

## ANNEX 3B. An Essential Package of Interventions to Address Musculoskeletal Disorders

Supplementary material for: Watkins, DA, DT Jamison, A Mills, R Atun, K Danforth, and others. 2018. “Universal Health Coverage and Essential Packages of Care.” In *Disease Control Priorities: Improving Health and Reducing Poverty* edited by DT Jamison, H Gelband, S Horton, P Jha, R Laxminarayan, CN Mock, and R Nugent. Volume 9 of *Disease Control Priorities, third edition*. Washington, DC: World Bank.

### Introduction

Musculoskeletal disorders are a heterogeneous group of conditions that affect the function of the musculoskeletal system, which includes the joints, muscles, tendons, and ligaments. Disorders of this system can arise from autoimmune phenomena (e.g., rheumatoid arthritis), degenerative processes (e.g., osteoporosis), or injury that may occur following repetitive stress (e.g., osteoarthritis) or acute trauma (e.g., meniscal tears or back sprain).

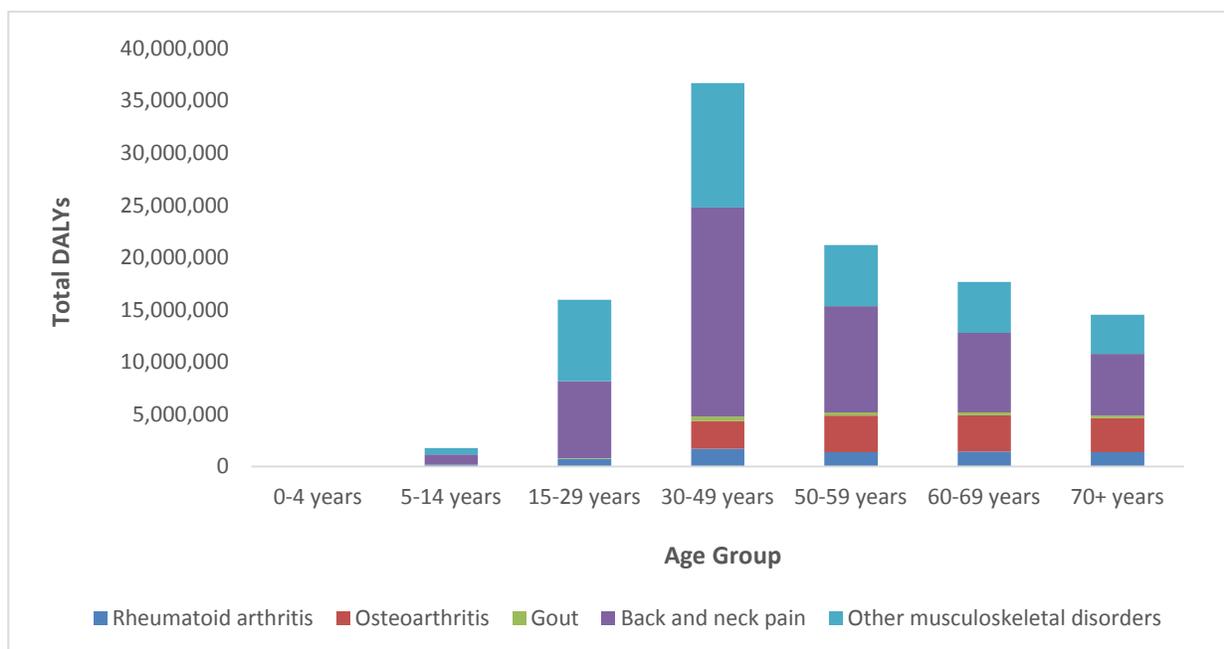
While musculoskeletal disorders are not among the top causes of global mortality, they are a major focus of outpatient healthcare and thus have major implications for health system planning in low- and middle-income countries. In many parts of the world, musculoskeletal symptoms are the most common reason for presenting to primary care facilities, including urgent care facilities. Oftentimes these symptoms are the result of minor injuries and are exacerbated by the work environment, a problem which spans across income groups and occupations.

