057	55.0	12.0	28.9	48.8	63.5	73.5	78.1
Ulcer & upper GI acid conditions	10,041	30.6	13.8	19.2	25.9	33.0	40.7	42.3
Osteoarthritis	9,595	29.2	2.4	8.4	21.2	33.4	45.5	52.6
Dermatitis	9,573	29.2	23.0	22.4	26.0	30.5	34.3	36.5

Chronic renal disease	8,046	24.5	4.2	6.2	9.8	21.6	44.6	64.8
Depression	6,587	20.1	20.8	21.7	23.1	20.1	17.3	16.5
Diabetes mellitus	6,454	19.7	4.6	10.2	17.1	23.8	27.4	22.7
Chronic lung disease	6,081	18.5	18.1	15.5	16.1	19.5	21.4	19.8
Erectile dysfunction	5,945	18.1	4.3	10.7	20.3	25.6	19.8	11.0
Coronary heart disease	5,558	16.9	0.9	3.4	9.0	18.9	29.6	34.2

Table 6 shows the percentage of patients diagnosed with gout, who have none (0), or multiple of the above 10 most common comorbidities (grouped conditions).

Table 6: Percentage of patients with multiple of the Top 10 grouped comorbidities: (all people with gout)

Number of conditions	Percentage
0	12.0
1	18.8
2	20.6
3	18.9
4	14.0
5	8.8
6	4.4
7	1.9
8	0.6
9	0.1
10	0.0

1.5 CKD

30,895 patients with gout have a record of a CKD test, 94.1% of the prevalent cohort.

Table 7: Number (%) of patients with gout by CKD stage.

CKD category	Number of patients	% of total cohort	eGFR test date		
			Minimum	Median	Maximum
No CKD/Stage 1+2	22,994	70.0	08/1999	04/2015	11/2015
CKD Stage 3	6,962	21.2	08/2003	07/2015	11/2015
CKD Stage 4+5	939	2.9	08/2004	08/2015	11/2015
No record of eGFR test	1,933	5.9			

1.6 Prescriptions

1.6.1 Treatment with Allopurinol or Febuxostat

Note, ULT is the Class of ULT drugs, and includes other products in addition to Allopurinol or Febuxostat. In addition, we also present prescriptions of Colchicine and Oral Nonsteroidal anti-inflammatory drugs (NSAIDs) as these are used in the treatment of acute gout.

Table 8: Number of patients on each type of urate lowering therapy (all people with gout)

	Currently treated		Previously treated		Ever treated	
	Number of patients	% of total cohort	Number of patients	% of total cohort	Number of patients	% of total cohort
Allopurinol	10,201	31.1	5,513	16.8	15,714	47.9
Febuxostat	226	0.7	160	0.5	386	1.2
Any ULT	10,440	31.8	5,342	16.3	15,782	48.1

Table 9: Prescribing ULTs and drugs used in acute gout by CKD category, percentage of each CKD category currently, or ever prescribed each drug (all patients with gout)

Drug of interest	Treatment timing	Number of patients	% of total cohort	No CKD/ Stage 1+2	CKD Stage 3	CKD Stage 4+5	No record of a test
Allopurinol	Current	10,201	31.1	30.0	37.4	44.9	14.2
Allopurinol	Ever	15,714	47.9	46.6	54.6	65.7	30.6
Febuxostat	Current	226	0.7	0.5	1.4	*	*
Febuxostat	Ever	386	1.2	0.8	2.3	*	*
Any ULT	Current	10,440	31.8	30.5	38.9	46.5	14.3
Any ULT	Ever	15,782	48.1	46.7	55.0	66.6	30.6
Colchicine	Current	1,134	3.5	3.0	4.9	7.0	1.8
Colchicine	Ever	10,960	33.4	30.2	44.5	56.9	19.2
Oral NSAID	Current	3,725	11.3	13.0	7.7	1.8	9.8
Oral NSAID	Ever	29,456	89.7	91.4	87.7	76.4	83.8

* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.

Table 10: Percentage of each age group with a current prescription of ULT and drugs used in acute gout (all patients with gout)

Drug of Interest	Under 45	45-54	55-64	65-74	75-84	Over 85
Allopurinol	20.7	26.5	30.8	34.1	34.6	30.5
Febuxostat	0.5	0.8	0.7	0.6	0.8	0.6
Any ULT	21.2	27.4	31.6	34.8	35.4	31.1
Oral NSAID	12.2	13.8	14.5	12.5	7.9	4.3
Colchicine	3.9	3.2	3.0	3.7	3.7	3.4

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1.6.2 Urate testing in people on urate lowering therapy (all people with gout)

25,554 patients with gout have a record of a urate test in their primary care records.

Table 11: Test result by time since last test (all patients with gout)

Urate Category	In the last year		1-2 years		2-5 years		5+ years	
	N	% of value category	N	% of value category	N	% of value category	N	% of value category
<300 umol/l	1,054	26.7	651	16.5	1,056	26.7	1,189	30.1
300-359 umol/l	1,031	27.4	601	16.0	1,013	26.9	1,120	29.7
360-480 umol/l	2,510	22.3	1,768	15.7	3,426	30.4	3,574	31.7
>480 umol/l	1,523	23.2	1,045	15.9	2,015	30.7	1,978	30.1

Table 12: Time since last urate test by ULT prescription status (all patients with gout)

Any ULT Status	In the last year		1-2 years		2-5 years		5+ years		No record of test	
	N	% of ULT Status	N	% of ULT Status	N	% of ULT Status	N	% of ULT Status	N	% of ULT Status
Currently prescribed	3,258	31.2	1,615	15.5	2,439	23.4	2,066	19.8	1,062	10.2
Previously prescribed	867	16.2	785	14.7	1,450	27.1	1,526	28.6	714	13.4
No record of treatment	1,993	11.7	1,665	9.8	3,621	21.2	4,269	25.0	5,498	32.3

Table 13: Time since last test by test result for those currently treated with any urate lowering therapy (prescription issued in the previous 84 days, all patients with gout)

Urate Category	In the last year		1-2 years		2-5 years		5+ years	
	N	% of value category	N	% of value category	N	% of value category	N	% of value category
<300 umol/l	871	37.5	441	19.0	567	24.4	444	19.1
300-359 umol/l	798	38.9	360	17.6	501	24.4	391	19.1
360-480 umol/l	1,088	33.2	578	17.7	882	26.9	725	22.2
>480 umol/l	501	28.9	236	13.6	489	28.2	506	29.2

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1.6.3 Co-prescribing

These are selected prescriptions of interest, which are *currently prescribed* (i.e. prescription date within 84 days of the index date, 164 days for Warfarin).

Table 14: Currently prescribed drugs of interest overall, and within CKD category (all patients with gout)

Drug of interest	Number of patients	% of cohort	No CKD/ Stage 1+2	CKD Stage 3	CKD Stage 4+5	No record of a test
Any diuretic[a]	6,501	19.8	14.2	38.1	52.5	5.2
Thiazide diuretic	2,979	9.1	8.3	13.6	8.5	2.6
Loop diuretic	3,450	10.5	5.6	24.3	45.4	2.5
Other diuretic	1,017	3.1	1.8	7.5	8.0	0.9
Any fibrate[a]	348	1.1	1.0	1.5	*	*
Fenofibrate	129	0.4	0.4	0.5	*	*
Other fibrate	219	0.7	0.6	1.0	*	*
Statins	13,411	40.9	38.6	54.8	55.3	10.0
Verapamil	157	0.5	0.4	0.8	*	*
Diltiazem	649	2.0	1.7	3.1	3.0	0.4
Digoxin	887	2.7	1.8	5.9	6.0	0.7
Amiodarone	165	0.5	0.2	1.3	*	*
Ketoconazole	0	0.0	0.0	0.0	0.0	0.0
Macrolides	676	2.1	1.9	2.8	2.9	0.9
Aspirin (antiplatelet dose)	5,618	17.1	14.6	27.3	31.0	3.6
Beta Blockers	7,841	23.9	19.5	39.7	48.5	6.8
ACE Inhibitors	9,648	29.4	27.9	40.5	31.1	6.5
Angiotensin Receptor blockers (all)[a]	4,645	14.1	11.7	23.6	24.3	4.8
Losartan	2,312	7.0	6.0	11.7	9.3	2.0
Other ARB	2,338	7.1	5.7	11.9	15.1	2.8
Tacrolimus	38	0.1	*	0.4	1.0	*
Ciclosporin	27	0.1	0.0	0.2	*	*
Oral anti-coagulants	3,295	10.0	7.6	18.6	20.7	3.4
[a] Totals for drug classes may be greater than the sum of individual drugs if more than one prescribed in the last 84 days, 168 days for Warfarin						
* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.						

We can also explore the distribution of these current prescriptions by age at index.

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Table 15: Percentage of each age group with a current prescription of each drug (all patients with gout)

Drug of Interest	Under 45	45-54	55-64	65-74	75-84	Over 85
Any diuretic[a]	2.0	5.0	11.4	20.5	33.7	42.5
Thiazide diuretic	0.9	3.0	7.5	11.3	13.8	11.6
Loop diuretic	0.9	1.7	3.7	8.7	19.9	31.0
Other diuretic	0.6	0.8	1.6	3.2	5.2	6.9
Any fibrate[a]	0.2	0.8	1.1	1.5	1.2	0.7
Fenofibrate	*	0.5	0.5	0.5	0.3	*
Other fibrate	0.0	0.3	0.6	0.9	0.9	0.7
Statins	5.2	16.5	35.0	53.6	57.0	47.7
Verapamil	*	*	0.2	0.6	0.9	0.7
Diltiazem	*	0.6	1.5	2.3	3.5	*
Digoxin	*	*	0.7	2.3	5.2	8.3
Amiodarone	*	*	0.2	0.6	0.8	1.1
Ketoconazole	0.0	0.0	0.0	0.0	0.0	0.0
Macrolides	1.2	1.2	1.9	2.0	2.8	3.0
Aspirin (antiplatelet dose)	1.4	4.1	10.9	20.5	28.1	29.5
Beta Blockers	4.3	8.1	16.8	28.3	37.0	37.6
ACE Inhibitors	7.5	17.4	28.2	35.0	37.3	34.4
Angiotensin Receptor blockers (all)[a]	1.6	5.7	11.4	17.6	21.2	17.9
Losartan	0.8	2.7	6.0	8.4	10.6	9.2
Other ARB	0.8	3.0	5.4	9.2	10.6	8.8
Tacrolimus	0.2	0.1	0.2	0.1	*	*
Ciclosporin	*	0.1	0.1	0.1	*	*
Oral anti-coagulants	0.6	1.9	3.9	10.4	19.8	20.7
a Totals for drug classes may be greater than the sum of individual drugs if more than one prescribed in the last 84 days, 168 for Warfarin						
* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.						

