BMJ Open

Cost–utility analysis of a multicomponent intervention for fibromyalgia syndrome in primary care versus usual clinical practice: study protocol for an economic evaluation of a randomised control trial

Victoria Mailen Arfuch ,[1,2] Carina Aguilar Martín,[1,3] Anna Berenguera ,[4,2] Rosa Caballol Angelats,[5,6] Noèlia Carrasco-Querol,[1] Gemma González Serra,[1,6] Maria Cinta Sancho Sol,[1,6] Immaculada Fusté Anguera,[5,6] José Fernández Sáez,[1] Alessandra Queiroga Gonçalves,[1,7] Marc Casajuana[4]

To cite: Arfuch VM, Aguilar Martín C, Berenguera A, *et al*. Cost–utility analysis of a multicomponent intervention for fibromyalgia syndrome in primary care versus usual clinical practice: study protocol for an economic evaluation of a randomised control trial. *BMJ Open* 2021;**11**:e043562. doi:10.1136/bmjopen-2020-043562

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-043562).

Received 07 August 2020
Revised 19 November 2020
Accepted 27 November 2020

For numbered affiliations see end of article.

Correspondence to
Mr Marc Casajuana;
mcasajuana@idiapjgol.org

ABSTRACT

Introduction Fibromyalgia syndrome (FMS) imposes a high cost on society. The significant economic burden from the use of healthcare and, especially, social resources is a spur to revising the usual clinical care (UCC) and to improving treatment strategies. FMS has a deleterious effect on the quality of life (QOL) and productivity, which considerably increase the indirect costs to society. This study reports an economic evaluation comparing the cost and health benefits in a multicomponent intervention programme and UCC of patients with FMS who attend primary healthcare centres of the Gerència Territorial Terres de L'Ebre region of Catalonia, Spain. This article is linked to the pre-results of a randomised control trial study on the implementation of this intervention programme (ClinicalTrials.gov: NCT04049006).

Method and analysis A cost–utility analysis will be conducted from a societal perspective. Quality-adjusted life years will be calculated from the results of the SF-36 questionnaire, a QOL measurement instrument. Direct and indirect healthcare costs will be obtained from official prices and reports published by the Spanish Public Health Administration and the National Statistics Institute. The incremental cost–utility ratio will be estimated to compare the two healthcare practices. Deterministic sensitivity analysis will also be used to compare different cost scenarios, modifying the items with the highest weight in the cost composition.

Ethics and dissemination The Clinical Research Ethics Committee of the IDIAPJGol Institute approved this study on 25 April 2018 (code P18/068) in accordance with the Helsinki/Tokyo Declaration. Information will be provided orally and in writing to participants, and their informed consent will be required. Participant anonymity will be guaranteed. The dissemination strategy includes publications in scientific journals and presentations in local and national media and at academic conferences.

Trial registration number: NCT04049006; Pre-results.

Strengths and limitations of this study

- This study will produce important and accurate information about the economic impact and health benefits of a new treatment strategy for fibromyalgia syndrome.
- The results of the analysis will help decision-makers to provide the best healthcare options and to consider stakeholders' opinions.
- The design of this study protocol is linked to a randomised control trial; it includes a broad perspective from society, and a 1-year horizon, which will enable long-term changes to be assessed.
- Although cost–utility analysis is a popular measurement tool, its methodological limitations make it controversial among some experts.
- The indirect-cost data source only includes patients who are linked to the social security system, which excludes self-employed and unemployed people, homemakers, and workers in the informal economy.

INTRODUCTION

Fibromyalgia is a chronic, medically unexplained syndrome that is characterised by persistent and widespread musculoskeletal pain, and that is also associated with psychological and social factors.[1–4] Disability is one of the main consequences of its impact on daily functioning, quality of life (QOL) and loss of productivity.[5] The prevalence of fibromyalgia syndrome (FMS) is significant in adults. A recent review suggests its prevalence in the general population of many countries ranges between 0.2% and 6.6%, and it is more frequent in women.[6] Specifically, it is present in 2.45% of the Spanish population.[7]

Therefore, healthcare for patients with this diagnosis is not only complicated from a clinical point of view but also costly from an economic perspective for both the health and social security systems.[5 8–13]

Available evidence has shown that FMS imposes a considerable cost on society, especially those associated with comorbidity and incapacity.[8 14–18] Among European countries, the estimated total annual costs of FMS were €7900 (direct €910, indirect €6990) for France, €7256 (direct €1765, indirect €5491) for Germany and €7814 (direct €5241, indirect €2573) for the Netherlands.[17 18] Additionally, FMS is responsible for the highest direct healthcare costs of all musculoskeletal conditions and chronic pain-related illnesses,[14] and higher rates of unemployment and number of days sick leave.[19]

