**SUPPLEMENTARY MATERIAL**

**Results of the content analysis of the literature**

***Preclinical disease states***

Three preclinical disease states of gout were identified, as shown in Table 2. The most frequently occurring cluster of disease elements was ‘hyperuricemia *without* clinical disease elements of gout’, present in 14.5% of total articles and universally labelled as ‘asymptomatic hyperuricemia’ (100% of articles referring to this disease state). The other two preclinical disease states identified were ‘imaging evidence of monosodium urate crystal deposition *without* clinical disease elements of gout’, most commonly labelled as ‘asymptomatic monosodium urate crystal deposition (43.8% of articles referring to this disease state); and ‘hyperuricemia *with* imaging evidence of monosodium urate crystal deposition and *without* clinical disease elements of gout’, most frequently referred to as ‘asymptomatic hyperuricemia with monosodium urate crystal deposition’ (90.6% of articles referring to this disease state).

***Clinical disease states***

There were six clinical disease states of gout identified (Table 2). Some were consistent in how they were labelled in the literature; for example, the ‘presence of monosodium urate crystals *with* at least one subcutaneous tophus’ was given the label ‘tophaceous gout’ in 81% of relevant articles. However, the labels for other disease states showed less consistency. For example, the cluster of ‘monosodium urate crystals *with* clinical disease elements of gout’ had 14 unique labels in the literature examined, the most common being ‘symptomatic gout’, used by 50.8% of articles referencing this disease state. Disease element clusters representing a state of high disease activity were common. One such disease state represented a wide range of clinical presentations: ‘the presence of monosodium urate crystals *with* any of the following: frequent recurrent gout flares, chronic gouty arthritis, subcutaneous tophi or imaging disease elements of gout’; this state was referred to in 13.4% of all articles examined and was given the non-specific label of ‘severe gout’ in 81.9% of these papers. Disease states characterising more specific elements of severity were also found. The cluster of ‘the presence of monosodium urate crystals *with* at least one subcutaneous tophus’ was a common finding, present in 19.7% of articles and labelled as ‘tophaceous gout’ in 81.1% of these. In contrast, the cluster of disease elements representing another important clinical sequela of gout, ‘the presence of monosodium urate crystals *with* clinical disease elements of gout and *with* at least one gouty bone erosion’, was uncommon, appearing in only 1.1% of articles in which it was invariably labelled ‘erosive gout’. Overall, disease element clusters representing less severe disease states were rare; the only example being the cluster ‘the presence of monosodium urate crystals *with* any of the following: gout flare, chronic gouty arthritis and *without* subcutaneous tophi’, labelled as ‘non-tophaceous gout’ in 80% of articles collectively describing these elements.

***States describing disease course***

There were four disease states identified that referred to the temporal course of disease (Table 2). Two disease states, ‘the first episode of gout flare *without* preceding intercritical gout’ and ‘more than one episode of gout flare *with* intercritical gout’, were relatively common and consistently labelled: ‘incident gout’ and ‘recurrent gout flares’ in 75.3% and 94.9% of relevant articles, respectively. Disease states referring to progression in the natural history of gout were non-specific and relevant time-frames were infrequently defined. These included ‘the presence of monosodium urate crystals *with* clinical disease elements of gout’ either ‘early’ or ‘late’ in the course of disease natural history; these were most commonly labelled ‘early gout’ and ‘longstanding gout’ (68.4% and 66.7% of relevant articles, respectively).

**Results of the Delphi exercise**

***Agreement about whether a disease state is meaningful***

Of the 13 disease states identified from the content analysis of the literature, nine were deemed ‘meaningful’ by consensus agreement; consensus agreement on all nine disease states occurred in the first Delphi round (Table 3). Two disease states were close to reaching consensus as meaningful, each with 74% agreement: ‘the presence of chronic gouty arthritis *with* at least one subcutaneous tophus’ and ‘the presence of monosodium urate crystal deposition *with* any of the following: gout flares or chronic gouty arthritis; but *without* subcutaneous tophi’. Regarding the first of these, some respondents argued that there is no meaningful distinction between this cluster of disease elements and the use of the element ‘chronic gouty arthritis’ in isolation.

Two other disease states related to the temporal progression of gout through its natural history did not reach consensus agreement on being ‘meaningful’: ‘the presence of monosodium urate crystal deposition *with* any of the following: gout flares, chronic gouty arthritis or subcutaneous tophi’ both ‘early’ and ‘late in the course of disease natural history’ reached 67% and 69% agreement, respectively, at the conclusion of the Delphi exercise. In their comments, respondents argued that disease states should not be defined according to temporal descriptors such as ‘late’ or ‘longstanding’; furthermore, some felt that defining meaningful time frames may be problematic given the variable period of monosodium crystal deposition prior to the emergence of clinical symptoms and signs.

There were a number of additional disease states proposed by respondents during the first round. Most of these proposed disease states included aspects of gout management or treatment outcomes; or comorbidities such as chronic kidney disease or cardiovascular disease. These were considered beyond the scope of the current project and did not represent clusters of disease elements; therefore, they were not included in subsequent rounds of the Delphi exercise.

