ECONOMIC EVALUATIONS AND HEALTH ECONOMIC MODELS OF SOFT TISSUE SARCOMAS: SYSTEMATIC LITERATURE REVIEW FROM A EUROPEAN AND NORTH AMERICAN PERSPECTIVE

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INTRODUCTION

- Soft tissue sarcomas (STS) are a group of solid tumors with over 50 histologic subtypes. They account for <1% of all new malignancies in adults and ~2% of cancer-related mortality[1].
- Prognosis for advanced STS is generally poor with a median overall survival of around 12-18 months [2].
- Surgery is the primary therapeutic option and may be supplemented with radiotherapy and/or chemotherapy either in the neo-adjuvant or in the adjuvant setting when the risk of recurrence/death is high, however, most patients develop local recurrence or metastases after surgery [3,4].
- **In the field of STS, there is no publicly available systematic literature review (SLR) on economic evaluations.**

OBJECTIVES

This SLR aimed to explore the literature on economic evaluations and health economic models related to STS.

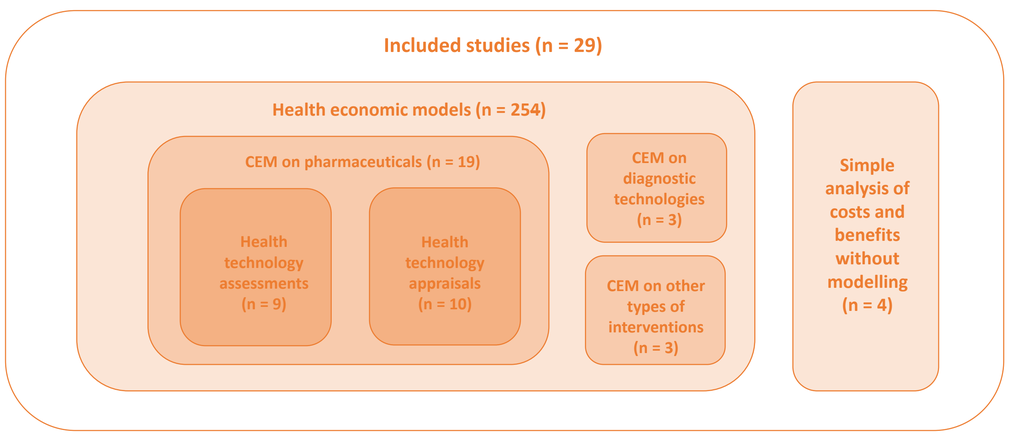
METHODS

- The literature search was performed on 22nd of August 2023, covering Medline, Embase, Scopus, Cochrane Library and PROSPERO with no restriction on publication date.
- Studies were considered eligible and selected for inclusion if they included patients with STS and contained data related to economic evaluations with a geographical focus on Europe and North America.
- Title and abstract screening, full-text screening, and data extraction were performed in Covidence.
- To increase the sensitivity and comprehensiveness of the SLR, backward and forward snowball searches and grey literature searches were also conducted.
- **The SLR protocol was registered in PROSPERO (ID: CRD42023483406)** [5].

RESULTS OF THE LITERATURE SEARCH

- The review of 1,638 records (852 peer-reviewed articles, 756 hits from snowball search, 30 records from grey literature search) resulted in 22 peer-reviewed articles, 5 HTA agency documents and 2 ISPOR posters.
- Of total 29 included studies, 25 reported information about a health economic model and 4 used a simple calculation of costs and benefits based on a clinical study without economic modelling.
- Cost-utility analysis was performed in 22 studies, where cost per quality adjusted life years (QALY) gain was the main outcome.
- Out of the 25 studies with economic models, 19 papers investigated pharmaceutical therapies, the majority (n=18) investigated trabectedin, pazopanib or olaratumab, while 3 studies focused on diagnostic technologies and 3 on other type of interventions.
- Out of the 19 studies investigated pharmaceuticals, 9 were original studies of economic evaluations and 10 were technology appraisals. (**Figure 1**)

FIGURE 1: CLASSIFICATION OF INCLUDED STUDIES



CEM: cost-effectiveness model

RESULTS OF HEALTH ECONOMIC MODELS ON PHARMACEUTICAL THERAPIES

- We identified 9 studies, where original health economic evaluations were reported (**Table 1**).
- Most studies were conducted in Europe (n = 7), while the 2 studies were from the USA and Canada.
- All European studies had a health care system perspective, the study from Canada also applied a societal perspective and the USA study used a private payer perspective.
- Advanced and previously treated STS was investigated in 5 studies, while another studies included patients with previously treated metastatic STS or advanced / metastatic leiomyosarcomas.
- Pazopanib or trabectedin were investigated in 8 studies, while the remaining study investigated the olaratumab + doxorubicin combination.
- The simulation of the patients was highly simplified; the "traditional" 3-state Markov cohort or partitioned-survival modelling approach (health states: progression-free; progressed; dead) was used in 7 cases, while the remaining studies applied a decision-tree and an analytical model without details.
- Majority of studies (n = 8) reported incremental cost per QALY gains and 5 of them reported incremental cost per incremental life-years (LY) gained as well. One study only reported incremental cost per progression-free life years gained.