1.7 Recently diagnosed: all patients diagnosed with gout in the year prior to the index date

2,126 patients with gout were diagnosed in the year 1 December 2014 to 30 November 2015, 6.5% of the total clinical population diagnosed with gout.

The age/sex breakdown of this recently diagnosed clinical population is:

Table 16: Sex and age breakdown (recently diagnosed gout)

Sex	Number of patients	%	Age at Diagnosis		Age at Index	
			Mean ± SD	Range	Mean ± SD	Range
Male	1,574	74	59.5 ± 15.1	21 - 97	59.6 ± 15.1	21 - 97
Female	552	26	69.2 ± 14.3	21 - 97	69.3 ± 14.3	21 - 98

Table 17: Age at diagnosis of gout by sex (recently diagnosed gout)

Age group	Male		Female		Total	
	N	% of age group	N	% of age group	N	% of cohort
<=44	289	90.0	32	10.0	321	15.1
45-54	329	86.1	53	13.9	382	18.0
55-64	313	75.2	103	24.8	416	19.6
65-74	360	71.7	142	28.3	502	23.6
75-84	226	60.6	147	39.4	373	17.5
>=85	57	43.2	75	56.8	132	6.2

Figure 4: Distribution of age at diagnosis by sex

(recently diagnosed Gout)

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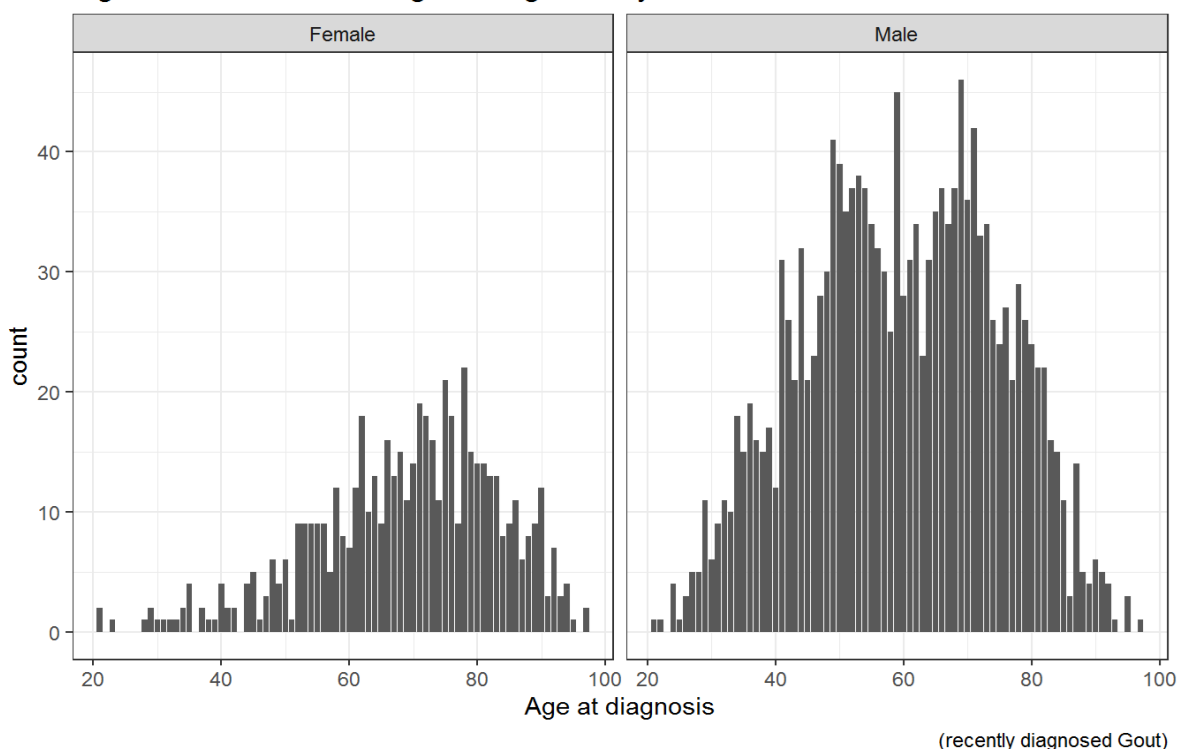
1.8 Comorbidities

These comorbidities are currently defined based on their Primary Care readcode defined conditions (+ biomedically defined CKD), as defined by the CALIBER project (https://github.com/spiros/chronological-map-phenotypes/tree/master/primary_care). Comorbidities are presented as individual conditions, and groups of conditions (e.g. Diabetes mellitus incorporates Type 1, Type 2 and uncertain diabetes)

Table 18: Individual comorbidities: Overall number (%) in recently diagnosed cohort with gout, and percentage of each age group with each comorbidity

Condition	N	%	Under 45	45-54	55-64	65-74	75-84	Over 85
Hypertension	998	46.9	13.4	25.4	44.0	61.3	67.9	85.0
Dermatitis	597	28.1	22.7	22.5	25.5	29.8	36.4	35.3
Osteoarthritis	512	24.1	*	*	18.3	31.2	46.8	54.1
Chronic Kidney Disease	501	23.6	4.7	5.8	11.1	23.6	53.2	75.2
Depression	412	19.4	16.8	24.6	20.0	20.8	14.7	16.5
Gastro-oesophageal Reflux Disease	316	14.9	6.2	13.5	15.1	17.5	18.4	18.8
Asthma	310	14.6	14.6	13.8	12.3	14.9	16.8	16.5
Anxiety	299	14.1	13.7	16.7	14.2	13.1	13.1	13.5
Erectile Dysfunction	296	13.9	5.0	10.3	15.4	20.4	17.4	6.8
Type 2 Diabetes Mellitus	268	12.6	1.6	3.7	13.5	16.3	22.7	19.5
* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.								

Table 19: Percentage of patients with multiple of the Top 10 individual comorbidities (recently diagnosed gout)

Number of comorbidities	Percentage
0	17.9
1	23.4
2	21.4
3	17.7
4	10.3
5	5.6
6	2.6
7	0.9
8	0.2

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Table 20: Grouped comorbidities: Overall number (%) in recently diagnosed cohort with gout, and percentage of each age group with each comorbidity (recently diagnosed gout)

Condition	N	%	Under 45	45-54	55-64	65-74	75-84	Over 85
Hypertension	998	46.9	13.4	25.4	44.0	61.3	67.9	85.0
Dermatitis	597	28.1	22.7	22.5	25.5	29.8	36.4	35.3
Ulcer and upper GI acid conditions	594	27.9	11.5	21.7	24.3	32.7	39.8	45.1
Chronic renal disease	515	24.2	5.3	6.9	11.8	24.4	53.5	75.2
Osteoarthritis	512	24.1	*	*	18.3	31.2	46.8	54.1
Depression	412	19.4	16.8	24.6	20.0	20.8	14.7	16.5
Chronic lung disease	388	18.3	15.0	14.6	14.9	19.8	23.5	26.3
Coronary heart disease	320	15.1	*	*	8.9	19.4	30.5	40.6
Anxiety	299	14.1	13.7	16.7	14.2	13.1	13.1	13.5
Erectile Dysfunction	296	13.9	5.0	10.3	15.4	20.4	17.4	6.8

* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.

Table 21: Percentage of patients with multiple of the Top 10 grouped comorbidities: (recently diagnosed gout)

Number of comorbidities	Percentage
0	16.3
1	21.2
2	20.6
3	18.2
4	11.6
5	6.9
6	2.8
7	2.0
8	0.3
9	0.1

1.9 CKD

1,989 Patients recently diagnosed with gout have a record of a CKD test, 93.6% of the recently diagnosed cohort.

Table 22: Number (%) of patients recently diagnosed with gout by CKD stage.

CKD category	Number of patients	% of total cohort	eGFR test date		
			Minimum	Median	Maximum
No CKD/Stage 1+2	1,488	70.0	08/2002	06/2015	11/2015
CKD Stage 3	446	21.0	12/2008	08/2015	11/2015
CKD Stage 4+5	55	2.6	05/2013	08/2015	11/2015
No record of eGFR test	137	6.4			

1.10 Prescriptions

1.10.1 Treatment with Allopurinol or Febuxostat

Note, ULT is the Class of ULT drugs, and includes other products in addition to Allopurinol or Febuxostat. In addition, we also present prescriptions of Colchicine and Oral Nonsteroidal anti-inflammatory drugs (NSAIDs) as these are used in the treatment of acute gout.

Table 23: Number of patients on each type of urate lowering therapy (recently diagnosed gout)

	Currently treated		Previously treated		Ever treated	
	Number of patients	% of total cohort	Number of patients	% of total cohort	Number of patients	% of total cohort
Allopurinol	433	20.4	125	5.9	558	26.2
Febuxostat	10	0.5	*	*	*	*
Any ULT	441	20.7	122	5.7	563	26.5
* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.						