In the Spanish context, the overall economic burden of FMS is considerable and has been estimated at more than €12 993 million annually.[20] According to the most recent data published by the Spanish National Institute of Social Security, the number of assigned temporary disabilities (short-term absenteeism because of days off sick) due to FMS has increased in recent years, as well as the average number of days of absence.[21] A cross-sectional and multicentre study involving a retrospective review of medical outpatient records in Catalonia between 2006 and 2007 showed that patients with FMS had considerably higher annual total costs of healthcare (including drugs, complementary tests, all types of medical visits, referrals and hospitalisations) and non-healthcare resource utilisation (sick leave days, and early retirement), under routine medical practice in the primary care setting, compared with a reference population. The study obtained an incremental adjusted per-patient per-year total cost of €5010 for patients with FMS, being €614 (12.3%) for direct costs and €4394 (87.7%) for indirect costs.[10]

In line with these findings, another cross-sectional study conducted in Spain, based on face-to-face patient interviews, encountered a mean total cost per patient per year of €9982, comprising €3245.8 (32.5%) of direct healthcare costs and €6736.2 (67.5%) of indirect costs attributable to productivity losses.[11] This study also showed that: (1) non-pharmacological therapies accounted for the highest costs of direct healthcare resources, involving three times more than the cost of drug treatments; (2) there was a significant direct association between disease severity and total costs; and (3) patients with a permanent working disability made the most extensive use of resources.[11] However, these findings were collated over a decade ago, and are in need of updating with reference to the Spanish public health system.

Health economic evaluation is essential in policy decision-making since it provides evidence enabling the efficiency of an intervention, programme, or project to be determined, thereby making it possible to optimise the benefits from limited resources.[22] Of the economic evaluation techniques, cost–utility analysis (CUA) estimates how much well-being is achieved for each monetary unit invested, taking into account both health outcomes and costs. This technique is a useful tool for comparing intervention strategies, especially those with quite different health outcomes because a standard utility unit is commonly used to measure all of them: the quality-adjusted life year (QALY).[23] Despite its limitations, especially in measuring the value that society attaches to different health status, CUA is better than other economic evaluation strategies and provides useful information for resource allocation processes.[24]

The economic evaluation of intervention programmes for FMS has been little studied. According to the published findings, non-pharmacological strategies, especially psychology-based therapies, have yielded positive results in terms of reducing the economic burden of FMS.[19 25–31] In Spain, some cost–utility studies comparing alternative interventions (ie, psychoeducational therapy, acceptance and commitment therapy, internet-delivered exposure therapy, and mindfulness-based stress reduction) with usual drug treatment have demonstrated the cost–utility from a healthcare and social perspective.[19 26–28 30] However, only the FibroQoL study has included a multicomponent intervention (MI) modality, and it had significant technical and methodological differences compared with the current proposal.[26 32]

This study aims to perform a CUA on an MI consisting of health education, physical activity, and cognitive-behavioural therapy, for patients with FMS compared with their treatment under usual clinical care (UCC),[33] provided within the 11 primary care centres of the Gerència Territorial Terres de L'Ebre of the Institut Català de la Salut, Spain. The results of this economic assessment are expected to support the evidence of the randomised clinical trial (RCT) related to this project[34] (ClinicalTrials.gov: NCT04049006).[35] It is hoped that this new proposed intervention will reinforce the UCC, enhance patients' QOL, and promote the efficient allocation of health and social resources.

METHOD

Design

This study protocol has been drafted based on a literature review and following the recommendations of the Consolidated Health Economic Evaluation Reporting Standards[36] about preliminary results. The UK Medical Research Council guidance[37] for complex interventions has been taken into account in planning the RCT study.

The design of this economic evaluation study requires a CUA to be conducted from a societal perspective so that indirect non-medical cost variables are included. Health outcomes and costs will be assessed over a 12-month duration to ensure that long-term outcomes are measured. This methodological decision is based on the clinical symptoms of FMS, its consequences, its tendency to chronicity, and the fact that its treatment is associated with ongoing clinical management.

The human capital approach has been judged the most suitable method for this study due to the limitations of

the data source, given that only full sick days, prescribed by the general practitioner (GP), and the period with a medical disability can be extracted from the computerised medical history programme (eCAP).

