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SCOPING REVIEW

Design and Features of Pricing and Payment Schemes for Health Technologies: A Scoping Review and a Proposal for a Flexible Need-Driven Classification

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Abstract

Background and Objective In a context of growing clinical and financial uncertainty, pricing and payment schemes can act as possible solutions to the problems of affordability and access to health technologies. However, a comprehensive categorization of the available schemes to help decision makers tackle these challenges is lacking. This work aims at mapping existing types of pricing and payment schemes, and proposes a new approach for their classification, in order to help decision makers and other stakeholders select the best type of scheme to meet their needs.

Methods A Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)-compliant scoping literature review was performed between 2010 and 2023 in three databases (PubMed, Web of Science, Scopus). The search strategy was developed around two groups of keywords, "pricing/payment schemes" and "scheme innovativeness". Eligible studies were those illustrating the unique design and features of each scheme type, which were extracted by two independent reviewers, and synthesized using a narrative format, including a detailed tabular description of each type of scheme.

Results A total of 70 unique types of pricing and payment schemes were identified. Around one third (33%) was only specified in principle, while two thirds (67%) had been implemented in practice. About half of the scheme types were proposed for drugs (34/70, 49%), and the vast majority were not designed for a specific therapeutic area (55/70, 79%). Each scheme type was categorized based on distinctive characteristics: the objectives, the outcome component, the timing/modalities of payments, and the evidence collection requirements.

Conclusions Instead of trying to fit the retrieved schemes into a rigid taxonomy, we propose a new approach that suggests a flexible need-driven use of the available scheme types, driven primarily by the specific objective that one might have, and allows leveraging of the other key characteristics of each type of scheme.

1 Introduction

1.1 Background

Decision makers, payers, and healthcare providers are increasingly challenged by the changing nature of new health technologies. Regarding medicinal products, in the past, the main challenges related to the financial impact of drugs delivered in primary care to large patient populations. In contrast, more recently licensed pharmaceuticals, such as gene and cell therapies, can be individualized treatments characterized by drug-target heterogeneity, to the extent that their patient-specific responses, culminating with precision medicine, is altering established trends of clinical evidence generation [1].

Innovative drugs are frequently characterized by greater uncertainty over their clinical efficacy upon market launch. For instance, target populations may be too small to be represented in traditional, parallel, double-blind, randomized controlled trials (RCTs), which as a result could be unfeasible or unethical to conduct [2]. In addition, there is a growing use of surrogate endpoints to predict clinical effectiveness [3], mainly in the field of oncology, but also in other fields such as the recently debated case of a reduction in brain amyloid beta plaque [4]. In this context, and in the interests of early patient access, regulatory agencies such as the European Medicines Agency and the US Food

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Key Points

Pricing and payment schemes have been proposed as possible solutions to the problems of affordability and access to health technologies. This work mapped existing types of pricing and payment schemes, and proposed a new approach for their classification.

Overall, 70 unique types of pricing and payments schemes around different technology types and therapeutic areas have been identified, both theoretical formulations and schemes applied in the real world. The schemes populate the Pay-for-Innovation Observatory, publicly accessible online.

Our proposed approach to categorize available types of pricing and payment schemes is to allow a flexible use of the entire repository of schemes, driven by the specific objective that different stakeholders might have, conscious that schemes can be better defined by using the combination of their key characteristics.

and Drug Administration have given new drugs market approval based on incomplete or limited evidence, de facto postponing the confirmation of their clinical efficacy to the post-marketing phase [3, 5–7].

In addition, the clinical uncertainty of recently authorized drugs is often associated with an increased operational complexity because of the intrinsic characteristics of new technologies. For instance, these may have to be produced by highly specialized manufacturers (laboratory-modified tissues, cells, or genes), delivered to patients with expensive logistics (transportation of human specimens), or entail novel modes of administration (single-administration drugs). Advanced therapy medicinal products (ATMPs) have often been cited as representative examples of technologies that encompass most of these challenges [8, 9]. Together, these factors have impacted the manufacturers' ability to scale up their production capacity and to reach economies of scale, resulting in extremely high launch prices for certain innovations. These high-cost drugs lead to significant budgetary impacts associated with their reimbursement or coverage decisions [10]. In the case of gene therapies, payers have been asked to make substantial upfront payments before any clinical benefits even accrue. Clinical uncertainty is thus intertwined with financial uncertainty.

