

SIZING THE PATIENT POTENTIAL FOR DISEASE MODIFYING OSTEOARTHRITIS THERAPIES IN USA & EU MARKETS

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Introduction:

Osteoarthritis is a highly prevalent, debilitating condition involving erosion of the joint and / or growth of bony protrusions into the joint capsule. Over time, the joint space between the bones of the joint lessens. Patients are often in a significant amount of pain, however the degree of joint destruction does not often correlate with the amount of pain experienced by the patient.

Treatment is largely focused on pain management, with whole joint replacement for patients with little to no remaining joint structure and functionality. Unlike other forms of arthritis, there are currently no licenced disease modifying treatments available for osteoarthritis (DMOATs).

Current DMOATs in development are focused on treating patients that still retain a certain amount of joint structure and function – the idea being that the DMOAT can restore joint functionality as long as there is sufficient residual tissue from which to rebuild joint function and form. Where the joint has been totally eroded, DMOATs are likely to be of limited (if any) use. Thus there is a narrowly defined range of joint destruction where DMOATs will be able to demonstrate efficacy. Coupled with the likely affordability of such treatments, DMOATs may also be reserved for patients that not only fit the clinical criteria in terms of joint structure / erosion but that also experience significant pain that interferes with daily life.

Methods:

A systematic search and review of published literature (including Medline, Embase, Cochrane CENTRAL) for studies reporting the prevalence of osteoarthritis was conducted to find published prevalence estimates in 5 EU markets and the USA. Papers were selected for inclusion in the analysis based on sample size and method of selection alongside diagnostic criteria (for prevalence estimates non-radiologic criteria for OA were allowed).

Sub-analyses and searches were also conducted to find information regarding severity of OA in patients using the Kellgren-Lawrence Grading System, based on radiological assessment of patients' joints and includes a combination of joint space narrowing, osteophyte formation, sclerosis and deformity of bone ends.

In addition, data were then sought regarding degree of impact that OA has on patients, using the WOMAC (Western Ontario and McMaster University) index. The Index consists of a 24-item questionnaire completed by the patients and focuses on three categories: pain, stiffness and physical function. Data regarding the pain scores in the index were extracted from the published data and aligned with the Kellgren-Lawrence grades determining joint function in order to assess the proportion of the population with OA according to both severity of OA and severity of pain experienced.

Countries included in the analysis were limited to France, Germany, Italy, Spain, UK and USA.

Results:

DMOATs are not clinically effective in patients with severe OA (K-L grade 4), thus while these patients were quantified, they were excluded from the final DMOAT quantification. Although DMOATs may be able to demonstrate clinical utility in patients with mild disease, these patients can be treated effectively with pain management. Patients with K-L Grade 0 / 1 osteoarthritis have also been excluded from the analysis since Grade 2 is the cut-off for radiographic diagnosis of OA. It is unlikely that there will be a strong cost-benefit rationale for widespread treatment of this patient group. For patients with moderate joint erosion, DMOATs are likely to demonstrate the greatest value-based proposition. Patients were further segmented with regards to the degree of pain experienced according to the WOMAC index. Those with more severe pain and thus lower utility scores would represent the optimal target population for DMOATs as they would be most likely to demonstrate cost-benefit. Of debate is the inclusion of those with grade 3 OA but only mild pain. There could be a clinical argument to intervene while there is sufficient joint structure remaining, despite lower reported pain by the patients.

		WOMAC PAIN SCORE		
		Mild	Moderate	Severe
KELLGREN-LAWRENCE GRADE	Grade 0	x	x	x
	Grade 1	x	x	x
	Grade 2*	x	✓	✓
	Grade 3	✓	✓	✓
	Grade 4	x	x	x

Figure 1. WOMAC vs. Kellgren-Lawrence Grade showing intersect where DMOATs could demonstrate highest patient benefit