Interventions that seek to prevent and manage musculoskeletal disorders are often focused on improving functional status and reducing the severity of disability. Because they rarely avert mortality, they are not often conceived as part of essential health services. Yet from the patient perspective, the economic benefits (increased productivity) and intangible gains (reduced pain and suffering) from musculoskeletal interventions are highly valued and can reasonably be considered within essential universal health coverage. Unfortunately, as is illustrated below, much of the literature in this domain has focused on high-income settings, making it challenging to identify a list of essential, cost-effective interventions for low-income settings.

### Disease burden

According to the WHO Global Health Estimates 2015, musculoskeletal disorders are a top cause of years lived with disability, comprising about 4% of total DALYs (110 million) as compared with 0.3% of total deaths (160,000) globally in 2015 (1). The most frequent cause of DALYs from musculoskeletal disorders in 2015 was back and neck pain (48%) followed by the residual category “other musculoskeletal disorders” (32%), osteoarthritis (12%), and rheumatoid arthritis (6.3%). It is worth noting that rheumatoid arthritis was responsible for the largest number of deaths (48,000) from any specific musculoskeletal disorder in 2015.

The age distribution of musculoskeletal disorders is an especially important feature of this group of conditions. With the exception of rheumatoid arthritis and osteoarthritis, which worsen over time with age, the highest number of DALYs by cause occurs in the prime working years (Figure 3B.1), owing to their sporadic and often work-related nature.



**Figure 3B.1** Global DALYs from musculoskeletal disorders by age (both sexes) in 2015

As suggested previously, this age distribution is important when considering the economic benefits of investing in health services for musculoskeletal disorders. Inasmuch as these disorders are disabling and result in high indirect costs, providing care for them can improve economic productivity. And because they are common disorders that often require repeat and ongoing engagement with the health system, reducing out-of-pocket payments for services can provide financial risk protection.

### Identification of effective interventions

Chapter 51 of Disease Control Priorities, 2<sup>nd</sup> Edition (*DCP2*) was devoted to musculoskeletal disorders and their interventions. This annex seeks to update the findings of that chapter and distill the recent literature into a package of essential interventions. Table 3B.1 summarizes the interventions that were appraised in *DCP2* and recommended for low- and middle-income countries (see text of that chapter for details on methods and data sources used in forming the chapter’s recommendations).

**Table 3B.1** Summary of intervention cost-effectiveness data on musculoskeletal interventions in *DCP2*

Condition	Strategy	Intervention
Osteoporosis	Primary prevention	Physical activity Calcium and vitamin D supplementation
	Secondary prevention	Calcium and vitamin D supplementation
Osteoarthritis	Secondary prevention	Exercise programs (if low-cost)
Rheumatoid arthritis	Self-care	Telephone help lines

	Treatment	Combination disease-modifying agents Corticosteroids
<b>Low back pain</b>	Treatment	Early interventions (addressing occupational injury)

A few additional comments can be made about the interventions above.

### Osteoporosis

Prevention of, and rehabilitation from, osteoporosis is becoming a growing concern for low- and middle-income countries. Disability and mortality due to falls in the elderly is increasing, and osteoporosis increases the risk of a fall leading to a fracture (1). Hip fractures in particular are associated with high mortality rates in this population, making prevention strategies especially urgent.

Primary prevention of osteoporosis can involve weight-bearing exercises and other strategies that support bone health, including healthy diet, smoking cessation, and limited use of alcohol. *DCP2* recommended calcium and vitamin D supplementation in high risk individuals, including women who are older, smoke, or have a family history of fragility fractures. Hormone replacement therapy, covered in *DCP2*, is no longer recommended for prevention of osteoporosis given its associations with cancer, cardiovascular disease, and venous thromboembolism following long-term use.

Secondary prevention of osteoporosis may be considered for individuals who have sustained a fragility fracture or who have undergone DEXA screening. (While the latter was not considered cost-effective in low- and middle-income countries, some individuals may have access to such screening and hence carry a diagnosis of osteoporosis on that basis.) Calcium and vitamin D appeared to be cost-effective for secondary prevention; hormone replacement therapy was not (for the reasons listed above). There has also been a growing interest in the use of bisphosphonates in recent decades, and these are frequently used in high-income countries. Bisphosphonates were not recommended in *DCP2* over concerns that they were not cost-effective.