As for medical devices (MDs), the evidence required for their licensing has traditionally been viewed as less robust when compared with drugs, given MDs' unique characteristics like incremental innovation and learning curves associated with repeated use [11, 12]. Randomized controlled trials are not often required for market authorization, and even when conducted can often be impractical or unfeasible because of the rapid technological advances introduced in the device under investigation. This challenge is compounded when it comes to drug-device combinations (including software-integrated devices and digital MDs), where frequent marginal improvements can rapidly render previous RCT findings obsolete.

In this context, decision makers at different levels (regulatory agencies, health technology assessment bodies, payers) are seeking ways to handle the financial impact and uncertainty surrounding the launch of new technologies. Novel pricing and payment schemes have been proposed as pragmatic tools to ensure timely patient access to promising innovations on the one hand, while simultaneously addressing financial sustainability on the other hand. Innovative pricing and payment schemes between manufacturers and payers have been designed to address the challenge of guaranteeing coverage for expensive technologies, while also guaranteeing that innovators are rewarded for their research and development (R&D) investments [13].

New pricing and payment schemes have been labeled differently and referred to as risk-sharing agreements [14], managed entry agreements [15], or innovative contracting [16]. Because of the increased number and types of pricing and payment schemes, decision makers and other stakeholders are likely to have difficulty in distinguishing between the different characteristics of schemes and in determining which one might best suit their specific purpose. Therefore, there is a need for a taxonomy or classification scheme that would help stakeholders in this process.

1.2 Existing Taxonomies of Innovative Pricing and Payment Models

Because of the diverse objectives and possible applications of these schemes, several authors have classified them using frameworks or taxonomies, clarifying how to navigate among them. An initial targeted review was conducted to identify existing taxonomies through a "pearl-growing" approach that, based on an initial sample of relevant sources known to the authors, allowed purposively selecting, from citations and references, of other relevant taxonomies that categorize pricing and payment schemes of health technologies (Table 1). Many of them distinguish between outcome-based (or performance-linked) schemes and non-outcome-based (or financial) schemes. Similarly, other researchers explored the primary reasons for employing MEAs, for instance categorizing such schemes based on four levels: the objectives (i.e., financial based vs performance based), the monitoring (i.e., the technology costs, use, and uncertainty), the instruments (e.g., outcome guarantees, registries, country-specific requirements), and the impact on certain variables (e.g., treatment interruption, initial free doses, periodic reassessments) [17]. Other frameworks focused on coverage options more broadly, distinguishing schemes with goals of evidence generation from those aiming for price reductions [18].

The existing taxonomies have been useful in helping us to understand the main features of schemes, but the categories

are often not mutually exclusive, and some are probably not granular enough. Some schemes have both an 'outcome' and a 'financial' component. For instance, performance-based instalment payment schemes for ATMPs allow for the generation of real-world evidence on the product performance, while also contributing to mitigating the financial impact on the payer's budget. Assigning a given scheme to a category might not be straightforward. For example, should a scheme generically named "pay-for-performance" be classified as outcome based or not? Some categories are very broad and could potentially include a wide range of differing schemes with multiple objectives. These difficulties suggest that to be able to differentiate between different types of schemes, or to identify a scheme that might suit an individual's purpose, a more detailed approach to developing a taxonomy might be required. A larger number of characteristics may be necessary to guide the selection of an innovative pricing and payment scheme that addresses the specific requirements of, or the challenges experienced by, a payer or a technology manufacturer.

1.3 Objectives

Given these premises, this work aims at enhancing the current understanding of the intricate landscape of pricing and payment schemes in the context of innovative health technologies. Our objectives are two-fold:

1. To conduct an extensive mapping of existing types of pricing and payment schemes for health technologies resulting in an open-access publicly accessible database that gathers their relevant dimensions, such as the primary reason for using the agreement, the type of technology, the disease area, or the presence and type of an outcome element.
2. To propose a new approach that overcomes the shortcomings of prior taxonomies, by classifying schemes based on the key characteristics that they possess, thereby helping decision makers and other stakeholders to select the best type of scheme to meet a specific purpose.