TABLE 1: ECONOMIC EVALUATION STUDIES INVESTIGATING PHARMACEUTICAL THERAPIES

Reference	Study country	Patient population	Investigated vs. comparator therapy	Model type	Time horizon
Amdahl, 2014	UK	Previously treated, advanced STS	Primary analysis: Pazopanib vs. Placebo Secondary analysis: Pazopanib vs. Trabectedin vs. Ifosfamide vs. Gemcitabine + docetaxel	1) Partitioned survival model 2) Markov cohort model	10 years
Daupin, 2017	France	Previously treated, advanced STS	Trabectedin vs. End-stage treatment	Decision tree cohort model*	NA
Delea, 2014	Canada	Previously treated, advanced STS	Pazopanib vs. Placebo	1) Markov cohort model 2) Partitioned survival model	10 years
Fernandez, 2017**	Scotland	Advanced, metastatic leiomyosarcomas	Trabectedin vs. Pazopanib	Analytical model without details	Lifetime
Guest, 2013	Italy, Spain, Sweden	Advanced STS patients with first-line treatment	Trabectedin vs. Doxorubicin + Ifosfamide	Markov simulation	2 years
Soini, 2011	Finland	Previously treated metastatic STS	Trabectedin vs. End-stage treatment	Markov cohort model	5 years
Verboom, 2019	the Netherlands	Previously treated, advanced STS***	Trabectedin vs. Ifosfamide	Partitioned survival model*	Lifetime
Villa, 2015	Spain	Previously treated, advanced STS	Pazopanib vs. Trabectedin	Partitioned survival model	10 years
Zuluaga-Sanchez, 2018	USA	Anthracycline-naïve advanced STS****	Olaratumab + Doxorubicin vs. Different alternatives***	Partitioned survival model	25 years

STS: soft tissue sarcoma; *Assumed from the model structure figure and description; **Conference poster available only; *** Sub-groups: L-sarcomas (leiomyosarcoma and liposarcoma); non-L-sarcomas; ***Different alternatives: Doxorubicin; Doxorubicin + Ifosfamide + Mesna; Gemcitabine + Docetaxel; Doxorubicin + Ifosfamide + Mesna + Dacarbazine; alternative dosing of Gemcitabine + Docetaxel; Pegylated Liposomal Doxorubicin; ****Both first or subsequent line of systemic therapy was possible for the patients

RESULTS OF HEALTH ECONOMIC MODELS ON DIAGNOSTIC TECHNOLOGIES

- We identified 3 studies, where diagnostic technologies were evaluated for STS patients (**Table 2**).
- All studies were conducted in the USA.
- Two studies used Markov cohort model design, and both studies reported incremental cost per QALY gained as an outcome. These studies had 3 health states: no evidence of disease, recurrence and death.
- One study applied decision tree cohort model with incremental cost per additional patient with pulmonary metastases detected outcome.
- The studies compared different various strategies for diagnosis and surveillance.

TABLE 2: STUDIES INVESTIGATING DIAGNOSTIC TECHNOLOGIES

Reference	Study country	Patient population	Investigated technologies	Model type	Time horizon
Chau, 2020*	USA	Patients with STS who had completed definitive treatment for stage II or III primary disease	Periodic chest x-ray vs. CT	Markov cohort model	3 years
Porter, 2002	USA	Patients with primary, non-recurrent STS measuring 5 cm in greatest dimension (T2)	Routine chest CT scanning vs. Selective chest CT scanning based on chest X-ray results	Decision tree cohort model	NA
Royce, 2017	USA	Patients with STS who had completed definitive treatment for stage II or III primary disease	Watchful waiting vs. Chest X-ray vs. Chest CT vs. PET/CT	Markov cohort model	Lifetime

*Conference poster available only; CT: computed tomography; PET/CT: Positron emission tomography–computed tomography; QALY: quality-adjusted life years

RESULTS OF HEALTH ECONOMIC MODELS ON OTHER TYPES OF TECHNOLOGIES

- We included 3 additional studies with other types of interventions (**Table 3**).
- All three health economic models were developed in the USA.
- One of the studies used Markov cohort model design, while two studies applied decision tree cohort model.
- The models compared different strategies for surgery combined with other types of interventions.
- Two studies expressed the result as an incremental cost per QALY gained, while one study applied incremental cost per incremental life-years.

TABLE 3: STUDIES INVESTIGATING OTHER TYPES OF INTERVENTIONS

Reference	Study country	Patient population	Investigated technologies	Model type	Time horizon
Porter, 2004	USA	Patients with STS pulmonary metastases	Pulmonary resection vs. Systemic chemotherapy vs. Pulmonary resection and systemic chemotherapy vs. No treatment	Decision tree cohort model	NA
Qu, 2017	USA	Patients with extremity STS	Preoperative radiotherapy prior surgery vs. Postoperative radiotherapy after surgery	Markov cohort model	5 years
Richard, 2016	USA	Patients with extremity STS	Preoperative intensity modulated radiation therapy vs. Preoperative 3-dimensional conformal radiation therapy	Decision tree cohort model	5 years

*Various events were defined based on local recurrence and toxicity grades; QALY: quality-adjusted life years; STS: soft tissue sarcoma

CONCLUSION

- **This is the first systematic literature review aimed to collect and summarize evidence on economic evaluations and health economic models related to STS.**
- The applied methodology of modelling, is mostly simplified and universally used across different jurisdictions. In most cases, Markov cohort models and partitioned survival models were applied, using the traditional approach for health states (i.e. progression-free, progressed disease, and death). Most models included patients with advanced STS who had undergone prior treatments and used primarily a healthcare system perspective.
- The majority of the identified studies focused on pharmaceuticals, while a few studies evaluating diagnostic technologies and other types of interventions were also reviewed. However, these areas of interventions are clearly underrepresented in the literature.
- Limitations of this review are that the identified studies included diverse patient populations and investigated a variety of health technologies, making direct comparisons challenging and the systematic literature review concentrated solely on studies from North America and Europe.

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REFERENCES