### Osteoarthritis

Osteoarthritis is usually the result of repetitive joint use and injury over time, and overweight and obese individuals appear to be at higher risk. Hence weight loss strategies, covered in several places in *DCP2*, were thought to be effective (though cost-effectiveness data on exercise for osteoarthritis prevention were lacking). Weight-bearing exercise programs showed some promise, though with limited economic evidence.

To address pain due to osteoarthritis, NSAIDs are commonly prescribed, often along with gastroprotective agents. *DCP2* found a lack of cost-effectiveness evidence for these medications. Similarly, synovial fluid replacement received some attention, though hard evidence on functional outcomes was limited, and its cost-effectiveness was deemed to depend on price to a large extent.

Finally, tertiary surgical interventions for osteoarthritis are a mainstay of care in high-income countries. Hip and knee arthroplasty were noted to be very cost-effective (\$0 – \$10,000 per QALY gained) in studies summarized in *DCP2*. The authors noted that provision of surgical care in lower-resource settings could potentially be cost-effective but would require more stringent case selection, looking for individuals with the highest degree of functional limitation.

## Rheumatoid arthritis

Rheumatoid arthritis is a progressive, debilitating, autoimmune disorder. In high-income settings, the standard of care for moderate-to-severe rheumatoid arthritis for many years has been combination therapy with “disease-modifying antirheumatic drugs” (DMARDs). Pharmacotherapy is very effective and can greatly reduce disability and disease progression. The main challenge, noted in *DCP2*, is that disease management is complex; general primary care nurses or practitioners may not have sufficient training to provide DMARDs.

Since the publication of *DCP2*, so-called “biologics” that suppress the immune system factors that drive the disease process have grown in popularity and are being used earlier in the disease course with good results. One particular advantage is that these drugs can spare the use of corticosteroids, the latter of which have high complication rates with long-term use. The main problem with biologics is their cost and complexity of delivery. *DCP2* did not recommend biologic therapies for rheumatoid arthritis.

## Other conditions

*DCP2* stressed the importance of conservative (non-pharmacologic) therapy for low back and neck pain, the most common musculoskeletal disorders. Early interventions, particularly for occupation-related back and neck pain, employ a multidisciplinary approach that includes exercise classes, biofeedback and pain management classes, group education sessions, case manager and occupational therapist sessions, and interdisciplinary team conferences. Such approaches were found to be cost-saving in high-income countries, though evidence was lacking in low- and middle-income settings.

## Review of economic evidence

After reviewing the findings of *DCP2*, the authors conducted a structured literature search for economic evaluations on musculoskeletal disorders in low- and middle-income countries (Table 3B.2). The search was restricted to January 1, 2000 to the present and to English-language studies with abstracts available. Studies were included if they reported cost-effectiveness or benefit-cost ratios comparing one or more interventions of relevance in low- and middle-income country settings. Reviews/editorials, studies from high-income settings, and cost analyses were excluded.

**Table 3B.2** Medline search strategy for economic studies of musculoskeletal disorders

### 1. Geography term

"south America" OR "latin America" OR afghanistan OR albania OR algeria OR angola OR argentina OR armenia OR armenian OR azerbaijan OR bangladesh OR benin OR belize OR bhutan OR bolivia OR botswana OR brazil OR "Burkina Faso" OR burundi OR cambodia OR "Khmer Republic" OR kampuchea OR