Table 24: Prescribing ULTs and drugs used in acute gout by CKD category (recently diagnosed gout)

Drug of interest	Treatment timing	Number of patients	% of cohort	No CKD/ Stage 1+2	CKD Stage 3	CKD Stage 4+5	No record of a test
Allopurinol	Current	433	20.4	19.5	25.8	29.1	8.8
Allopurinol	Ever	558	26.4	25.0	33.0	38.2	13.1
Febuxostat	Current	10	0.5	*	*	*	*
Febuxostat	Ever	*	*	*	*	*	*
Any ULT	Current	441	20.7	19.6	27.1	29.1	8.8
Any ULT	Ever	563	26.5	25.1	33.9	38.2	13.1
Colchicine	Current	245	11.5	10.0	16.1	27.3	6.6

Colchicine	Ever	810	38.1	35.4	50.0	56.4	21.2
Oral NSAID	Current	381	17.9	20.1	11.0	5.5	21.9
Oral NSAID	Ever	1,812	85.2	87.8	79.6	69.1	82.5
<mark>* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.</mark>							

Table 25: Percentage of each age group with a current prescription of ULT or drugs used in acute gout (recently diagnosed gout)

Drug of Interest	Under 45	45-54	55-64	65-74	75-84	Over 85
Allopurinol	18.7	18.0	23.1	20.4	21.9	18.0
Febuxostat	<mark>*</mark>	<mark>*</mark>	<mark>*</mark>	<mark>*</mark>	<mark>*</mark>	<mark>*</mark>
Any ULT	19.0	18.3	23.3	21.0	22.5	18.0
Colchicine	7.2	8.5	10.3	15.5	12.6	16.5
Oral NSAID	17.1	19.0	23.3	18.8	13.1	9.8
<mark>* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.</mark>						

1.10.2 Urate testing in people on urate lowering therapy (recently diagnosed gout)

1,634 patients recently diagnosed with gout have a record of a urate test in their primary care records.

Table 26: Test result by time since last test (recently diagnosed gout)

	In the last year		1-2 years		2-5 years		5+ years	
Urate Category	N	% of value category	N	% of value category	N	% of value category	N	% of value category
<360umol/l	249	88.6	6	2.1	10	3.6	16	5.7
360-480 umol/l	680	84.4	37	4.6	47	5.8	42	5.2
>480 umol/l	475	86.8	33	6.0	22	4.0	17	3.1
Note: Value categories collapsed to avoid disclosive results								

Table 27: Time since last urate test by ULT prescription status (recently diagnosed gout)

	In the last year		1-2 years		2-5 years		5+ years		No record of test	
ULT Status	N	% of ULT Status	N	% of ULT Status	N	% of ULT Status	N	% of ULT Status	N	% of ULT Status
Currently	382	86.6	12	2.7	8	1.8	9	2.0	30	6.8

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prescribed										
Previously prescribed	93	76.2	9	7.4	*	*	*	*	15	12.3
No record of treatment	929	59.4	55	3.5	68	4.4	64	4.1	447	28.6
* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.										

Table 28: Time since last test by test result for those currently treated with urate lowering therapy (prescription issued in the previous 84 days, recently diagnosed gout)

	In the last year			1+ years	
Urate Category	**N**	**% of value category**		**N**	**% of value category**
<360umol/l	*	*		*	*
360-480 umol/l	160	89.4		19	10.6
>480 umol/l	109	94.0		7	6.0
Note: Value and time categories collapsed to avoid disclosive results					
* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.					

1.10.3 Co-prescribing

These are selected prescriptions of interest, which are *currently prescribed* (i.e. prescription date within 84 days of the index date, 168 for Warfarin).

Table 29: Currently prescribed drugs of interest by CKD category (recently diagnosed gout)

Drug of interest	Number of patients	% of cohort	No CKD/ Stage 1+2	CKD Stage 3	CKD Stage 4+5	No record of a test
Any diuretic[a]	472	22.2	14.7	47.8	67.3	2.9
Thiazide diuretic	242	11.4	8.9	21.5	23.6	0.7
Loop diuretic	241	11.3	5.8	27.6	54.5	*
Other diuretic	69	3.2	1.9	7.8	9.1	*
Any fibrate[a]	11	0.5	0.7	*	*	*
Fenofibrate	*	*	*	*	*	*
Other fibrate	*	*	*	*	*	*
Statins	703	33.1	29.0	54.0	43.6	4.4
Verapamil	10	0.5	0.5	*	*	0.0
Diltiazem	34	1.6	1.3	2.9	1.8	0.7
Digoxin	57	2.7	1.3	7.0	10.9	0.0
Amiodarone	11	0.5	*	1.6	*	0.0

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Ketoconazole	0	0.0	0.0	0.0	0.0	0.0
Macrolides	60	2.8	2.2	5.4	*	*
Aspirin (antiplatelet dose)	289	13.6	10.7	26.5	20.0	*
Beta Blockers	463	21.8	15.9	43.9	47.3	3.6
ACE Inhibitors	555	26.1	23.8	40.1	29.1	4.4
Angiotensin Receptor blockers (all)[a]	261	12.3	8.3	25.1	41.8	*
Losartan	105	4.9	3.4	11.4	*	*
Other ARB	156	7.3	4.9	13.7	34.5	2.2
Tacrolimus	*	*	*	*	*	*
Ciclosporin	*	*	*	*	*	*
Oral anti-coagulants	216	10.2	7.0	20.4	34.5	*

[a] Totals for drug classes may be greater than the sum of individual drugs if more than one prescribed in the last 84 days, 168 for Warfarin

* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.

We can also explore the distribution of these current prescriptions by age at index.

Table 30: Percentage of each age group with a current prescription of each drug (recently diagnosed gout)

Drug of Interest	Under 45	45-54	55-64	65-74	75-84	Over 85
Any diuretic[a]	3.7	6.1	15.6	28.4	39.8	60.2
Thiazide diuretic	2.5	3.7	10.8	17.5	16.6	18.8
Loop diuretic	1.6	2.4	4.6	11.5	24.9	42.9
Other diuretic	*	*	3.1	2.2	5.6	12.0
Any fibrate[a]	*	*	1.0	*	*	0.8
Fenofibrate	*	*	*	*	*	*
Other fibrate	*	*	*	*	*	*
Statins	3.7	13.2	29.8	49.4	57.5	39.8
Verapamil	*	*	*	1.2	*	*
Diltiazem	*	*	1.4	2.8	1.9	*
Digoxin	*	*	*	2.8	6.4	10.5
Amiodarone	*	*	*	*	*	*
Ketoconazole	0.0	0.0	0.0	0.0	0.0	0.0
Macrolides	1.6	1.9	3.1	1.8	4.8	6.0
Aspirin (antiplatelet dose)	*	4.0	9.4	19.2	25.7	30.8
Beta Blockers	4.7	7.9	16.1	29.0	39.0	44.4
ACE Inhibitors	8.1	16.1	26.7	34.7	35.8	36.1

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Angiotensin Receptor blockers (all)[a]	2.5	6.6	9.4	17.5	19.5	21.1
Losartan	*	*	4.1	6.7	8.6	7.5
Other ARB	1.6	4.2	5.3	10.7	11.0	13.5
Tacrolimus	*	*	*	*	*	*
Ciclosporin	*	*	*	*	*	*
Oral anti-coagulants	*	*	4.3	15.3	21.9	18.0

[a] Totals for drug classes may be greater than the sum of individual drugs if more than one prescribed in the last 84 days, 168 for Warfarin

* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.

2. What this document contains

<u>Example: three trials of treatment of gout flares</u>

This document contains information about three trials of treatments for acute flares of gout (chosen from the list from the Committee where they required more detailed information about the population included). The clinical population examined was the prevalent population with gout on 30/11/2015. The inclusion and exclusion criteria applied by each trial, and the way that these were operationalised in the CPRD data, are described in the appendix.

The aim was to provide the Committee with some examples of data. Any information of interest to the Committee, or trials they were interested in examining, could be specified and displayed in tables (e.g. particular comorbidities or co-prescribing).

There are three types of table in this document (see below). The following questions were posed to the committee to extract the specific information they required:

1. Table 1 is a summary across all trials. **Question** – what information would you like to see in the columns of such a summary table? This is constrained by the available space although if we show it in landscape then we can add some additional columns.
2. Table 2 is more detail for all trials, although if we look at *all* trials then it won't fit on one page (we can probably get four or maybe five trials per table/page). **Question** – what information would you like to see in the rows of such a summary table?
3. Tables 3-6 is more detail for each trial. **Question** – does this add anything/what might you want to see in such a table?

Question - is there a better/more informative way of doing this?

Trials 1 to 3: Trials of treatment for gout flares

Table 1: Overall summary for trials of treatments for gout flares (all patients with gout)

	N (%)	Median age at index (IQR)	% Men	% Women
All patients with gout	32,828 (100)	67 (56 to 77)	79.3	20.7
Exclusions from individual trials				
	No (%) NOT eligible	Median age at Index (IQR) of those NOT eligible	% of Men NOT eligible	% of Women NOT eligible
Janssens 2008 (Prednisolone v naproxen)	12,026 (36.6)	74 (65 to 81)	34.4	45.3
Rainer 2016 (Prednisolone vs indomethacin)	8,920 (27.2)	73 (63 to 81)	25.8	32.3
Roddy 2020 (Naproxen vs colchicine)	10,217 (31.1)	74 (64 to 81)	30.3	34.4

Table 2: Percentage of people with gout excluded from trials of treatment of gout flares (all patients with gout)