The elements to be compared in this study are the UCC[21 33 38 39] for patients with FMS, and the UCC plus an MI provided in primary care centres. The MI consists of a 12-week group programme of 2 hours per week combining: 7 health education instructions, 11 items of physical activity and physical health training, and 7 interventions of psychological therapy based on cognitive-behavioural strategies and pain management. Group therapy is being delivered by the GP specialised in FMS, the physiotherapist, and the psychologist, with the support of the head nurses of each health centre involved.

Study population

The patients recruited for the study sample are shortlisted from the electronic medical records system eCAP of the Catalan Health Service (CatSalut) and the Institut Català de la Salut. Only the medical records of the 11 primary care centres of the Gerència Territorial Terres de L'Ebre in Catalonia, Spain, are included. Patients are allocated at random to study groups from lists provided by the health centres in order to obtain a representative sample giving patient's sociodemographic diversity throughout the territory. The inclusion criteria are set out in detail in the RCT protocol study.[34]

Patient and public involvement

Neither patients nor the public will be involved in the design or execution of our research, or the reporting and dissemination of its results.

Outcomes measures and data collection

Health outcomes

The utilities will be obtained based on the results of the health-related QOL SF-36 questionnaire[40] (Optum, license number QM048943) and the QALY estimates. This measurement instrument is administered to the study sample at baseline, immediately after the intervention, and at 6 and 12 months of follow-up. Sociodemographic and clinical variables are registered at baseline and are fully described in the RCT study protocol.[35] A software application, specially designed for the study and linked to digital medical records, is employed to register the collected data.

Cost outcomes

Direct and indirect costs, related to the use of health and social resources, will be estimated in euros (€) based on the official prices for the public sector, which are published in the Diari Oficial de la Generalitat de Catalunya (DOGC)[41] (updated in 2019), and in the Spanish National Statistics Institute (NSI), respectively. Table 1 shows the cost variables and data sources that will be collected retrospectively, 12 months before the start date, and 12 months after the end of the MI.

Direct costs include visits to primary care services, other professional referrals, and emergency services, clinical tests for diagnosis and medical follow-up, pharmacological treatments, and hospitalisations. Costs will be calculated based on unit service prices, which will be obtained from the DOGC. Additionally, drug prices will be obtained from the Council of Pharmaceutical Colleges of Catalonia.

Indirect non-medical costs include temporary and permanent disability. As stated in the Spanish General Law of Social Security (Law 20/2014; Royal Legislative Decree 8/2015),[42] the term 'temporary disability' refers to sick leave days due to short-term common or professional illness, whereas 'permanent disability' refers to the impossibility of working due to the permanent and total or partial loss of working capacity in the long-term. In the former case, a GP determines whether a patient is unable to work in the short term. In the latter case, a medical board conducts an in-depth assessment of the medical background, including the physical and mental condition of the person, in order to determine whether a permanent disability should be declared. These measurements will be estimated from the number of full sick leave days and the months spent with a disability, respectively.

We will not collect data on other non-medical costs, such as presenteeism and unpaid lost time, because of the limitations of the data available from our data source (eCap).

The weighted price of the social costs will be determined by calculating a total annual average salary (including regular and extra payments) for the Catalonia region, based on the official records of the NSI.[43] This estimate will take into account part-time and full-time working schedules, and all activity sectors (industry, construction, and all services except housework).

Data collection is expected to be completed by April 2021.

Sample size

In order to detect a score difference of at least five points in the SF-36 questionnaire, it has been calculated that 260 participants (130 subjects per study arm) are needed to ensure an adequate sample size, assuming an α error of 0.05, a β error of 0.05 in a bilateral contrast, and a dropout rate of 20%.[34] Consequently, between 10 and 13 MI groups, with their respective control groups (UCC), including 10–12 patients per group, are required.

Statistical analysis

SPSS V.25 and Stata V.15 for Windows will be used for the statistical analyses. First, a descriptive analysis of the sample will be carried out that will compare the characteristics of the two study arms.

As an economic evaluation outcome measure, the incremental ratio of the cost–utility will be estimated, dividing the difference in total mean costs in both UCC and MI by the differences in QALYs of each study arm. 95% CIs will be calculated for all parameter estimates.