cameroon OR cameroons OR cameron OR cameron OR "Cape Verde" OR "Central African Republic" OR chad OR china OR colombia OR comoros OR comoro islands OR comores OR mayotte OR congo OR zaire OR "Costa Rica" OR "Cote d'Ivoire" OR "Ivory Coast" OR djibouti OR "French Somaliland" OR dominica OR "Dominican Republic" OR "East Timor" OR "East Timor" OR "Timor Leste" OR ecuador OR egypt OR "United Arab Republic" OR "El Salvador" OR eritrea OR ethiopia OR fiji OR gabon OR "Gabonese Republic" OR gambia OR gaza OR georgia OR ghana OR grenada OR guatemala OR guinea OR guiana OR guyana OR haiti OR honduras OR india OR maldives OR indonesia OR kenya OR kiribati OR "Lao PDR" OR laos OR lesotho OR basutoland OR liberia OR libya OR madagascar OR "Malagasy Republic" OR sabah OR sarawak OR malawi OR nyasaland OR mali OR "Marshall Islands" OR mauritania OR mauritius OR "Agalega Islands" OR mexico OR micronesia OR moldova OR moldova OR moldovan OR mongolia OR montenegro OR morocco OR ifni OR mozambique OR myanmar OR myanmar OR burma OR namibia OR nepal OR "Netherlands Antilles" OR nicaragua OR niger OR nigeria OR muscat OR pakistan OR palau OR palestine OR panama OR paraguay OR peru OR philippines OR philippines OR philippines OR philippines OR rwanda OR ruanda OR nevis OR "Saint Lucia" OR "St Lucia" OR "Saint Vincent" OR "St Vincent" OR grenadines OR samoa OR "Samoan Islands" OR "Navigator Island" OR "Navigator Islands" OR "Sao Tome" OR senegal OR serbia OR montenegro OR seychelles OR "Sierra Leone" OR "Sri Lanka" OR ceylon OR "Solomon Islands" OR somalia OR sudan OR suriname OR surinam OR swaziland OR tajikistan OR tadjikistan OR tadjik OR tanzania OR thailand OR togo OR "Togolese Republic" OR tonga OR tunisia OR turkey OR turkmenistan OR turkmen OR uganda OR ukraine OR vanuatu OR "New Hebrides" OR venezuela OR vietnam OR "Viet Nam" OR zambia OR zimbabwe OR "Africa, Northern" OR "Northern Africa" OR "North Africa" OR "Africa South of the Sahara" OR "sub-Saharan Africa" OR "subsaharan Africa" OR "Africa, Central" OR "central Africa" OR "Africa, Eastern" OR "Eastern Africa" OR "east Africa" OR "Africa, Southern" OR "southern Africa" OR "Africa, Western" OR "western Africa" OR "west Africa" OR "Caribbean Region" OR caribbean OR "Central America" OR "Panama Canal Zone" OR "French Guiana" OR borneo OR "Mekong Valley" OR "mekong delta" OR "Republic of Congo" OR congo-brazzaville OR "Democratic Republic of the Congo" OR DRC OR congo kinshasa OR "South Sudan" OR "South Africa" OR guinea-bissau OR Africa OR developing countr\*[All Fields] OR low and middle-income countr\*[All Fields] OR LMIC[All Fields]

**2. Economics term**

cost-effective\*[All Fields] OR cost-benefit[All Fields] OR cost-utility[All Fields] OR econom\*[All Fields]

**3. Health condition term**

"Musculoskeletal Diseases"[Mesh]

The search was run on May 8, 2017, and yielded 953 records. The literature contained a large number of articles on the economic impact of musculoskeletal disorders. A few studies reported on quality-of-life reductions due to rheumatologic conditions in low- and middle-income countries. A small literature was found on surgical missions to provide orthopedic care, with significant overlap with the interventions recommended in Volume 1 of *Disease Control Priorities, 3<sup>rd</sup> Edition (DCP3)* and in the congenital and genetic disorders package of DCP3 (Annex 3A of this chapter).

Table 3B.3 summarizes the interventions for which cost-effectiveness estimates have been published in low- and middle-income countries. (As is standard in *DCP3*, incremental cost-effectiveness ratios, summarized in the last column of the Table, were converted and deflated to 2012 US dollars.)

**Table 3B.3** Summary of economic evaluations of interventions for musculoskeletal disorders in low- and middle-income countries

Author/year	Location	Intervention	Comparator	Finding
-------------	----------	--------------	------------	---------

(reference)

