

Background and objectives

ATMPs are cutting-edge therapeutic drugs for human use derived from genes, tissues, or cells, offering substantial clinical benefits.

The field of ATMPs is experiencing rapid growth but faces significant challenges, particularly due to the high costs associated with these therapies.

To ensure patient access and to address the uncertainties regarding their long-term effectiveness and financial impact on both manufacturers and payers, innovative contracting models have been developed.

An effective risk-sharing arrangement between the payer and the manufacturer could improve access to costly and innovative technologies that might otherwise face limited reimbursement or be denied access.

This research aims to review the existing types of innovative contracts, evaluate their added value, and assess their limitations, with a special focus on France, Italy, and the United States.

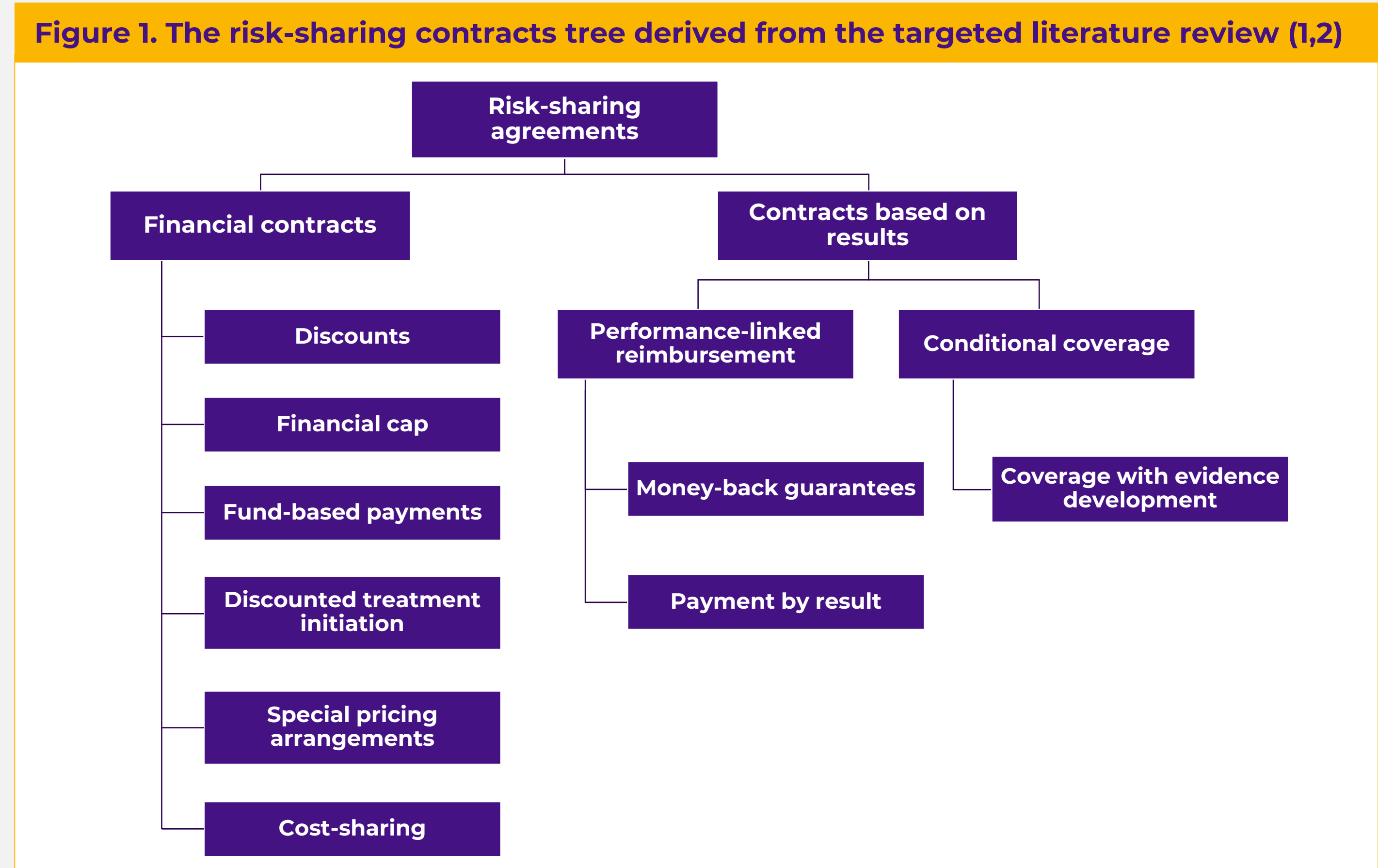
Results

A total of 193 articles were reviewed. 57 were included based on the relevance of their title/abstract and then the outcome of the full-paper review.

Most of the contracts described were performance-based arrangements, of which the majority were OBCs. OBCs included performance-linked reimbursement contracts and conditional coverage contracts, with the first type being predominant.

These risk-sharing agreements could be with deferred or non-deferred payment and had a general aim of reducing payer uncertainty about clinical outcomes while compensating manufacturers for their product's value.

To visually synthesise the results of the literature review, the following contract tree allows for the differentiation of the various types of risk-sharing contracts (**Figure 1**).



Methods

A TLR was conducted on PubMed and supplemented by grey literature searches, conference abstracts, and presentations (including from the 2024 EPA congress and Sharing risks, sharing value 2024). The review included publications released between 2005 and 2023 and covered Europe and the United States, with a focus on France and Italy for Europe.