Table 1 Cost outcome measurements and data collection

Cost outcomes				
Cost outcome	**Cost outcome description**	**Data source**	**Cost data source**	**Cost calculation**
Direct healthcare costs				
Primary care visits	► General practitioner ► Nurse ► Physiotherapist ► Psychologists	eCAP	DOGC	Number of visits×price
Professional referral visits	► Traumatology ► Psychiatry ► Rehabilitation ► Other specialities	eCAP	DOGC	Number of visits×price
Clinical tests	► Blood test ► Diagnostic imaging techniques ► Other tests	eCAP	DOGC	Test performed x price
Pharmacological prescriptions	► Muscle relaxants -Analgesics ► Corticoids ► Antidepressants ► Anxiolytics ► Antiseizure -Gastric protectors ► Other drugs	eCAP	Council of Pharmaceutical Colleges of Catalonia	Medicines bought ×price
Emergency visits		eCAP	DOGC	Number of visits×price
Hospitalizations		eCAP	DOGC	Number of hospitalisation days×price
Indirect non-medical costs				
Temporary disability (TD)		eCAP	NS	Number of full sick leave days×salary
Permanent disability (PD)		eCAP	NSI	Number of months with PD×salary

DOGC, Diario Oficial de la Generalitat de Catalunya; eCAP, computerised medical history programme; NSI, Spanish National Statistics Institute.

To avoid possible biases as far as possible, the intention-to-treat principle will be applied in order not to affect the random distribution. In addition, to address the loss of follow-up and non-response, multiple imputation approaches to substitute missing values will be implemented.

Sensitivity analysis

A deterministic sensitivity analysis will be performed to assess the robustness of the results.[44] Items with a higher cost will be modified in order to compare them with the initial results.

DISCUSSION

This study aims to address FMS as a public health problem with economic repercussions.[10] FMS compromises the health status of a considerable number of people, who consequently consume substantial health and social resources in the short and long terms. Therefore, this study is expected to support the inclusion of an MI for FMS in primary care settings in order to improve patient QOL and to reduce its economic burden.

The literature review indicates that the indirect costs attributable to sick leave and permanent work disability exceed the direct costs of healthcare.[8–11 14–20] Therefore, preventing productivity loss should be prioritised since this imposes the highest cost on the community. This study adopts a societal perspective, including indirect non-medical cost variables that will allow us to assess the impact of the burden of FMS on the social security system.

More accurate methods, such as the friction cost approach, have been acknowledged as being effective for estimating productivity costs. However, the human capital approach has been considered the most suitable for this study, given the data available. However, a sensitivity analysis will be performed to assess alternative cost scenarios that take into account the limitations of this methodological approach. It will include different direct healthcare

costs and, if necessary, the weighted price of the social cost, considering that the salary rate will be an overall annual average estimate without distinction between the type of activity or the working schedule.

Additionally, another economic concern involves the costs of the diagnostic process since it is purely clinical.[45] Before FMS is diagnosed, other possible diseases must be ruled out with objective tests and by a variety of medical specialists. This process is often long and exhausting for patients, frustrating for doctors, and expensive from the perspective of the health system.[46] Furthermore, the presence of comorbidities can hinder and delay the diagnosis, as well as complicating the choice of a treatment strategy.[47] Hence, the study sample could show differences in the use of resources between patients depending on the year of diagnosis and the medical records. However, it is expected that the randomised allocation will balance these differences between the study arms.

Given the evidence about the economic burden of FMS,[8 14–21] particularly related to the loss of productivity, UCC does not seem to be entirely helpful for reducing the effects of chronicity or for preventing disability. Thus, FMS treatment should not be limited to short-term pain relief. It should also promote the acceptance of the condition, the self-management of symptoms, and empowering patients to deal with FMS in their daily lives. Non-pharmacological approaches could address the consequences of chronicity, reducing healthcare over-provision and overmedication. Indeed, the proposed MI aims to address these challenges by combining physical, psychological, and health educational methods.

Findings regarding the efficacy of MI for patients with this condition have proved helpful for improving QOL, physical function, psychological variables, and or pain after 3–12 months of follow-up.[48–53] However, more studies are required to address the economic efficiency of this type of intervention, particularly in the context of the Spanish public health system.

Evidence of efficiency is essential for decision-making in order to allow budgets to be prioritised for those treatment options that prove to be cost-efficient and to fulfil patients' health needs. Economic evaluation is key to overcoming the obstacles arising from the uncertainty about the real costs and the sustainability of particular interventions.[54] The CUA is a popular measurement tool that combines quantity data and QOL, based on the opinions of the healthcare users, associated with a monetary cost. It involves a participatory and economic evidence-based decision-making strategy that considers stakeholders' preferences.[55] However, this methodology is controversial,[56] the main points of contention being: (1) the lack of transparency about data collection and analysis regarding the measurement of the value that society assigns to a state of health; (2) that the gain in health depends on the severity of the condition, so the value is affected by patients' perception of their pain and health status; (3) the limited value of this measurement tool for long-term diseases such as FMS, where disability accumulates over time since it assumes that the utility of a health state is independent of the time the patient has experienced it, and the influence of previous and subsequent health conditions.[24] Although all these factors pose methodological challenges, CUA is still a valid and effective strategy for carrying out health economic evaluations and collaborating with decision-makers in choosing between intervention alternatives.[24]

Another limitation related to the instruments and the data collection stems from the QOL being a multifactorial variable that could be influenced by non-medical circumstances such as family dynamics, working conditions, and economic and political contexts, among others.[57] Sociodemographic variables will therefore be analysed in the models in order to control for these possible effects.