*Rheumatoid arthritis and other autoimmune disorders*

Bamrungsawad 2015 (2)	Thailand	IVIG plus corticosteroids for steroid-refractory dermatomyositis	Azathioprine or methotrexate plus corticosteroids for steroid-refractory dermatomyositis	Cost saving
Kostić 2014 (3)	Serbia	Tocilizumab plus methotrexate for rheumatoid arthritis	Methotrexate for rheumatoid arthritis	Dominated
Valle-Mercado 2013 (4)	Colombia	Biologic therapy (one of five standard drugs) for rheumatoid arthritis	Methotrexate for rheumatoid arthritis	US\$ 260,000 per QALY gained
Wu 2012 (5)	China	Biologic therapy (six single or dual agent regimens)	Traditional DMARDs	Expansion pathway, assuming DMARDs already being used, starts with infliximab (US\$ 29,000 per QALY gained) and adds or substitutes others thereafter
Wu 2015 (6)	China	Multiple strategies for rheumatoid arthritis, including initiation with Yisaipu (biosimilar to etanercept) in all cases	Traditional DMARDs	Only strategy that is cost-effective at current Chinese thresholds is induction with Yisaipu followed by methotrexate maintenance and DMARDs if methotrexate fails (about US\$ 8000 per QALY gained)

*Osteoporosis and other degenerative disorders*

Brandão 2012 (7)	Brazil	Systematic review of economic evaluations of drugs to treat postmenopausal osteoporosis	Varies; see text	Reasonable to start with vitamin D (and hormone replacement in selected groups) and expand to teriparatide and ultimately bisphosphonates as resources permit
Chen 2012 (8)	Nicaragua	Orthopedic surgical mission (including training and provision of care for well-selected cases)	Doing nothing	US\$ 530 per DALY averted
Kingkaew 2012 (9)	Thailand	Multiple strategies for primary and secondary prevention of osteoporosis in postmenopausal women	Doing nothing	Generally not cost-effective at current thresholds; alendronate most cost-effective (about US\$ 15,000-18,000 depending on age)

Panichkul 2006 (10)	Thailand	Multiple strategies for screening, including universal treatment, of osteoporosis in perimenopausal women	Doing nothing	Targeted DEXA in high-risk patients was the most cost-effective (US\$ 89,000 per fracture averted) but not acceptable at current thresholds
Turajane 2012 (11)	Thailand	Celecoxib for osteoarthritis	Standard (nonselective) NSAIDs for osteoarthritis	US\$ 47 per QALY gained
<i>Musculoskeletal injuries and pain syndromes</i>				
Falavigna 2016 (12)	Brazil	Discectomy for severe lumbar disk herniation	Conservative treatment for severe lumbar disk herniation	US\$ 15,000 per QALY gained
Ornelas 2012 (13)	Mexico	Multiple pharmacological strategies for fibromyalgia	Amitriptyline	Pregabalin is the most cost-effective option (US\$ 4500-6300 per case of pain controlled)

Note: interventions that provide good value for money in low- and middle-income countries, according to incremental cost-effectiveness ratios below usual levels of willingness-to-pay in these settings, are shown in red. IVIG = intravenous immunoglobulin. NSAIDS = non-steroidal anti-inflammatory drugs.

A few general themes emerge from the studies in Table 3B.3.

For autoimmune disorders, the authors found one study that looked at intravenous immunoglobulin for dermatomyositis. While this intervention appeared to be very cost-effective, the condition is quite rare and unlikely to be a priority for most countries. The remainder of the studies focused on rheumatoid arthritis. The weight of evidence from these studies supports a basic DMARD regimen built on methotrexate and corticosteroids, both of which are on the WHO's model list of essential medicines. Most biologic regimens assessed were not cost-effective compared to traditional DMARDs, though studies of a biosimilar called Yisaipu (similar to etanercept, but developed in China) suggested this drug was cost-effective in the Chinese context.

A variety of studies looked at screening and treatment strategies for osteoporosis. Compared to doing nothing, most drug treatment approaches were found to be cost-effective. The data from a systematic review on postmenopausal osteoporosis supported the notion that vitamin D supplementation would be the preferred first step in management, and that teriparatide and bisphosphonates would be reasonable second-line approaches. Screening for osteoporosis did not appear to be cost-effective in general, though if such screening were desired, it would be most cost-effective if implemented in a targeted fashion (i.e., in high-risk groups only).