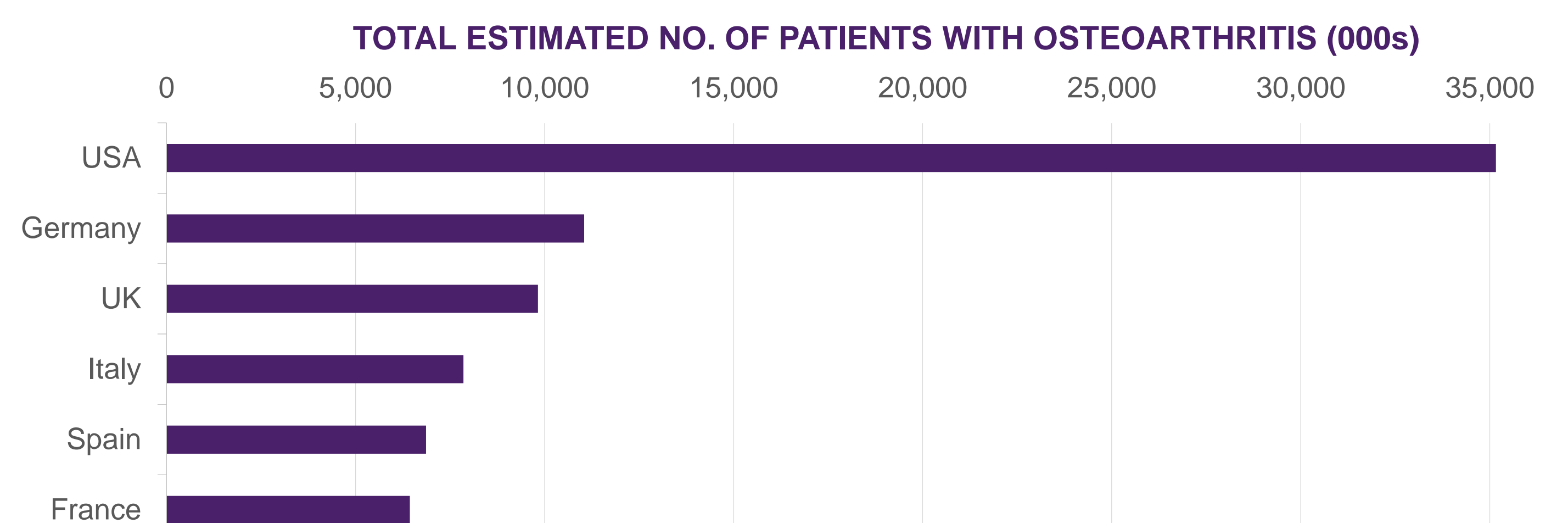


Figure 2. Overall Estimated Prevalence of OA in EU 5 countries & USA, 2018

		WOMAC PAIN SCORE		
		Mild	Moderate	Severe
KELLGREN-LAWRENCE GRADE	Grade 0	11.4%	1.4%	0.0%
	Grade 1	12.0%	1.4%	0.6%
	Grade 2	35.7%	4.7%	2.1%
	Grade 3	17.8%	3.6%	0.9%
	Grade 4	5.6%	2.2%	0.7%

Figure 3. Distribution of OA Patients according to K-L Grade vs. WOMAC pain score

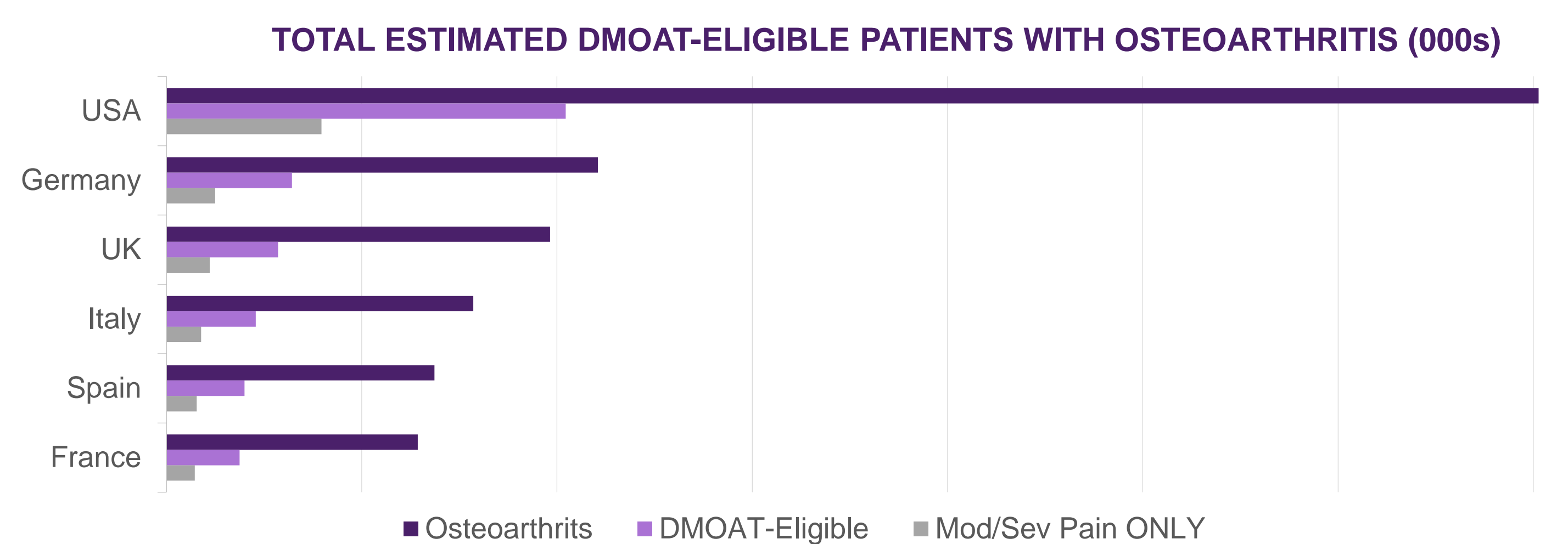


Figure 4. Estimated DMOAT-eligible patient population by country, 2018 vs total prevalent OA