This health region covers a wide and varied territory. However, all the primary care centres participating in the study are run by the public health administration, meaning that clinical care protocols and direct medical costs are both standardised according to official regulations and will be homogeneous for the entire sample.

Regarding the indirect costs, only those people who are linked to the social security system and who have access to its benefits will be able to provide data about productivity costs. The study sample, therefore, excludes self-employed and unemployed people, homemakers, and workers in the informal economy. In this sense, although the human capital approach could overestimate productivity costs, it could be offset by the missed data of these population subgroups that contribute to the productivity loss to society due to the side effects of their illness.

Finally, this study could be affected by sample loss to follow-up given the 1-year time horizon. This methodological characteristic is also a strength of the study since it will allow long-term changes to be assessed. In order to minimise the number of participants abandoning the study, reminders of upcoming interviews will be sent, and different data collection methods, such as telephone calls and online survey platforms, may even be used.

If the results indicate that the intervention is utility cost effective, this study will support, through efficiency evidence, the inclusion of an MI as part of the usual practice for FMS in primary care centres in Catalonia, Spain. Additionally, enhancements of patient QOL and cost reductions for health and social resources are expected. We hope that this new proposed intervention could be replicated throughout the rest of Catalonia and Spain, and used more extensively as a guide within other European health systems.

ETHICS AND DISSEMINATION

This study was designed in accordance with the Helsinki/Tokyo Declaration. It was approved by the Clinical Research Ethics Committee of the Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (IDIAPJGol), on 25 April 2018 (code P18/068). Information is delivered to participants orally

and in writing before their necessary informed consent is obtained. This project respects the data protection laws guaranteeing participant anonymity. Dissemination strategy includes publications in scientific journals and through presentations in the local and national media and at academic conferences.

Author affiliations
[1]Unitat de Suport a la Recerca Terres de l'Ebre, IDIAP Jordi Gol, Barcelona, Catalunya, Spain
[2]Department of Pediatrics, Obstetrics and Gynecology, and Preventive Medicine, Universitat Autonoma de Barcelona, Barcelona, Catalunya, Spain
[3]Unitat d'Avaluació, Direcció d'Atenció Primària Terres de l'Ebre, Institut Català de la Salut, Tortosa, Catalunya, Spain
[4]Central Research Unit, IDIAP Jordi Gol, Barcelona, Catalunya, Spain
[5]Equip d'Atenció Primària Tortosa Est, Institut Català de la Salut, Tortosa, Catalonia, Spain
[6]Unitat d'Expertesa en Síndromes de Sensibilització Central Terres de l'Ebre, Institut Català de la Salut, Tortosa, Catalonia, Spain
[7]Unitat Docent de Medicina de Família i Comunitària Tortosa-Terres de L'Ebre, Institut Català de la Salut, Tortosa, Catalonia, Spain

Correction notice This article has been corrected since it first published. The provenance and peer review statement has been included.

Twitter Anna Berenguera @ABerenguera

Acknowledgements All authors thank the contributions of the Institut Català de la Salut, especially those of the Gerència Territorial Institut Catalá de la Salut Terres de l'Ebre, the Direcció d'Atenció Primària de Terres de l'Ebre, and the Unitat de Sistemes d'informació de la Gerència Territorial Terres de l'Ebre. The participation and support of all the healthcare and non-healthcare professionals involved in implementing this study and collecting the data are appreciated.

Contributors VMA, MC, CAM, AB, JFS and AQG designed the study. VMA wrote the draft versions, which all the other authors reviewed. RCA, NC-Q, GGS, MCSS, IFA, AQG, AB, CAM, JFS and VMA are involved in the development of the general project and the RCT study from which this qualitative study is related.