The focus of the TLR was interesting because it allowed the comparison of France with Italy—a European country with a similar national healthcare system—and with the United States, which has a completely different system. This comparison could help draw valuable lessons from the different national approaches.

Two appropriate algorithms oriented towards innovative contracts have been developed respectively for PubMed and for Value in Health.

A double screening, based on review of titles and abstracts followed by a reading of the full text, was used to include or exclude articles depending on whether they were deemed relevant.

Articles were excluded if they made no mention of ATMPs; made no mention of at least one economic aspect; covered a geographic area outside the scope of interest (Europe and the United States); were duplicates; or were published before 2013.


Innovative contracts support the management of uncertainty associated with ATMPs, secure patient access to these innovative therapies, and maintain the sustainability of the healthcare system.

Uncertainties may be clinical, concerning the long-term effectiveness of treatments or their safety, but they can also be financial, commercial, and legal, driven by significant development costs, constantly changing funding models, and an evolving regulatory framework associated with ATMPs (3).


Because they face regulatory obstacles or lack a framework that satisfies the interests of all stakeholders, the adoption of innovative contracts comes with constraints such as collecting real-world data or quantifying uncertainty. Risk-sharing contracts also encounter a regulatory obstacle. A structural change in the reimbursement policies of most states would be necessary to support these new financing mechanisms (3).

Results showed that, depending on the country, innovative contracts can take different forms. Their terms generally reflect the public health strategy of the country concerned. Indeed, differences in healthcare systems as well as political and budgetary orientations lead to the implementation of distinct mechanisms. All are driven by the desire to facilitate access to innovative treatments while managing expenditure.




**Table 1** presents the French, Italian, and American cases.



In France and Italy, innovative contracts are designed with the objective of making ATMPs sustainable in the long term, unlike in the United States, where the healthcare system is based on private insurance.



**Key success factors** include ensuring the contract's completeness, establishing a centralised registry to manage data collection, choosing the simplest indicator possible, defining success criteria with a strict timeline and conducting frequent reevaluations, and ensuring organisational feasibility through stakeholder collaboration and compromise (4,5).

Table 1. Comparison of outcome-based contracts in France, Italy, and the United States			
	Types of contract	Database	Specifics
 France	<ul style="list-style-type: none"><li>• <b>Performance-based payment</b> for ATMPs over 5 years:<ul style="list-style-type: none"><li>- <b>PRMs</b> (a new contract type)</li><li>- <b>Satisfied or your money back</b> contracts</li></ul></li><li>• CEPS is no longer in favor of <b>conditional payment models</b></li></ul>	<ul style="list-style-type: none"><li>• There is no official national registry, but there are a few very specific registries, such as DESCAR-T (LYSARC) or Roche's database for its PRM</li></ul>	<ul style="list-style-type: none"><li>• Very few risk-sharing contracts were signed in the past 7 years because of the significant legal and financial risks they entail, as well as the lack of infrastructure for real-world data collection</li><li>• The LFSS 2023 recommends that instalment payments (based on risk-sharing agreements correlated with the monitoring of the drug's effectiveness for at least 5 years) replace conditional payment models</li></ul>
 Italy (6)	<ul style="list-style-type: none"><li>• <b>Payment by result:</b> industry gives back money if treatment fails</li><li>• <b>Hidden discount + payment at result:</b> industry is paid if the treatment is effective</li></ul>	<ul style="list-style-type: none"><li>• A centralised database has been managed by AIFA since 2012</li></ul>	<ul style="list-style-type: none"><li>• The Italian experience is the longest and most productive in terms of performance-based reimbursements in Europe</li><li>• Evaluation/appraisal/negotiation are managed by the same agency using a multicriteria approach</li><li>• Renegotiation occurs at the end of the contract (2 years) or if market conditions change</li></ul>
 United States (7,8)	<ul style="list-style-type: none"><li>• <b>Outcome-based rebates based on IPD</b></li><li>• <b>Payments in installments + outcomes-based rebates based on IPD</b></li><li>• <b>Outcome-based payment offered to healthcare providers for all patients based on IPD:</b> no invoice for all patients who do not receive a response in a few days</li><li>• <b>Money-back guarantee, coverage with evidence development</b></li></ul>	<ul style="list-style-type: none"><li>• Databases are private and held by the insurance companies</li></ul>	<ul style="list-style-type: none"><li>• Treatments are generally short term because of the private insurance system</li><li>• There is a limited amount of information because of the confidentiality to which these contracts are subject</li></ul>

**Abbreviations:** AIFA, Agenzia Italiana del Farmaco; ATMP, advanced therapy medicinal product; CEPS, Comité économique des produits de santé; EPA, European Psychiatric Association; IPD, individual patient data; LFSS, Loi de financement de la sécurité sociale; OBC, outcome-based contract; PRM, personalised reimbursement model; TLR, targeted literature review

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Conclusions

The adoption of innovative contracts demonstrates a collective commitment from all parties to improve access to ATMPs, despite the limitations these contracts present. Among these innovative contracts, financial contracts continue to outnumber performance-based contracts, because financial contracts are easier to implement.

Even if many databases or registers have been put in place to collect and derive real-world evidence, further efforts in collecting and utilising real-world data could significantly improve the effectiveness and implementation of these contracts.

There are 2 limitations to this TLR. From a methodologic point of view, it is difficult to establish an exhaustive review of the different types of contracts given the lack of harmonisation in the terminology of innovative contracts. Moreover, the confidentiality and lack of transparency associated with negotiations and contracts complicate interpretations.