	All people with gout	% of all people	Janssens 2008 (Prednisolone vs naproxen) % of row NOT eligible	Rainer 2016 (Prednisolone vs indomethacin) % of row NOT eligible	Roddy 2020 (Naproxen vs colchicine) % of row NOT eligible
All people with gout	32,828	100	36.6	27.2	31.1
Men	26,044	79.3	34.4	25.8	30.3
Women	6,784	20.7	45.3	32.3	34.4
Age Group at Index					
Median (IQR)	67 years (56 to 77)		74 years (65 to 81)	73 years (63 to 81)	74 years (64 to 81)
Age Group: <45	2,443	7.4	11.6	14.0	13.9
Age Group: 45-64	11,669	35.5	22.4	18.6	19.3
Age Group: 65-74	8,652	26.4	39.2	27.1	31.9
Age Group: 75-84	7,016	21.4	55.5	39.3	45.9
Age Group: 85+	3,048	9.3	60.3	42.9	53.9
Top 10 most common conditions[1]					
Hypertension	18,057	55.0	44.4	31.8	38.0
Osteoarthritis	9,595	29.2	49.8	35.9	40.6
Dermatitis	9,573	29.2	42.5	31.2	35.5
Chronic Kidney Disease	7,901	24.1	58.7	40.7	49.8
Depression	6,587	20.1	41.7	34.2	37.1
Type 2 Diabetes	6,303	19.2	47.2	33.7	42.9
Erectile Dysfunction	5,945	18.1	44.8	32.7	37.9
Anxiety	4,898	14.9	41.3	34.9	36.8
Gastro-oesophageal reflux	4,872	14.8	66.4	58.6	40.0
Asthma	4,676	14.2	40.4	30.9	34.1

	All people with gout	% of all people	Janssens 2008 (Prednisolone vs naproxen) % of row NOT eligible	Rainer 2016 (Prednisolone vs indomethacin) % of row NOT eligible	Roddy 2020 (Naproxen vs colchicine) % of row NOT eligible
All people with gout	32,828	100	36.6	27.2	31.1
Other conditions[1] of interest					
Ulcer and upper GI	10,041	30.6	65.4	56.9	45.8
Coronary Heart Disease	5,558	16.9	73.9	41.7	70.9
CKD Stage 3	6,962	21.2	53.1	35.8	43.1
CKD Stage 4 or 5	939	2.9	100.0	77.2	100.0
Dementia	762	2.3	55.9	100.0	100.0
Prescriptions[2] of interest					
Allopurinol	10,201	31.1	42.3	31.1	37.5
Febuxostat	226	0.7	50.0	31.9	45.1
Thiazides	2,979	9.1	39.7	27.6	32.4
Oral Anticoagulants	3,295	10.0	100.0	86.6	100.0
Oral NSAIDs	3,736	11.4	27.5	18.3	19.9

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

Table 3: Characteristics of people with gout eligible and ineligible for "Janssen et al 2008 (prednisolone vs naproxen)

	All people with gout N = 32,828	% of all people	Eligible N= 20,802 (63.4%) % of Eligible	Ineligible N = 12,026 (36.6%) % of Ineligible
Men	26,044	79.3	82.2	74.4
Women	6,784	20.7	17.8	25.6
Age at Index				
Median (IQR)	67 years (56 to 77)		63 years (52 to 72)	74 years (65 to 81)
Mean (sd)	66.1 years (14.2)		62.6 years (14)	72.2 years (12.2)
Age Group: <45	2,443	7.4	10.4	2.4
Age Group: 45-64	11,669	35.5	43.5	21.8
Age Group: 65-74	8,652	26.4	25.3	28.2
Age Group: 75-84	7,016	21.4	15.0	32.4
Age Group: 85+	3,048	9.3	5.8	15.3
Top 10 most common conditions[1]				
Hypertension	18,057	55.0	24.3	21.6
Osteoarthritis	9,595	29.2	11.6	12.9
Dermatitis	9,573	29.2	13.3	11.0
Chronic Kidney Disease	7,901	24.1	7.9	12.5
Depression	6,587	20.1	9.3	7.4
Type 2 Diabetes	6,303	19.2	8.0	8.0
Erectile Dysfunction	5,945	18.1	7.9	7.2
Anxiety	4,898	14.9	6.9	5.5
Gastro-oesophageal reflux	4,872	14.8	4.0	8.7
Asthma	4,676	14.2	6.7	5.1
Other conditions[1] of interest				
Ulcer and upper GI	10,041	30.6	40.8	41.7
Coronary Heart Disease	5,558	16.9	17.0	26.1
CKD Stage 3	6,962	21.2	38.3	23.5
CKD Stage 4 or 5	939	2.9	0.0	6.0
Dementia	762	2.3	3.9	2.7
Prescriptions[2] of interest				
Allopurinol	10,201	31.1	56.0	43.5
Febuxostat	226	0.7	1.1	1.1
Thiazides	2,979	9.1	17.1	11.9
Oral Anticoagulants	3,295	10.0	0.0	33.2
Oral NSAIDs	3,736	11.4	25.8	10.3

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

Table 4: Characteristics of people with gout eligible and ineligible for Rainer 2016 (Prednisolone vs indomethacin)

	All people with gout N = 32,828	% of all people	Eligible N= 23,908 (72.8%) % of Eligible	Ineligible N = 8,920 (27.2%) % of Ineligible
Men	26,044	79.3	80.8	75.5
Women	6,784	20.7	19.2	24.5
Age at Index				
Median (IQR)	67 years (56 to 77)		65 years (54 to 75)	73 years (63 to 81)
Mean (sd)	66.1 years (14.2)		64.3 years (14.1)	71 years (13.2)
Age Group: <45	2,443	7.4	8.8	3.8
Age Group: 45-64	11,669	35.5	39.8	24.3
Age Group: 65-74	8,652	26.4	26.4	26.3
Age Group: 75-84	7,016	21.4	17.8	30.9
Age Group: 85+	3,048	9.3	7.3	14.7
Top 10 most common conditions[1]				
Hypertension	18,057	55.0	24.3	20.7
Osteoarthritis	9,595	29.2	12.1	12.4
Dermatitis	9,573	29.2	13.0	10.8
Chronic Kidney Disease	7,901	24.1	9.2	11.6
Depression	6,587	20.1	8.6	8.1
Type 2 Diabetes	6,303	19.2	8.2	7.7
Erectile Dysfunction	5,945	18.1	7.9	7.0
Anxiety	4,898	14.9	6.3	6.2
Gastro-oesophageal reflux	4,872	14.8	4.0	10.3
Asthma	4,676	14.2	6.4	5.2
Other conditions[1] of interest				
Ulcer and upper GI	10,041	30.6	35.3	47.6
Coronary Heart Disease	5,558	16.9	26.5	19.3
CKD Stage 3	6,962	21.2	36.5	20.8
CKD Stage 4 or 5	939	2.9	1.7	6.0
Dementia	762	2.3	0.0	6.3
Prescriptions[2] of interest				
Allopurinol	10,201	31.1	54.8	41.7
Febuxostat	226	0.7	1.2	0.9
Thiazides	2,979	9.1	16.8	10.8
Oral Anticoagulants	3,295	10.0	3.4	37.5
Oral NSAIDs	3,736	11.4	23.8	9.0

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

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Table 5: Characteristics of people with gout who would be eligible and ineligible for Roddy 2020 (Naproxen vs colchicine)

	All people with gout N = 32,828	% of all people	Eligible N= 22,611 (68.9%) % of Eligible	Ineligible N = 10,217 (31.1%) % of Ineligible
Men	26,044	79.3	80.3	77.1
Women	6,784	20.7	19.7	22.9
Age at Index				
Median (IQR)	67 years (56 to 77)		64 years (53 to 73)	74 years (64 to 81)
Mean (sd)	66.1 years (14.2)		63.5 years (13.9)	71.9 years (12.9)
Age Group: <45	2,443	7.4	9.3	3.3
Age Group: 45-64	11,669	35.5	41.6	22.1
Age Group: 65-74	8,652	26.4	26.1	27.0
Age Group: 75-84	7,016	21.4	16.8	31.5
Age Group: 85+	3,048	9.3	6.2	16.1
Top 10 most common conditions[1]				
Hypertension	18,057	55.0	23.5	22.2
Osteoarthritis	9,595	29.2	12.0	12.6
Dermatitis	9,573	29.2	13.0	11.0
Chronic Kidney Disease	7,901	24.1	8.3	12.8
Depression	6,587	20.1	8.7	7.9
Type 2 Diabetes	6,303	19.2	7.6	8.8
Erectile Dysfunction	5,945	18.1	7.8	7.3
Anxiety	4,898	14.9	6.5	5.8
Gastro-oesophageal reflux	4,872	14.8	6.1	6.3
Asthma	4,676	14.2	6.5	5.2
Other conditions[1] of interest				
Ulcer and upper GI	10,041	30.6	49.4	34.7
Coronary Heart Disease	5,558	16.9	14.7	29.8
CKD Stage 3	6,962	21.2	36.0	22.6
CKD Stage 4 or 5	939	2.9	0.0	7.1
Dementia	762	2.3	0.0	5.8
Prescriptions[2] of interest				
Allopurinol	10,201	31.1	55.4	42.8
Febuxostat	226	0.7	1.1	1.1
Thiazides	2,979	9.1	17.5	10.8
Oral Anticoagulants	3,295	10.0	0.0	36.9
Oral NSAIDs	3,736	11.4	26.0	8.3

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

Comparing across Trials

Another way of looking at this data is to examine who would be ineligible for all trials. Across all three trials, 54.5% of all people diagnosed with gout are eligible for all three, whilst 15.4% are ineligible for all three.

Question – is this of any interest? For example, we could add an 'ineligible for any trial' row to tables 1 and 2 (overall summary) column to tables 3 and 4 (summary of trials).

Multiple exclusions

Some people with gout are only excluded by one criteria, some are excluded by multiple. Some criteria dominate exclusion, and others only have minor effects.

Question – we're not quite sure how to show this, but is it of interest and we can design something? For example, % of people excluded by each criteria; % of people *only* excluded by each criteria

Janssens 2008 (Prednisolone vs naproxen)
- 24.0% of the cohort are excluded by only meeting one criteria, and the maximum number of conditions met by any one patient is 6 (0.4% of patients).
- Ulcer and upper GI acid conditions (either primary or hospitalisation record in the previous 5 years) excluded the largest proportion of patients (14.4%), followed by 10% excluded due to current use of anticoagulants.

Rainer 2016 (Prednisolone vs indomethacin)
- 23.3% of the cohort are excluded by only meeting one criteria, and the maximum number of conditions met by any one patient is 4 (0.2% of patients).
- Ulcer and upper GI acid conditions (either primary or hospitalisation record in the previous 5 years) excluded the largest proportion of patients (14.4%), followed by a current prescription for warfarin (8%).