Funding This project was funded by a research grant from the Instituto de Salud Carlos III (ISCIII), awarded in 2018, with reference PI1800943, as part of the Health Strategy Action 2017–2020 within the National Research ProgramProgramme; the Technical, Scientific and Innovation Research National Plan 2017–2020. It is also co-funded by the European Union ERDF (European Regional Development Fund). VMA received a predoctoral grant for training in health research from the ISCIII (2019; reference FI19/00254). This project also received funding through a scholarship from the Dr Ferran Foundation in 2017. The funders financed the project but will not participate in any phase of the research, and will have no authority over any of the project's activities.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Victoria Mailen Arfuch http://orcid.org/0000-0001-5935-6907
Anna Berenguera http://orcid.org/0000-0002-0889-2002

REFERENCES

1 Wolfe F, Smythe HA, Yunus MB, *et al*. The American College of rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria Committee. *Arthritis Rheum* 1990;33:160–72.
2 Wolfe F, Clauw DJ, Fitzcharles M-A, *et al*. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR preliminary diagnostic criteria for fibromyalgia. *J Rheumatol* 2011;38:1113–22.
3 Wolfe F, Clauw DJ, Fitzcharles M-A, *et al*. 2016 revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum* 2016;46:319–29.
4 Helfenstein M, Goldenfum MA, Siena CAF. Fibromyalgia: clinical and occupational aspects. *Rev Assoc Med Bras* 2012;58:358–65.
5 Skaer TL. Fibromyalgia: disease synopsis, medication cost effectiveness and economic burden. *Pharmacoeconomics* 2014;32:457–66.
6 Marques AP, Santo AdeSdoE, Berssaneti AA, *et al*. Prevalence of fibromyalgia: literature review update. *Rev Bras Reumatol Engl Ed* 2017;57:356–63.
7 Seoane-Mato D, Sánchez-Piedra C, Silva-Fernández L, *et al*. Prevalence of rheumatic diseases in adult population in Spain (EPISER 2016 study): aims and methodology. *Reumatol Clin* 2019;15:90–6.
8 Robinson RL, Birnbaum HG, Morley MA, *et al*. Economic cost and epidemiological characteristics of patients with fibromyalgia claims. *J Rheumatol* 2003;30:1318–25.
9 Epidemiology SM. Costs, and the economic burden of fibromyalgia. *Arthritis Res Ther* 2009;11:2–3.
10 Sicras-Mainar A, Rejas J, Navarro R, *et al*. Treating patients with fibromyalgia in primary care settings under routine medical practice: a claim database cost and burden of illness study. *Arthritis Res Ther* 2009;11:1–14.
11 Rivera J, Rejas J, Esteve-Vives J, *et al*. Resource utilisation and health care costs in patients diagnosed with fibromyalgia in Spain. *Clin Exp Rheumatol* 2009;27:S39–45.
12 Thompson JM, Luedtke CA, Oh TH, *et al*. Direct medical costs in patients with fibromyalgia: cost of illness and impact of a brief multidisciplinary treatment program. *Am J Phys Med Rehabil* 2011;90:40–6.
13 Vervoort VM, Vriezekolk JE, Olde Hartman TC, *et al*. Cost of illness and illness perceptions in patients with fibromyalgia. *Clin Exp Rheumatol* 2016;34:S74–82.
14 White KP, Speechley M, Harth M, *et al*. The London fibromyalgia epidemiology study: direct health care costs of fibromyalgia syndrome in London, Canada. *J Rheumatol* 1999;26:885–9.
15 Berger A, Dukes E, Martin S, *et al*. Characteristics and healthcare costs of patients with fibromyalgia syndrome. *Int J Clin Pract* 2007;61:1498–508.
16 Berger A, Sadosky A, Dukes EM, *et al*. Patterns of healthcare utilization and cost in patients with newly diagnosed fibromyalgia. *Am J Manag Care* 2010;16:S126–37.
17 Boonen A, van den Heuvel R, van Tubergen A, *et al*. Large differences in cost of illness and wellbeing between patients with fibromyalgia, chronic low back pain, or ankylosing spondylitis. *Ann Rheum Dis* 2005;64:396–402.
18 Winkelmann A, Perrot S, Schaefer C, *et al*. Impact of fibromyalgia severity on health economic costs. *Appl Health Econ Health Policy* 2011;9:125–36.
19 Feliu-Soler A, Borràs X, Peñarrubia-María MT, *et al*. Cost-Utility and biological underpinnings of Mindfulness-Based stress reduction (MBSR) versus a psychoeducational programme (FibroQoL) for fibromyalgia: a 12-month randomised controlled trial (EUDAIMON study). *BMC Complement Altern Med* 2016;16:1–16.
20 Cabo-Meseguer A, Cerdá-Olmedo G, Trillo-Mata JL. Fibromyalgia: prevalence, epidemiologic profiles and economic costs. *Med Clin* 2017;149:441–8.
21 Instituto Nacional de la Seguridad social. Guia de actualización en La valoración de fibromialgia, sÍndrome de fatiga crónica, sensibilidad química múltiple Y electrosensibilidad. *Segunda Edición* 2019 https://www.semg.es/images/documentos/guia_fibromialgia_2019.pdf
22 Chisholm D, Evans DB. Economic evaluation in health: saving money or improving care? *J Med Econ* 2007;10:325–37.
23 Franklin M. Cost utility analysis. in: mental health economics: the costs and benefits of psychiatric care. *Cham. Springer International Publishing* 2017:89–119.
24 Mccabe C. What is cost-utility analysis? *Hayward Med Commun* 2009:1–6 http://www.bandolier.org.uk/painres/download/whatis/What_is_cost-util.pdf
25 Goossens ME, Rutten-van Mölken MP, Leidl RM, *et al*. Cognitive-educational treatment of fibromyalgia: a randomized clinical trial. II. economic evaluation. *J Rheumatol* 1996;23:1246–54.