Overall, the total % of patients with OA of a suitable clinical grade (as defined by the Kellgren-Lawrence grading scale) coupled with sufficient pain associated with the disease was approximately 28% of the overall osteoarthritis population (reduced to ~11% when K-L Grade 3 with mild pain was removed). Of ~77 million OA patients in Europe & USA, this would equate with approximately 22 million patients (~8.7 million when K-L Grade 3 with mild pain was removed) being eligible for DMOAT treatment.

Conclusion:

There is no reliable correlation between osteoarthritis severity and level of pain experienced by patients with OA. Selection of a suitable target population that would benefit from DMOAT therapy needs to consider both the clinical setting in which the DMOAT would be able to demonstrate disease modifying activity balanced against the patient quality of life and impairment that arises from the condition. Patients with moderate OA disease (K-L Grade 2-3) experiencing mild/moderate to severe pain would be most likely to benefit from DMOAT therapy. This represents approximately 28% of the overall OA population, ~22 million patients. If patients with K-L Grade 3 with mild pain are removed from the analysis, only ~11% of the overall OA population would remain eligible for DMOAT therapy, corresponding to ~8.7 million patients. Those with lower K-L grades are not considered to meet diagnostic criteria for OA and thus would likely be ineligible for DMOAT treatment. Those with K-L Grade 4 disease have lost nearly complete joint function and would be considered eligible for total joint replacement.

While there is reasonable data regarding the prevalence of OA in Europe, data regarding radiographic severity of the disease is lacking in many studies and where available may represent a bias toward those more likely to come forward for diagnosis i.e. symptomatic patients experiencing pain. This would reduce the true proportion of patients with OA that would be eligible for DMOAT therapy according to these criteria.

Bibliography:

- Black Swan Analysis (2018). Epimic Patient Segmentation Database. [Accessed June 2019]
- De Filippis L et al. Epidemiologia e fattori di rischio dell'osteoartrite: review della letteratura e dati dal progetto OASIS. *Reumatismo*. 2004; 56 (1), 169-184.
- Felson DT et al. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum*. 1987; 30 (8), 914-918.
- Fuchs J et al. Prevalence of selected musculoskeletal conditions in Germany Results of the German Health Interview and Examination Survey for Adults (DEGS1). *Bundesgesundheitsbl*. 2013; 56 (1), 678-686.
- Guillemin F et al. Prevalence of symptomatic hip and knee osteoarthritis: a two-phase population-based study. *Osteoarthritis Cartilage*. 2011; 19 (11), 1314-1322.
- Guillemin F et al. The KHOA cohort of knee and hip osteoarthritis in France. *Joint Bone Spine*. 2012; 79 (6), 597-603.
- Kingsbury SR et al. Osteoarthritis in Europe: impact on health status, work productivity and use of pharmacotherapies in five European countries. *Rheumatology*. 2014; 53(5):937-947.
- Kohn MD et al. Classifications in Brief: Kellgren-Lawrence Classification of Osteoarthritis. *Clin Orthop Relat Res*. 2016; 474(8):1886-1893.
- Le Pen C et al. Financial cost of osteoarthritis in France. The "COART" France study. *Joint Bone Spine*. 2005; 72 (6), 567-570.
- Lo GH et al. Knee Osteoarthritis Symptom Assessments That Combine Pain and Physical Activity Are Superior to Pain Alone. *ACR/ARHP Annual Meeting*. 2012; (1):239.
- Lo GH et al. Symptom assessment in knee osteoarthritis needs to account for physical activity level. *Arthritis Rheum*. 2015; 67(11):2897-2904.
- Postler A et al. Prevalence and treatment of hip and knee osteoarthritis in people aged 60 years or older in Germany: an analysis based on health insurance claims data. *Clin Interv Aging*. 2018; 13(1):2339-2349.
- Salaffi F et al. Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2003; 11(8):551-560.
- Skou ST et al. Knee Confidence as It Relates to Self-reported and Objective Correlates of Knee Osteoarthritis: A Cross-sectional Study of 220 Patients. *J Orthop Sports Phys Ther*. 2015; 45(10):765-771.