Roddy 2020 (Naproxen vs colchicine)
- 21.1% of the cohort are excluded by only meeting one criteria, and the maximum number of conditions met by any one patient is 6 (0.2% of patients).
- Current prescriptions for anticoagulants excluded the largest proportion of patients (10%), followed by 6% due to a primary care record or hospitalisation for angina in the previous 5 years.

2.1 Appendix: criteria applied

Inclusion and Exclusion criteria for trials were extracted from: the trial registrations where available and from the main trial paper if no registration information.

We applied each trial's inclusion and exclusion criteria to the cohort of all patients diagnosed with gout, as far as was reasonably possible, given we are limited to using administrative data. The tables show what the stated inclusion and exclusion criteria were, and how we applied them.

Where comorbidities are specified, they are either ever diagnosed (primary care record on or before 30/11/2015), or within the previous 5 years (primary care diagnosis or hospital admission in the 5 years prior to 30/11/2015). Where non-specific exclusions, such as "Any significant co-morbidity", are used, we provide a reasonable attempt.

Trial 1: Janssens et al. (2008) "Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double-blind, randomised equivalence trial"

	Criteria	Interpretation
Inc	Participants were patients with a monoarticular gout arthritis confirmed by identification of monosodium urate crystals in the synovial fluid of the affected joint.	Diagnosis of gout in primary care, by 30/11/2015
Inc	All patients provided written informed consent.	Not applied
Excl	current use of anticoagulants	Section = "anticoagulants" Current = 84 days
Excl	Unstable condition (prevalent angina pectoris, myocardial infarction, severe renal failure, manifest heart failure , renal transplant, or cancer)	• Angina (Stable + unstable) last 5 years • Myocardial infarction last 5 years • Cancers (not non-melanoma skin) last 5 years • End stage renal disease, ever • CKD stage 4/5 ever • Heart failure last 5 years • Dilated cardiomyopathy last 5 years
Excl	chronic rheumatic diseases	Connective tissue disorders ever
Excl	Medical history of upper gastrointestinal diseases.	Ulcer and upper GI acid conditions in last five years
Excl	Patients were not excluded on the basis of age.	Not applied
Excl	We did not allow the use of NSAIDs or other analgesics (including colchicine) within 24 h before baseline assessments or for the duration of the trial.	Not applied

Trial 2: Rainer et al. (2016) "Oral Prednisolone in the Treatment of Acute Gout A Pragmatic, Multicenter, Double-Blind, Randomized Trial"

	Criteria	**Interpretation**
Incl.	Aged greater than 18 years, either sex	Age at index date
Incl.	Presenting to the Emergency Department [..] with an acute arthritis suggestive of gout	Diagnosis of gout in primary care, by 30/11/2015
	3. Present within 3 days of symptom onset	
	4. Have a clinical diagnosis of an acute monoarthritis suggestive of gout	
	5. For the purpose of this study the diagnosis of acute gout is made if BOTH of the following TWO criteria are met:	
	5.1. Criteria 1: The presence of rapid onset of severe pain, swelling, tenderness and erythema of an affected joint, which is maximal by 6 to 12 hours	
	5.2. Criteria 2: The presence of one or more of the following:	
	5.2.1. Metatarsal-phalangeal (MTP) joint involvement (podagra); or	
	5.2.2. Knee or ankle joint involvement; or wrist or elbow joint involvement WITH either:	
	5.2.2.1. Gouty tophi present, or	
	5.2.2.2. Previous joint aspiration confirming the diagnosis of gout, or	
	5.2.2.3. The presence of hyperuricaemia,	
	5.2.2.4. A clinical history of one or more clinical gouty arthritis attack	
	If none of B1 to B4 is present then we will seek to confirm the diagnosis by visual and microscopic examination of joint aspirate containing crystals.	
Excl.	Suspicion of sepsis or other joint disease (e.g. rheumatoid arthritis)	Not applied

Excl.	Follow up is not possible because of lack of transport or lack of telephone contact	Not applied
Excl.	Any significant co-morbidity which would interfere with assessment	• Schizophrenia ever • Intellectual disability ever • Down syndrome ever • Dementia ever • Alcohol misuse in the last five years • Substance misuse in the last five years
Excl.	Dementia	Dementia, ever
Excl.	Confusion	Not applied
Excl.	Active gastrointestinal symptoms	Ulcer and upper GI acid conditions Recorded in last five years
Excl.	Renal insufficiency with serum creatinine greater than 200 umol/L	Serum creatinine < 200 umol/L Recorded on or before 30/11/2015
Excl.	Bleeding disorder	• Primary or idiopathic thrombocytopenia • Secondary or other thrombocytopenia Recorded on or before 30/11/2015
Excl.	Warfarin	Name = Warfarin Current use = 168 days
Excl.	Allergy to a study drug	Not applied
Excl.	Joint aspirate which excluded the diagnosis of gout	Not applied

Trial 3: Roddy et al. (2020) "Open-label randomised pragmatic trial (CONTACT) comparing naproxen and low-dose colchicine for the treatment of gout flares in primary care"

	Criteria	Interpretation
Incl.	Adults aged 18 years and over	Age at index
Incl.	Consultation with GP, primary care out-of-hours service or walk-in-centre	Diagnosis of gout in primary care, by 30/11/2015
Incl.	Current attack of acute gout (first attack or recurrent).	Diagnosis of gout in primary care, by 30/11/2015
Incl.	Patient has capacity and willingness to give consent and complete the trial paperwork	Not applied
Excl.	Known unstable medical conditions (such as ischaemic heart disease, impaired liver function)	- Angina (any) last five years - Myocardial infarction last five years - Ischaemic cardiomyopathy last five years - TIA last five years - Hepatic failure ever - Chronic liver disease (excl fatty liver) ever - ALT, AST, GGT, or Bilirubin > 2 ULN last three years
Excl.	Known stage 4/5 kidney disease (eGFR/creatinine clearance <30ml/min)	CKD Stage 4/5 ever
Excl.	Recent surgery or gastrointestinal bleed	Not applied
Excl.	History of gastric ulcer	Peptic Ulcer ever
Excl.	Current anticoagulant use	Section = "anticoagulants" Current use = 84 days (168 for Warfarin)
Excl.	Allergy to aspirin/NSAID	Not applied
Excl.	Previous inability to tolerate naproxen or low-dose colchicine	Not applied
Excl.	Other contraindication to either study drug in accordance with the Summary of Product Characteristics (SPC)	Prescribing of Verapamil and Dilitazem Current use = 84 days
Excl.	Prescription of naproxen or colchicine in the previous 24 hours	Not applied

Excl.	Pregnant or lactating females	Not applied
Excl.	Potentially vulnerable	• Schizophrenia ever • Intellectual disability ever • Down syndrome ever • Dementia ever • Alcohol misuse in the last five years • Substance misuse in the last five years
Excl.	Previous participation in the CONTACT trial during a previous acute attack of gout.	Not applied
Excl.	Involvement in another clinical trial of an investigational medicinal product in the last 90 days or any other research within the last 30 days	Not applied

3. What this document contains

Example: three trials of urate lowering therapy

The document contains information about three trials of treatments for urate lowering therapy (chosen from the list from the Committee where they required more detailed information about the population included). The inclusion and exclusion criteria applied by each trial and the way that these were operationalised in the CPRD data are described in the appendix. Two clinical populations were examined:

1. The prevalent population of people with gout on 30/11/2015 (irrespective of duration).
2. The 'recently diagnosed' population of people with gout on 30/11/2015 (first record of gout 1/12/2014 to 30/11/2015)

The Committee were queried as to which of the above populations were the most appropriate for this question, or data could be requested for both populations (depending on what they were interested in).

The aim was to provide the Commitee with some examples of data. Any information of interest to the Committee, or trials they were interested in examining, could be specified and dispalayed in tables (e.g particular comorbidities or co-prescribing)

There are three types of table in this document (see below). The following questions were posed to the committee to extract the specific information they required:

4. Tables 1 and 2 are a summary across all trials for the two populations. *Question* – what information would you like to see in the columns of such a summary table? This is constrained by the available space although if we show it in landscape then we can add some additional columns.
5. Tables 3 and 4 have more detail for all trials for the two populations, although if we look at *all* trials then neither will fit on one page (we can probably get four or maybe five trials per table/page). *Question* – what information would you like to see in the rows of such a summary table?
6. Tables 5-10 show more detail for each trial for each population. *Question* – does this add anything/what might you want to see in such a table?

Question - is there a better/more informative way of doing this?