26 Luciano JV, Sabes-Figuera R, Cardeñosa E, *et al*. Cost-Utility of a psychoeducational intervention in fibromyalgia patients compared with usual care: an economic evaluation alongside a 12-month randomized controlled trial. *Clin J Pain* 2013;29:702–11.
27 Luciano JV, D'Amico F, Cerdà-Lafont M, *et al*. Cost-Utility of cognitive behavioral therapy versus U.S. food and drug administration recommended drugs and usual care in the treatment of patients with fibromyalgia: an economic evaluation alongside a 6-month randomized controlled trial. *Arthritis Res Ther* 2014;16:1–17.
28 Luciano JV, D'Amico F, Feliu-Soler A, *et al*. Cost-Utility of group acceptance and commitment therapy for fibromyalgia versus recommended drugs: an economic analysis alongside a 6-month randomized controlled trial conducted in Spain (EFFIGACT study). *J Pain* 2017;18:868–80.
29 Hedman-Lagerlöf M, Hedman-Lagerlöf E, Ljótsson B, *et al*. Cost-Effectiveness and cost-utility of internet-delivered exposure therapy for fibromyalgia: results from a randomized, controlled trial. *J Pain* 2019;20:47–59.
30 Pérez-Aranda A, D'Amico F, Feliu-Soler A, *et al*. Cost–Utility of Mindfulness-Based stress reduction for fibromyalgia versus a multicomponent intervention and usual care: a 12-month randomized controlled trial (EUDAIMON study). *JCM* 2019;8:1068.
31 D'Amico F, Feliu-Soler A, Montero-Marín J, *et al*. Cost-Utility of Attachment-Based compassion therapy (ABCT) for fibromyalgia compared to relaxation: a pilot randomized controlled trial. *J Clin Med* 2020;9:726.
32 Luciano JV, Martínez N, Peñarrubia-María MT, *et al*. Effectiveness of a psychoeducational treatment program implemented in general practice for fibromyalgia patients: a randomized controlled trial. *Clin J Pain* 2011;27:383–91.
33 Celaya M, Ibáñez D, Laseca N. Guia per a l'avaluació de la fibromi lgia i de la síndrome de fatiga crònica. *Generalitat de Catalunya*, 2017. Available: https://canalsalut.gencat.cat/web/.content/_A-Z/F/fibromialgia/documents/guia_avaluacio_fibromialgia_fatiga_cronica.pdf [Accessed 20 Feb 2020].
34 Caballol Angelats R, Gonçalves AQ, Aguilar Martín C, *et al*. Effectiveness, cost-utility, and benefits of a multicomponent therapy to improve the quality of life of patients with fibromyalgia in primary care. *Medicine*2019;98:e17289.
35 Caballol Angelats R, Gonçalves AQ, Aguilar Martín C, *et al*. Effectiveness, cost-utility, and benefits of a multicomponent therapy to improve the quality of life of patients with fibromyalgia in primary care: a mixed methods study protocol. *Medicine* 2019;98:e17289.
36 Husereau D, Drummond M, Petrou S, *et al*. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)--explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value Health* 2013;16:231–50.
37 Craig P, Dieppe P, Macintyre S, *et al*. Developing and evaluating complex interventions: the new medical Research Council guidance. *Int J Nurs Stud* 2013;50:587–92.
38 Nishishinya Aquino B, Requeijo Lorenzo C, Roqué Fíguls M. Evaluación Y abordaje de la fibromialgia. Actualización de las evidencias científicas. *Barcelona. Ministerio de Sanidad, Servicios Sociales e Igualdad. Agència de Qualitat i Avaluació Sanit ries de Catalunya. Departament de Salut. Generalitat de Catalunya* 2017. (Informes de Evaluación de Tecnologías Sanitarias) https://aquas.gencat.cat/web/.content/minisite/aquas/publicacions/2017/Fibromialgia_actualizacion_RedETS2017.pdf