***Disease state labels***

Of the nine disease states deemed to be meaningful by consensus agreement following the Delphi exercise, seven disease states reached consensus agreement on their preferred label: ‘asymptomatic hyperuricemia’, ‘asymptomatic monosodium urate crystal deposition’, ‘severe gout’, ‘tophaceous gout’, ‘erosive gout’, ‘first gout flare’ and ‘recurrent gout flares’ (Table 4).

Two of the disease states determined to be meaningful failed to reach consensus agreement on their label. One state was close to reaching agreement: ‘hyperuricemia *with* imaging evidence of monosodium urate crystal deposition *without* gout flares, chronic gouty arthritis or subcutaneous tophi’, the label for which, ‘asymptomatic hyperuricemia with monosodium urate crystal deposition’, reached 79% agreement after round three. The remaining disease state, ‘the presence of monosodium urate crystal deposition *with* any of the following: gout flares, chronic gouty arthritis or subcutaneous tophi’ was not close to reaching consensus agreement. However, the most preferred label for this state was ‘gout’, for which there was 56% agreement. While it was not the original intention of this project to define gout, this label was proposed by respondents during round one of the Delphi exercise and progressively gained popularity throughout the remaining two rounds.

**Supplementary Table S1.** Journals used in a content analysis of gout- and hyperuricemia†-related literature concerning the disease states of gout. In descending order: the ten highest-ranked general rheumatology journals, and the five highest-ranked general internal medicine journals (according to Impact Factor, 2016 Thomson-Reuters Journal Citation Reports) published between 1st January 2013 and 31st January 2018.

|  |  |  |
| --- | --- | --- |
| Specialty | Journal | Number of gout-related articles identified |
| General rheumatology journals | Annals of the Rheumatic Diseases | 118 |
| Nature Reviews Rheumatology | 38 |
| Arthritis and Rheumatism/Arthritis and Rheumatology | 45 |
| Rheumatology | 92 |
| Seminars in Arthritis and Rheumatism | 36 |
| Current Opinion in Rheumatology | 21 |
| Arthritis Research and Therapy | 62 |
| Best Practice and Research in Clinical Rheumatology | 5 |
| Rheumatic Disease Clinics of North America | 19 |
| Arthritis Care and Research | 51 |
| General internal medicine journals | The New England Journal of Medicine | 2 |
| Lancet | 4 |
| Journal of the American Medical Association | 8 |
| British Medical Journal | 14 |
| Annals of Internal Medicine | 24 |
| Total |  | **539** |

†In British English, hyperuricaemia.

**Supplementary Table S2.** Voting results from the face-to-face consensus meeting. Consensus defined as 80% or more agreement.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Item proposed** | **Voting** | | | |
| **For (%)** | **Against** | **Abstain** | **Consensus achieved** |
| Only disease states that met consensus as being meaningful during the Delphi exercise are included within the final disease state consensus statement. | 35 (100%) | 0 | 0 | Yes |
| ‘Gout’ as the label for the disease state: The presence of monosodium urate crystals ***with*** clinical disease elements of gout. | 34 (100%) | 0 | 1 | Yes |
| ‘Asymptomatic hyperuricemia† with monosodium urate crystal deposition’ as the label for the disease state: Hyperuricemia† ***with*** imaging evidence of monosodium urate crystal deposition but ***without*** clinical disease elements of gout. | 33 (94%) | 2 | 0 | Yes |
| ‘Gout’ definition: A disease caused by monosodium urate crystal deposition with any of the following clinical presentations: gout flare, chronic gouty arthritis or subcutaneous tophus. | 35 (100%) | 0 | 0 | Yes |
| ‘Asymptomatic hyperuricemia†’ definition: Hyperuricemia† in the absence of gout. | 34 (97%) | 1 | 0 | Yes |
| ‘Asymptomatic monosodium urate crystal deposition’ definition: Evidence of monosodium urate crystal deposition in the absence of gout. Monosodium urate crystal deposition may be demonstrated by imaging or microscopic analysis. | 33 (100%) | 0 | 0 | Yes |
| ‘Asymptomatic hyperuricemia† with monosodium urate crystal deposition’ definition: Hyperuricemia† with evidence of monosodium urate crystal deposition in the absence of gout. Monosodium urate crystal deposition may be demonstrated by imaging or microscopic analysis. | 33 (100%) | 0 | 0 | Yes |
| ‘Severe gout’ should not be included in the nomenclature. | 32 (100%) | 0 | 1 | Yes |
| ‘Tophaceous gout’ definition: Gout with at least one subcutaneous tophus. | 31 (100%) | 0 | 0 | Yes |
| ‘Erosive gout’ definition: Gout with at least one gouty bone erosion. | 31 (100%) | 0 | 0 | Yes |
| ‘First gout flare’ definition: The first episode of gout flare. | 30 (100%) | 0 | 1 | Yes |
| ‘Recurrent gout flares’ definition: More than one gout flare. | 28 (100%) | 0 | 0 | Yes |
| Additional recommendation on disease states not addressed by the nomenclature: Where there is more than one disease state present, these can be combined (for example: tophaceous and erosive gout). Where there are additional elements present, not recognized as disease states, these will be labelled as the recognized disease state with or without additional disease elements (for example: tophaceous gout with chronic gouty arthritis). | 27 (100%) | 0 | 1 | Yes |

†In British English, hyperuricaemia.