Trials 4 to 6: Use of Urate Lowering Therapy

*Table 1: Overall summary for trials of urate lowering therapy (**all patients with gout**)*

	No (%)	Median age at index (IQR)	% Men	% Women
All patients with gout	32,828 (100)	67 (56 to 77)	79.3	20.7
Exclusions from individual trials				
	No (%) NOT eligible	Median age at Index (IQR) of those NOT eligible	% of Men NOT eligible	% of Women NOT eligible
Becker 2005 (Febuxostat vs Allopurinol, FACT)	12,452 (37.9)	69 (58 to 78)	39.2	33.2
Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS)	21,170 (64.5)	71 (61 to 80)	62.3	72.9
Yu 2016 (Febuxostat vs Allopurinol)	16,887 (51.4)	73 (64 to 81)	47.6	66.4

*Table 2: Overall summary for trials of urate lowering therapy (**patients recently diagnosed with gout**)*

	No (%)	Median age at index (IQR)	% Men	% Women
Recently diagnosed with gout	2,126 (100)	63 (51 to 74)	74.0	26.0
Exclusions from individual trials				
	No (%) NOT eligible	Median age at Index (IQR) of those NOT eligible	% of Men NOT eligible	% of Women NOT eligible
Becker 2005 (Febuxostat vs Allopurinol, FACT)	806 (37.9)	65 (53 to 75)	38.8	35.5
Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS)	1,407 (66.2)	68 (55 to 77)	63.0	75.4
Yu 2016 (Febuxostat vs Allopurinol)	1,044 (49.1)	71 (61 to 79)	43.6	64.7

*Table 3: Percentage of people with gout excluded from trials of urate lowering therapy (**all patients with gout**)*

	All people with gout	% of all people	Becker 2005 (Febuxostat vs Allopurinol, FACT) % of row NOT eligible	Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS) % of row NOT eligible	Yu 2016 (Febuxostat vs Allopurinol) % of row NOT eligible
All people with gout	32,828	100	37.9	64.5	51.4
Men	26,044	79.3	39.2	62.3	47.6
Women	6,784	20.7	33.2	72.9	66.4
Age at Index					
Median (IQR)	67 years (56 to 77)		69 years (58 to 78)	71 years (61 to 80)	73 years (64 to 81)
Age Group: <45	2,443	7.4	25.5	34.8	21.7
Age Group: 45-64	11,669	35.5	36.1	51.9	33.9
Age Group: 65-74	8,652	26.4	40.7	68.8	53.6
Age Group: 75-84	7,016	21.4	40.5	80.5	73.9
Age Group: 85+	3,048	9.3	41.1	87.3	84.6
Top 10 most common conditions[1]					
Hypertension	18,057	55.0	46.2	76.5	65.0
Osteoarthritis	9,595	29.2	40.8	76.3	65.4
Dermatitis	9,573	29.2	40.1	69.3	57.3
Chronic Kidney Disease	7,901	24.1	51.5	100.0	100.0
Depression	6,587	20.1	41.8	68.3	56.4
Type 2 Diabetes	6,303	19.2	46.3	76.0	67.0
Erectile Dysfunction	5,945	18.1	44.7	72.3	58.1
Anxiety	4,898	14.9	41.6	68.1	56.1
Gastro-oesophageal reflux	4,872	14.8	40.8	71.7	60.9
Asthma	4,676	14.2	39.2	66.5	53.6

	All people with gout	% of all people	Becker 2005 (Febuxostat vs Allopurinol, FACT) % of row NOT eligible	Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS) % of row NOT eligible	Yu 2016 (Febuxostat vs Allopurinol) % of row NOT eligible
All people with gout	32,828	100	37.9	64.5	51.4
Other conditions[1] of interest					
Ulcer and upper GI	10,041	30.6	41.9	73.9	63.1
Coronary Heart Disease	5,558	16.9	44.0	92.9	90.3
CKD Stage 3	6,962	21.2	45.4	100.0	100.0
CKD Stage 4 or 5	939	2.9	96.6	100.0	100.0
Dementia	762	2.3	36.4	100.0	100.0
Prescriptions[2] of interest					
Allopurinol	10,201	31.1	44.4	72.2	58.5
Febuxostat	226	0.7	52.2	78.3	69.5
Thiazides	2,979	9.1	100.0	100.0	100.0
Oral Anticoagulants	3,295	10.0	45.4	82.3	77.9
Oral NSAIDs	3,736	11.4	37.0	100.0	44.2

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

*Table 4: Percentage of people with gout excluded from trials of urate lowering therapy (**patients recently diagnosed with gout**)*

	Recently diagnosed N	% of recently diagnosed	Becker 2005 (Febuxostat vs Allopurinol, FACT) % of row NOT eligible	Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS) % of row NOT eligible	Yu 2016 (Febuxostat vs Allopurinol) % of row NOT eligible
Recently diagnosed gout	2,126	100	37.9	66.2	49.1
Men	1,574	74	38.8	63.0	43.6
Women	552	26	35.5	75.4	64.7
Age at Index					
Median (IQR)	63 years (51 to 74)		65 years (53 to 75)	68 years (55 to 77)	71 years (61 to 79)
Age Group: <45	321	15.1	24.3	37.7	17.4
Age Group: 45-64	794	37.3	39.5	59.9	35.6
Age Group: 65-74	504	23.7	41.7	74.4	56.9
Age Group: 75-84	374	17.6	38.0	83.2	79.9
Age Group: 85+	133	6.3	46.6	93.2	89.5
Top 10 most common conditions[1]					
Hypertension	998	46.9	48.4	79.8	67.5
Dermatitis	597	28.1	38.4	68.3	54.3
Osteoarthritis	512	24.1	41.8	81.6	69.3
Chronic Kidney Disease	501	23.6	54.7	100.0	100.0
Depression	412	19.4	41.5	70.4	55.1
Gastro-oesophageal reflux	316	14.9	41.8	75.3	64.2
Asthma	310	14.6	36.5	71.3	50.6
Anxiety	299	14.1	37.5	64.9	50.8
Erectile Dysfunction	296	13.9	46.3	74.0	59.5
Type 2 Diabetes	268	12.6	50.7	81.0	72.8

	Recently diagnosed N	% of recently diagnosed	Becker 2005 (Febuxostat vs Allopurinol, FACT) % of row NOT eligible	Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS) % of row NOT eligible	Yu 2016 (Febuxostat vs Allopurinol) % of row NOT eligible
Recently diagnosed gout	2,126	100	37.9	66.2	49.1
Other conditions[1] of interest					
Ulcer and upper GI	594	27.9	40.6	75.1	63.5
Coronary Heart Disease	320	15.1	41.6	94.4	92.8
CKD Stage 3	446	21.0	49.3	100.0	100.0
CKD Stage 4 or 5	55	2.6	98.2	100.0	100.0
Dementia	31	1.5	29.0	100.0	100.0
Prescriptions[2] of interest					
Allopurinol	433	20.4	45.0	75.8	56.8
Febuxostat	10	0.5	50.0	100.0	80.0
Thiazides	242	11.4	100.0	100.0	100.0
Oral Anticoagulants	216	10.2	46.3	84.7	81.0
Oral NSAIDs	382	18.0	34.0	100.0	39.3

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

*Table 5: Characteristics of **all people with gout** who would be eligible and ineligible for Becker 2005 (Febuxostat vs Allopurinol, FACT)*

	All people with gout N = 32,828	% of all people	Eligible N= 20,376 (62.1%) % of Eligible	Ineligible N = 12,452 (37.9%) % of Ineligible
Men	26,044	79.3	77.8	81.9
Women	6,784	20.7	22.2	18.1
Age at Index				
Median (IQR)	67 years (56 to 77)		66 years (55 to 76)	69 years (58 to 78)
Mean (sd)	66.1 years (14.2)		65.2 years (14.5)	67.6 years (13.4)
Age Group: <45	2,443	7.4	8.9	5.0
Age Group: 45-64	11,669	35.5	36.6	33.8
Age Group: 65-74	8,652	26.4	25.2	28.3
Age Group: 75-84	7,016	21.4	20.5	22.8
Age Group: 85+	3,048	9.3	8.8	10.1
Top 10 most common conditions[1]				
Hypertension	18,057	55.0	22.0	24.3
Osteoarthritis	9,595	29.2	12.9	11.4
Dermatitis	9,573	29.2	13.0	11.2
Chronic Kidney Disease	7,901	24.1	8.7	11.8
Depression	6,587	20.1	8.7	8.0
Type 2 Diabetes	6,303	19.2	7.7	8.5
Erectile Dysfunction	5,945	18.1	7.5	7.7
Anxiety	4,898	14.9	6.5	5.9
Gastro-oesophageal reflux	4,872	14.8	6.6	5.8
Asthma	4,676	14.2	6.5	5.3
Other conditions[1] of interest				
Ulcer and upper GI	10,041	30.6	44.0	38.2
Coronary Heart Disease	5,558	16.9	23.4	22.3
CKD Stage 3	6,962	21.2	28.6	28.8
CKD Stage 4 or 5	939	2.9	0.2	8.2
Dementia	762	2.3	3.7	2.5
Prescriptions[2] of interest				
Allopurinol	10,201	31.1	57.1	43.1
Febuxostat	226	0.7	1.1	1.1
Thiazides	2,979	9.1	0.0	28.4
Oral Anticoagulants	3,295	10.0	18.1	14.2
Oral NSAIDs	3,736	11.4	23.7	13.2

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

*Table 6: Characteristics of **people recently diagnosed with gout** who would be eligible and ineligible for Becker 2005 (Febuxostat vs Allopurinol, FACT)*

	Recently diagnosed N = 2,126	%	Eligible N= 1,320 (62.1%) % of Eligible	Ineligible N= 806 (37.9%) % of Ineligible
Men	1,574	74	73	75.7
Women	552	26	27	24.3
Age at Index				
Median (IQR)	67 years (56 to 77)		66 years (55 to 76)	69 years (58 to 78)
Mean (sd)	66.1 years (14.2)		65.2 years (14.5)	67.6 years (13.4)
Age Group: <45	321	15.1	18.4	9.7
Age Group: 45-64	794	37.3	36.4	39.0
Age Group: 65-74	504	23.7	22.3	26.1
Age Group: 75-84	374	17.6	17.6	17.6
Age Group: 85+	133	6.3	5.4	7.7
Top 10 most common conditions[1]				
Hypertension	998	46.9	20.5	24.1
Dermatitis	597	28.1	14.7	11.4
Osteoarthritis	512	24.1	11.9	10.7
Chronic Kidney Disease	501	23.6	9.1	13.7
Depression	412	19.4	9.6	8.5
Gastro-oesophageal reflux	316	14.9	7.3	6.6
Asthma	310	14.6	7.9	5.6
Anxiety	299	14.1	7.5	5.6
Erectile Dysfunction	296	13.9	6.3	6.8
Type 2 Diabetes	268	12.6	5.3	6.8
Other conditions[1] of interest				
Ulcer and upper GI	594	27.9	44.7	36.7
Coronary Heart Disease	320	15.1	23.7	20.2
CKD Stage 3	446	21.0	28.6	33.5
CKD Stage 4 or 5	55	2.6	*	8.2
Dementia	31	1.5	2.8	1.4
Prescriptions[2] of interest				
Allopurinol	433	20.4	39.0	29.0
Febuxostat	10	0.5	0.8	0.7
Thiazides	242	11.4	0.0	36.0
Oral Anticoagulants	216	10.2	19.0	14.9
Oral NSAIDs	382	18.0	41.2	19.3

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)
* Percentage based on small cell counts of <5 patients, and where necessary, the next lowest cell count, have been supressed for disclosure control.