39 Gándara M, Muñoz G. Evaluación Y abordaje de la fibromialgia Y El síndrome de fatiga crónica. Día Mundial de la Fibromialgia Y El Síndrome de Fatiga Crónica. *Oficial Nacional de Salud Pública-AEMPPI Ecuador* 2017 https://www.elsevier.com/es-es/connect/actualidad-sanitaria/dia-mundial-de-la-fibromialgia-y-el-sindrome-de-fatiga-cronica?aaref=https%3A%2F%2Fwww.google.com%2F
40 Alonso J*et al*. Versión española de SF-36v2TM health survey © 1996, 2000, adapted by J. Alonso, et al. *Heal Surv* 2003:1–8 http://www.ser.es/wp-content/uploads/2015/03/SF36_CUESTIONARIOpdf.pdf
41 Catalunya Gde. Diari Oficial de la Generalitat de Catalunya. Available: https://dogc.gencat.cat/es
42 España Gde. Real Decreto 8/2015 POR El que Se aprueba El texto refundido de la Ley General de la Seguridad social. *Boletín Oficial del Estado* 2015:1–157 http://www.boe.es/boe/dias/1994/06/29/pdfs/A20658-20708.pdf
43 Estadística INde. (ine). Coste laboral POR trabajador, comunidad autónoma, sectores de actividad. Available: https://www.ine.es/jaxiT3/Tabla.htm?t=6061 [Accessed 20 Mar 2020].
44 Andronis L, Barton P, Bryan S. Sensitivity analysis in economic evaluation: an audit of NICE current practice and a review of its use and value in decision-making. *Health Technol Assess* 2009;13.
45 Wang S-M, Han C, Lee S-J, *et al*. Fibromyalgia diagnosis: a review of the past, present and future. *Expert Rev Neurother* 2015;15:667–79.
46 Briones-Vozmediano E. The social construction of fibromyalgia as a health problem from the perspective of policies, professionals, and patients. *Glob Health Action* 2017;10:1275191.
47 Lichtenstein A, Tiosano S, Amital H. The complexities of fibromyalgia and its comorbidities. *Curr Opin Rheumatol* 2018;30:94–100.
48 Giusti EM, Castelnuovo G, Molinari E. Differences in multidisciplinary and interdisciplinary treatment programs for fibromyalgia: a mapping review. *Pain Res Manag* 2017;2017:1–19.
49 Bourgault P, Lacasse A, Marchand S, *et al*. Multicomponent interdisciplinary group intervention for self-management of fibromyalgia: a mixed-methods randomized controlled trial. *PLoS One* 2015;10:e0126324.
50 Ollevier A, Vanneuville I, Carron P. A 12-week multicomponent therapy in fibromyalgia improves health but not in concomitant moderate depression, an exploratory pilot study. *Disabil Rehabil* 2019;0:1–8.
51 Martín J, Torre F, Padierna A, *et al*. Six-and 12-month follow-up of an interdisciplinary fibromyalgia treatment programme: results of a randomised trial. *Clin Exp Rheumatol* 2012;30:103–11.
52 Saral I, Sindel D, Esmaeilzadeh S, *et al*. The effects of long- and short-term interdisciplinary treatment approaches in women with fibromyalgia: a randomized controlled trial. *Rheumatol Int* 2016;36:1379–89.
53 Stein KF, Miclescu A. Effectiveness of multidisciplinary rehabilitation treatment for patients with chronic pain in a primary health care unit. *Scand J Pain* 2013;4:190–7.
54 Eisman AB, Kilbourne AM, Dopp AR, *et al*. Economic evaluation in implementation science: making the business case for implementation strategies. *Psychiatry Res* 2020;283:112433.
55 Anneliese P, Hoch J. Understanding cost-utility analysis in health care. *Univ Toronto Med J* 2006;83(2 http://utmj.org/index.php/UTMJ/article/view/734
56 McGregor M. Cost-Utility analysis: use QALYs only with great caution. *CMAJ* 2003;168:433–4.
57 Tarter T, Johnson G, Johnson R. Neuropsychology of Cancer and Oncology.. In: Noggle CA, Dean RS, eds. New York: Springer Publishing Company, 2013: 3–5.