There are a variety of indications for surgical repair of musculoskeletal injuries, including for injuries (such as ligamentous tears or long bone fractures) and degenerative changes (such as severe osteoarthritis). One study evaluated the cost-effectiveness of a mission to train providers in specialized orthopedic repairs on 30 well-selected cases. That study found favorable average

costs per case and incremental cost-effectiveness ratios. It is unclear whether costs and outcomes would be significantly different at scale, but this study does add to the growing literature that supports building capacity for specialized surgical care in a focused manner. Importantly, this study did not look at the long-term cost of complex surgical repairs such as arthroplasties (requiring prosthetic implants); while these procedures can be cost-effective (as noted in *DCP2*), specialist capacity is required to deal with complications, such as prosthetic joint infections, that can be costly.

Finally, there were a couple of studies on the management of chronic pain conditions. Surgical approaches to low back pain caused by lumbar disk herniation do not appear to be cost-effective. Non-opioid pharmacotherapy for fibromyalgia can be cost-effective, with amitriptyline and pregabalin being especially attractive options. It should be noted that the first line of care for chronic injuries is usually physical therapy, but this intervention was not assessed in the context of chronic musculoskeletal pain; a systematic review of interventions for low back pain in high-income countries concluded that interdisciplinary rehabilitation programs were likely to be cost-effective. (Chapter 16 of *DCP3* Volume 9 deals with rehabilitation care in low- and middle-income country settings.)

## Recommendations

Based on the evidence above and recommendations from other areas of *DCP3*, the authors developed an essential package for musculoskeletal disorders (Table 3B.4). The criteria for including an intervention in this package were: (1) likely to provide good value for money in low- and middle-income country settings, (2) feasible to implement by 2030, and (3) addressed a significant disease burden.

The authors support the use of rehabilitation services to address musculoskeletal disorders such as low back and neck pain. The literature suggests that early intervention following injury or symptom onset leads to better functional outcomes. The authors strongly recommend against opioid therapy for chronic pain; its role should be restricted to severe acute injuries, particularly those requiring surgical repair.

There is sufficient evidence for the authors to recommend outpatient care for osteoporosis and rheumatoid arthritis. Calcium and vitamin D supplementation are the preferred approach to primary and secondary prevention of osteoporosis. It is unclear whether screening for osteoporosis is cost-effective, and pharmacotherapies besides calcium and vitamin D (such as bisphosphonates) while effective can be very expensive. This question will need to be reassessed in the coming years as the burden of age-related bone disease increases in lower-income countries due to demographic changes and the prices of these medications fall.

While uncommon, rheumatoid arthritis is a severe debilitating condition that has cost-effective pharmacologic options. The authors recommend that care for this condition, which is complex, be managed by physicians (preferably specialist physicians) at outpatient departments of first-level hospitals. Branded biologics are probably not cost-effective in most countries, though the experience with developing “biosimilars” in middle-income countries suggests that these drugs may become attractive options in the near future.

Finally, there is an evolving evidence base for the role of specialized orthopedic surgical care in low- and middle-income countries. Selected elective repairs of severe injuries are likely to provide good value for money. However, similar to the case of cancer care (see Chapter 11 of *DCP3* Volume 3), in most countries, all that would be feasible by 2030 would be to establish a national-level orthopedic surgical center that could also serve as a hub for training. It is also important to note that demographic changes are increasing the incidence of (age-related) fragility fractures, a problem which has become a costly epidemic in many high-income countries. Low- and middle-income countries with an interest in orthopedic surgery need to be aware of the very large financial costs that will be incurred by expanding access to surgery for orthopedic trauma in older adults.

**Table 3B.4** Essential package of interventions for musculoskeletal disorders in low- and middle-income countries

Intersectoral policies	Population-based health services	Community	Health centers	First-level hospitals	Referral and specialty hospitals
1. Improvements to the built environment to encourage physical activity	3. Media campaigns to encourage nutrition and physical activity and to reduce tobacco and alcohol use	4. Training, retraining, and exercise programs that address musculoskeletal injuries and disorders	5. Calcium and vitamin D supplementation for primary prevention of osteoporosis in high-risk individuals*	7. Calcium and vitamin D supplementation for secondary prevention of osteoporosis	10. Urgent, definitive surgical management of orthopedic injuries (e.g., by open reduction and internal fixation)
2. Tobacco and alcohol control policies			6. Exercise programs for upper extremity injuries and disorders	8. Combination therapy, including low-dose corticosteroids and generic disease-modifying antirheumatic drugs (including methotrexate), for individuals with moderate to severe rheumatoid arthritis	11. Elective surgical repair of common orthopedic injuries (e.g., meniscal and ligamentous tears) in individuals with severe functional limitation
				9. Basic first-level hospital care for orthopedic injuries (e.g., closed reduction, external fixation)	