*Table 7: Characteristics of **all people with gout** who would be eligible and ineligible for Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS)*

	All people with gout N = 32,828	% of all people	Eligible N= 11,658 (35.5%) % of Eligible	Ineligible N= 21170 (64.5%) % of Ineligible
Men	26,044	79.3	84.3	76.6
Women	6,784	20.7	15.7	23.4
Age at Index				
Median (IQR)	67 years (56 to 77)		60 years (50 to 69)	71 years (61 to 80)
Mean (sd)	66.1 years (14.2)		59.8 years (13.6)	69.6 years (13.2)
Age Group: <45	2,443	7.4	13.7	4.0
Age Group: 45-64	11,669	35.5	48.2	28.6
Age Group: 65-74	8,652	26.4	23.1	28.1
Age Group: 75-84	7,016	21.4	11.7	26.7
Age Group: 85+	3,048	9.3	3.3	12.6
Top 10 most common conditions[1]				
Hypertension	18,057	55.0	22.1	23.3
Osteoarthritis	9,595	29.2	11.8	12.4
Dermatitis	9,573	29.2	15.3	11.2
Chronic Kidney Disease	7,901	24.1	0.0	13.3
Depression	6,587	20.1	10.9	7.6
Type 2 Diabetes	6,303	19.2	7.9	8.1
Erectile Dysfunction	5,945	18.1	8.6	7.3
Anxiety	4,898	14.9	8.1	5.6
Gastro-oesophageal reflux	4,872	14.8	7.2	5.9
Asthma	4,676	14.2	8.1	5.3
Other conditions[1] of interest				
Ulcer and upper GI	10,041	30.6	86.9	34.9
Coronary Heart Disease	5,558	16.9	13.1	24.3
CKD Stage 3	6,962	21.2	0.0	32.8
CKD Stage 4 or 5	939	2.9	0.0	4.4
Dementia	762	2.3	0.0	3.6
Prescriptions[2] of interest				
Allopurinol	10,201	31.1	81.8	43.4
Febuxostat	226	0.7	1.4	1.0
Thiazides	2,979	9.1	0.0	17.6
Oral Anticoagulants	3,295	10.0	16.8	16.0
Oral NSAIDs	3,736	11.4	0.0	22.0

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

Table 8: Characteristics of **people recently diagnosed with gout** who would be eligible and ineligible for Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS)

	Recently diagnosed N = 2126	%	Eligible N= 719 (33.8%) % of Eligible	Ineligible N= 1407 (66.2%) % of Ineligible
Men	1,574	74	81.1	70.4
Women	552	26	18.9	29.6
Age at Index				
Median (IQR)	67 years (56 to 77)		60 years (50 to 69)	71 years (61 to 80)
Mean (sd)	66.1 years (14.2)		59.8 years (13.6)	69.6 years (13.2)
Age Group: <45	321	15.1	27.8	8.6
Age Group: 45-64	794	37.3	44.2	33.8
Age Group: 65-74	504	23.7	17.9	26.7
Age Group: 75-84	374	17.6	8.8	22.1
Age Group: 85+	133	6.3	1.3	8.8
Top 10 most common conditions[1]				
Hypertension	998	46.9	20.1	22.7
Dermatitis	597	28.1	18.8	11.7
Osteoarthritis	512	24.1	9.3	11.9
Chronic Kidney Disease	501	23.6	0.0	14.3
Depression	412	19.4	12.1	8.3
Gastro-oesophageal reflux	316	14.9	7.7	6.8
Asthma	310	14.6	8.8	6.3
Anxiety	299	14.1	10.4	5.5
Erectile Dysfunction	296	13.9	7.6	6.3
Type 2 Diabetes	268	12.6	5.1	6.2
Other conditions[1] of interest				
Ulcer and upper GI	594	27.9	89.2	34.8
Coronary Heart Disease	320	15.1	10.8	23.6
CKD Stage 3	446	21.0	0.0	34.8
CKD Stage 4 or 5	55	2.6	0.0	4.3
Dementia	31	1.5	0.0	2.4
Prescriptions[2] of interest				
Allopurinol	433	20.4	76.1	28.6
Febuxostat	10	0.5	0.0	0.9
Thiazides	242	11.4	0.0	21.1
Oral Anticoagulants	216	10.2	23.9	16.0
Oral NSAIDs	382	18.0	0.0	33.4

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

*Table 9: Characteristics of **all people with gout** who would be eligible and ineligible for Yu 2016 (Febuxostat vs Allopurinol)*

	All people with gout N = 32,828	% of all people	Eligible N= 15,941 (48.6%) % of Eligible	Ineligible N= 16887 (51.4%) % of Ineligible
Men	26,044	79.3	85.7	73.3
Women	6,784	20.7	14.3	26.7
Age at Index				
Median (IQR)	67 years (56 to 77)		61 years (51 to 69)	73 years (64 to 81)
Mean (sd)	66.1 years (14.2)		60.3 years (13.1)	71.5 years (12.9)
Age Group: <45	2,443	7.4	12.0	3.1
Age Group: 45-64	11,669	35.5	48.4	23.4
Age Group: 65-74	8,652	26.4	25.2	27.5
Age Group: 75-84	7,016	21.4	11.5	30.7
Age Group: 85+	3,048	9.3	2.9	15.3
Top 10 most common conditions[1]				
Hypertension	18,057	55.0	23.1	23.0
Osteoarthritis	9,595	29.2	12.1	12.3
Dermatitis	9,573	29.2	14.9	10.8
Chronic Kidney Disease	7,901	24.1	0.0	15.5
Depression	6,587	20.1	10.5	7.3
Type 2 Diabetes	6,303	19.2	7.6	8.3
Erectile Dysfunction	5,945	18.1	9.1	6.8
Anxiety	4,898	14.9	7.9	5.4
Gastro-oesophageal reflux	4,872	14.8	7.0	5.8
Asthma	4,676	14.2	7.9	4.9
Other conditions[1] of interest				
Ulcer and upper GI	10,041	30.6	87.2	31.7
Coronary Heart Disease	5,558	16.9	12.8	25.1
CKD Stage 3	6,962	21.2	0.0	34.8
CKD Stage 4 or 5	939	2.9	0.0	4.7
Dementia	762	2.3	0.0	3.8
Prescriptions[2] of interest				
Allopurinol	10,201	31.1	59.5	44.8
Febuxostat	226	0.7	1.0	1.2
Thiazides	2,979	9.1	0.0	22.4
Oral Anticoagulants	3,295	10.0	10.2	19.3
Oral NSAIDs	3,736	11.4	29.3	12.4

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

*Table 10: Characteristics of **people recently diagnosed with gout** who would be eligible and ineligible for Yu 2016 (Febuxostat vs Allopurinol)*

	Recently diagnosed N = 2,126	%	Eligible N= 1082 (50.9%) % of Eligible	Ineligible N= 1044 (49.1%) % of Ineligible
Men	1,574	74	82	65.8
Women	552	26	18	34.2
Age at Index				
Median (IQR)	67 years (56 to 77)		61 years (51 to 69)	73 years (64 to 81)
Mean (sd)	66.1 years (14.2)		60.3 years (13.1)	71.5 years (12.9)
Age Group: <45	321	15.1	24.5	5.4
Age Group: 45-64	794	37.3	47.2	27.1
Age Group: 65-74	504	23.7	20.1	27.5
Age Group: 75-84	374	17.6	6.9	28.6
Age Group: 85+	133	6.3	1.3	11.4
Top 10 most common conditions[1]				
Hypertension	998	46.9	21.0	22.7
Dermatitis	597	28.1	17.7	10.9
Osteoarthritis	512	24.1	10.2	12.0
Chronic Kidney Disease	501	23.6	0.0	16.9
Depression	412	19.4	12.0	7.7
Gastro-oesophageal reflux	316	14.9	7.3	6.8
Asthma	310	14.6	9.9	5.3
Anxiety	299	14.1	9.5	5.1
Erectile Dysfunction	296	13.9	7.8	5.9
Type 2 Diabetes	268	12.6	4.7	6.6
Other conditions[1] of interest				
Ulcer and upper GI	594	27.9	90.4	31.3
Coronary Heart Disease	320	15.1	9.6	24.6
CKD Stage 3	446	21.0	0.0	37.0
CKD Stage 4 or 5	55	2.6	0.0	4.6
Dementia	31	1.5	0.0	2.6
Prescriptions[2] of interest				
Allopurinol	433	20.4	40.5	30.0
Febuxostat	10	0.5	0.4	1.0
Thiazides	242	11.4	0.0	29.5
Oral Anticoagulants	216	10.2	8.9	21.3
Oral NSAIDs	382	18.0	50.2	18.3

[1] Diagnosed with condition ever (not just in previous 5 years)
[2] Current prescribing, 84 days prior to index date (168 days for Warfarin)

Comparing across trials

Another way of looking at this data is to examine who would be ineligible for all trials. Across the three trials here, 32.6% of people with gout are eligible for all three trials, whilst 27.2% are ineligible for all three trials.

Question – is this of any interest? For example, we could add an 'ineligible for any trial' row to tables 1 and 2 (overall summary) column to tables 3 and 4 (summary of trials).

Multiple exclusions

Some people with gout are only excluded by one criteria, some are excluded by multiple. Some criteria dominate exclusion, and others only have minor effects.

Question – we're not quite sure how to show this, but is it of interest and we can design something? For example, % of people excluded by each criteria; % of people *only* excluded by each criteria

Becker 2005 (Febuxostat vs Allopurinol, FACT)
- 28.9% of the cohort are excluded by meeting only one criteria, and the maximum number of exclusion criteria met by any one patient is 7 (0.003% of patients).
- The criteria which excludes the largest proportion of the cohort is drinking more than 14 units of alcohol per week (15%), followed by a current prescription for thiazide diuretics (9%).

Becker 2010 (Febuxostat vs Allopurinol, CONFIRMS)
- 32.7% of the cohort are excluded by meeting only one criteria, and the maximum number of conditions met by any one patient is 10 (0.003% of patients).
- The criteria which excludes the largest proportion of the cohort is chronic renal disease (ever, 24.5%), followed by 15% excluded for consuming more than 14 units of alcohol per week.

Yu 2016 (Febuxostat vs Allopurinol)
- 27.0% of the cohort are excluded by meeting only one criteria, and the maximum number of conditions met by any one patient is 10 (0.003% of patients).
- The criteria which excludes the largest proportion of the cohort is chronic renal risease (ever, 24.5%), followed by 12.5% excluded by coronary heart disease in the previous 5 years.

3.1 Appendix: criteria applied

Inclusion and Exclusion criteria for trials were extracted from: the trial registrations where available and from the main trial paper if no registration information.

We applied each trial's inclusion and exclusion criteria to the cohort of all patients diagnosed with gout and separately to those 'recently diagnosed with gout', as far as was reasonably possible, given we are limited to using administrative data. The tables show what the stated inclusion and exclusion criteria were, and how we applied them.

Where comorbidities are specified, they are either ever diagnosed (primary care record on or before 30/11/2015), or within the previous 5 years (primary care diagnosis or hospital admission in the 5 years prior to 30/11/2015). Where non-specific exclusions, such as "Any significant co-morbidity", are used, we provide a reasonable attempt.

Trial 4: Becker et al. (2005) "Febuxostat Compared with Allopurinol in Patients with Hyperuricemia and Gout (FACT)"

	Criteria	Interpretation
Incl.	The subjects met the preliminary criteria of the American College of Rheumatology for acute arthritis of gout	Diagnosis of gout in primary care, by 30/11/2015
Incl.	serum urate concentrations of at least 8.0 mg per deciliter (480 µmol/l)	Not applied
Excl.	serum creatinine concentration of more than 1.5 mg per deciliter (133 µmol/l)	Serum creatinine
Excl.	pregnancy or lactation	Not applied
Excl.	use of urate-lowering agents, azathioprine, 6-mercaptopurine, thiazide diuretics, or medications containing aspirin (more than 325 mg daily) or other salicylates	• Name = Azathioprine • Name = mercaptopurine • Class = Thiazide diuretics • Aspirin - Angelgesics class • Aminosalicylates - oral Current prescribing = 84 days
Excl.	body-mass index (the weight in kilograms divided by the square of the height in meters) of more than 50	BMI estimated using: Height (most recent) Weight (most recent in last 3 years)
Excl.	a history of xanthinuria, active liver disease, or hepatic dysfunction;	Chronic liver disease (excl fatty liver) ever ALT, AST, GGT, or Bilirubin > 1.5 ULN last three years Recorded on or before 30/11/2015
Excl.	use of prednisone at more than 10 mg per day	Name = "Prednisone" or Name = "Prednisolone", Strength > 10 mg, oral treatments only Current prescribing = 84 days
Excl.	change in hormone-replacement therapy or oral-contraceptive therapy within the previous three months	Not applied
Excl.	history of alcohol abuse or an alcohol intake of more than 14 drinks per week.	• Alcohol Problems ever • Last recorded alcohol units, 3 year lookback

Trial 5: Becker et al. (2010) "The urate-lowering efficacy and safety of febuxostat in the treatment of the hyperuricemia of gout: the CONFIRMS trial"

	Criteria	Interpretation
Incl.	Has one or more of the American Rheumatism Association criteria for the diagnosis of gout.	Diagnosis of gout in primary care, by 30/11/2015
Incl.	Females of childbearing potential who are sexually active must agree to use adequate contraception, and can neither be pregnant nor lactating from Screening throughout the duration of the study.	Not applied
Incl.	Must have a serum urate level greater than or equal to 8.0 milligram per deciliter (mg/dL).	Not applied
Excl.	Have a severe, unstable, or life threatening medical condition that would likely prevent them from completing this study.	• Schizophrenia ever • Intellectual disability ever • Down syndrome ever • Dementia ever • Alcohol misuse in the last five years • substance misuse in the last five years
Excl.	Has a known body reaction to febuxostat, allopurinol, naproxen, any other non-steroidal anti-inflammatory drug (NSAID), aspirin, lansoprazole, colchicine, or any components in their formulation.	Not applied
Excl.	History of xanthinuria.	Not applied
Excl.	Alcohol consumption greater than 14/week.	Last recorded alcohol units, three year lookback
Excl.	History of significant concomitant illness.	• Cancer in the last 5 years (excl non-melanoma skin cancer) • Coronary heart disease (any) in last 5 years • Heart failure in last 5 years • Primary pulmonary HT ever • Thromboembolic and other non-haemorrhagic stroke/TIA in last 5 years • Cerebral haemorrhage in last 5 years • Cardiomyopathy in last 5 years • Inflammatory bowel disease in last 5 years • Chronic renal disease ever • Chronic liver disease (excl fatty liver) ever • COPD ever • Alcohol and substance misuse in last 5 years • Intellectual disability ever • Down syndrome ever • Multiple sclerosis ever

			- Parkinson's Disease ever - Myasthenia gravis ever - Motor neurone disease ever - Dementia ever - Schizophrenia, schizotypal and delusional disorders ever - Connective tissue disease ever
Excl.	Active liver or peptic ulcer disease.		- Chronic liver diseases (excl fatty liver) ever - Peptic ulcer in the last five years
Excl.	Has rheumatoid arthritis requiring treatment.		Rheumatoid arthritis ever
Excl.	Has estimated creatinine clearance less than 30 milliliter per minute (mL/min) calculated using the Cockcroft-Gault formula corrected for ideal body weight.		CKD 4 or CKD 5 on last record
Excl.	Requires therapy with any other urate-lowering drug other than the study drug; long-term use of NSAIDs and COX-2 inhibitors; Salicylates; thiazide diuretics; losartan; azathioprine; mercaptopurine; theophylline; intravenous (IV) colchicine; cyclosporine; cyclophosphamide; pyrazinamide; sulfamethoxazole; trimethoprim.		- Section = "Oral and parenteral NSAIDS" - Aminosalicylates - oral - Class = Thiazides - Class = ARBs + Name contains Losartan - Name = Azathioprine - Name = mercaptopurine (08010100) - Class = Theophylline - Ciclosporin - Name = Pyrazinamide - Section = Sulfonamides and Trimethoprim + Name = Trimethoprim (excludes Trimethoprim in Antibacterials) Current prescribing = 84 days

Trial 6: Yu et al. (2016) "Safety and efficacy of oral febuxostat for treatment of HLA-B*5801-negative gout: a randomized, open-label, multicentre, allopurinol-controlled study"

	Criteria	Interpretation
Incl.	Subjects will also have a history or presence of gout as defined by the American College of Rheumatology (ACR) criteria	Diagnosis of gout in primary care, by 30/11/2015
Incl.	Subject has serum urate level >= 8.0 mg/dL at the screening Visit	Not applied
Excl.	Female subject who is breast-feeding or pregnant	Not applied
Excl.	Subject has a history of xanthinuria	Not applied
Excl.	Subject who is intolerant of allopurinol, ie hypersensitivity, Steven-Johnson syndrome/topic epidermal necrolysis	Not applied
Excl.	Subject who takes allopurinol > 300 mg/day and with serum urate level > 8mg/dL	Not applied
Excl.	Subject who is HLA B*5801 positive	Not applied
Excl.	Subject who is receiving thiazide diuretic therapy	Class = Thiazide diuretics Current use = 84 days
Excl.	Subject who has secondary hyperuricemia	Not applied
Excl.	Subject who requires concurrent therapy with any systemic or topical medications, prescribed or non-prescribed, containing aspirin or other salicylates (low doses of aspirin will be allowed (ie. =< 325mg/day)	• Section = Analgesics • Aminosalicylates - all
Excl.	Subject who requires therapy with prednisone > 10 mg/ day during the study	Name = "Prednisone" or Name = "Prednisolone", Strength >10mg, route = oral, Current prescribing = 84 days
Excl.	Subject who has active liver disease or hepatic dysfunction, defined as both ALT and AST > 1.5 times the upper limit of normal	Chronic liver disease (excl fatty liver) ever ALT AST Most recent test in 2012-2015
Excl.	Subject who has serum creatinine >= 1.5mg/dL	serum creatinine >= 1.5mg/dL Most recent test ever
Excl.	Subject who has any another significant medical condition as defined by the investigator that would interfere with the treatment, safety or compliance with the protocol (eg. A clinically significant ECG result)	• Cancer in the last 5 years (excl non-melanoma skin cancer) • Coronary heart disease (any) in last 5 years • Heart failure in last 5 years • Primary pulmonary HT ever • Thromboembolic and other non-haemorrhagic stroke/TIA in last 5 years • Cerebral haemorrhage in last 5 years • Cardiomyopathy in last 5 years

		- Inflammatory bowel disease in last 5 years - Chronic renal disease ever - Chronic liver disease (excl fatty liver) ever - COPD ever - Alcohol and substance misuse in last 5 years - Intellectual disability ever - Down syndrome ever - Multiple sclerosis ever - Parkinson's Disease ever - Myasthenia gravis ever - Motor neurone disease ever - Dementia ever - Schizophrenia, schizotypal and delusional disorders ever - Connective tissue disease ever
Excl.	Subject who has a history of cancer (other than basal cell carcinoma of the skin) within 5 years prior to the study, or has taken any systemic cancer chemotherapy within 5 years prior to the study	Primary (not non-melanoma skin) malignancy Secondary (not non-melanoma skin) malignancy, in last 5 years
Excl.	Subject who has previously participated in a clinical study in which febuxostat was administered	Not applied
Excl.	Subject who has participated in another investigational trial within the 30 days prior to the study	Not applied