\* High-risk individuals are those with multiple risk factors including: advanced age, personal history of fracture, parental history of hip fracture, current tobacco use, excessive alcohol use, low body weight, or long-term glucocorticoid use (e.g., for rheumatoid arthritis).

## REFERENCES

1. WHO. Global Health Estimates (GHE). Geneva: World Health Organization; 2017.
2. Bamrungsawad N, Chaiyakunapruk N, Upakdee N, Pratoomsoot C, Sruamsiri R, Dilokthornsakul P. Cost-utility analysis of intravenous immunoglobulin for the treatment of steroid-refractory dermatomyositis in Thailand. *Pharmacoeconomics*. 2015;33(5):521-31.
3. Kostic M, Jovanovic S, Tomovic M, Milenkovic MP, Jankovic SM. Cost-effectiveness analysis of tocilizumab in combination with methotrexate for rheumatoid arthritis: a Markov model based on data from Serbia, country in socioeconomic transition. *Vojnosanit Pregl*. 2014;71(2):144-8.
4. Valle-Mercado C, Cubides MF, Parra-Torrado M, Rosselli D. Cost-effectiveness of biological therapy compared with methotrexate in the treatment for rheumatoid arthritis in Colombia. *Rheumatol Int*. 2013;33(12):2993-7.
5. Wu B, Wilson A, Wang FF, Wang SL, Wallace DJ, Weisman MH, et al. Cost effectiveness of different treatment strategies in the treatment of patients with moderate to severe rheumatoid arthritis in china. *PloS one*. 2012;7(10):e47373.
6. Wu B, Song Y, Leng L, Bucala R, Lu LJ. Treatment of moderate rheumatoid arthritis with different strategies in a health resource-limited setting: a cost-effectiveness analysis in the era of biosimilars. *Clin Exp Rheumatol*. 2015;33(1):20-6.
7. Brandao CM, Machado GP, Acurcio Fde A. Pharmacoeconomic analysis of strategies to treat postmenopausal osteoporosis: a systematic review. *Rev Bras Reumatol*. 2012;52(6):924-37.
8. Chen AT, Pedtke A, Kobs JK, Edwards GS, Jr., Coughlin RR, Gosselin RA. Volunteer orthopedic surgical trips in Nicaragua: a cost-effectiveness evaluation. *World J Surg*. 2012;36(12):2802-8.
9. Kingkaew P, Maleewong U, Ngarmukos C, Teerawattananon Y. Evidence to inform decision makers in Thailand: a cost-effectiveness analysis of screening and treatment strategies for postmenopausal osteoporosis. *Value Health*. 2012;15(1 Suppl):S20-8.
10. Panichkul S, Panichkul P, Sritara C, Tamdee D. Cost-effectiveness analysis of various screening methods for osteoporosis in perimenopausal Thai women. *Gynecol Obstet Invest*. 2006;62(2):89-96.
11. Turajane T, Chaweevanakorn U, Sungkhun P, Larbphiboonpong V, Wongbunnak R. Cost-utility analysis and economic burden of knee osteoarthritis treatment: the analysis from the real clinical practice. *J Med Assoc Thai*. 2012;95 Suppl 10:S98-104.
12. Falavigna A, Scheverin N, Righesso O, Teles AR, Gullo MC, Cheng JS, et al. Economic value of treating lumbar disc herniation in Brazil. *J Neurosurg Spine*. 2016;24(4):608-14.
13. Arreola Ornelas H, Rosado Buzzo A, Garcia L, Dorantes Aguilar J, Contreras Hernandez I, Mould Quevedo JF. Cost-effectiveness analysis of pharmacologic treatment of fibromyalgia in Mexico. *Reumatol Clin*. 2012;8(3):120-7.