This work is centered around the defining elements and distinctive features that characterize each type of pricing and payment scheme, focusing equally on schemes that are used in real-life contexts and schemes that have only been proposed by the scientific community. The specific details of each agreement negotiated in a given real-life context (e.g., country of implementation, duration of the agreement, outcome data to be collected), and the evaluation results of such schemes, are not part of the present analysis.

1.4 Introductory Definitions

Textbox 1 gives the definitions of some relevant concepts that underpin the basis for this research.

Pricing and payment schemes.
Pricing schemes refer to any approach or methodology to calculate, measure or quantify a fair price for health technologies, and are those establishing what the manufacturer will seek to be rewarded for, typically in light of the value of the product to patients and the larger society. *Payment schemes* refer to the formulation of any aspect that has to be defined to govern the payment of health innovations, including, but not limited to, the types and number of stakeholders involved, the moment in which the payment occurs, the split of payments over time, the linkage to an outcome component, or ways to reach a balance between financial sustainability for payers, whilst rewarding the manufacturers for the technologies produced. While pricing and payment schemes might be reflective of the same monetary value from the perspectives of different stakeholders, this is not always the case.

Innovativeness.
For the purposes of this study, "innovative payment and pricing schemes" were defined as arrangements that go beyond price per pill/vial (or more broadly, unit) of the technology, including simple price/volume agreements or expenditure caps. Innovativeness of a pricing or payment scheme might refer to the characteristics of a scheme (i.e., scheme type), and/or to the way a given scheme is employed (i.e., scheme use). Therefore, none of the schemes was qualified as "innovative" based on its ex-ante perceived innovativeness, the rationale being that it is not the scheme per se which is innovative, but rather its application or use in each context.

Taxonomy.
An approach that allows the qualification, characterization and classification of the distinctive features of pricing and payment schemes.

2 Methods

2.1 Overview

The mapping of existing types of pricing and payment schemes for health technologies was performed according to a scoping review methodology, following the updated methodological guidance for scoping reviews [26] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews guidelines (PRISMA-ScR) [27]. The review was previously registered within the International Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD42023444824. All the methodological details are provided in the published research protocol [28]; the most relevant aspects are summarized hereafter.

2.2 Key Search Details

As for the scientific literature, three scientific databases were searched: PubMed (MEDLINE), Web of Science, and Scopus. The search strategy was developed around two blocks of keywords, "pricing and payment/reimbursement schemes" and "innovativeness," and comprised combinations of the following terms: performance-based, value-based, evidence-based, risk-sharing, reimbursement, rebate, pricing, contract, scheme, guarantee, and health system. In addition, to arrive at a manageable amount of retrieved records, database-specific addendums were used, specifically Mesh Terms for PubMed, Web of Science categories for Web of Science, and index terms for Scopus. The full search strategy can be found in Table 1 of the Electronic Supplementary Material (ESM).

As for the gray literature, reports, White papers, and websites of pertinent institutions, including international organizations, industry and patient associations, health technology assessment bodies, and consulting firms, were searched, such as the Organization for Economic Cooperation and Development, International HTA Database, European Federation of Pharmaceutical Industries and Associations, and others. Further information specific to the search performed can be found in the published protocol [28].

2.3 Inclusion Criteria

Studies illustrating the defining elements and distinctive features of each type of pricing and payment schemes of health technologies, with a level of detail that is sufficient to explain their general functioning and rationale, were deemed eligible to be included in this review. Theoretical schemes (i.e., schemes that had only been proposed) and implemented schemes (i.e., schemes that had practical applications) were equally considered to retrieve the design features of each scheme type. No exclusions were made based on the type of study design. For this reason, editorials, commentaries, and perspective articles were included when a given scheme type was proposed and discussed.

2.4 Data Items and Synthesis

First, information on the selected papers (i.e., publication year, location of corresponding author, type of study, journal of publication) was extracted. Then, for each type of scheme, several characteristics were mapped and extracted, such as the name of the scheme type, its description, objective, if theoretical or applied, whether it had an outcome component (including if on a patient or population level), and the evidence collection requirements. In total, data on up to 21 items (characteristics) of each scheme were extracted. Further information on the data extracted is available in the published protocol [28]. In addition, the list of data items extracted from each scheme is given in Table 2 of the ESM.

Study results were reported mostly with a narrative format, using tables where relevant. Through this, the main characteristics of the included papers were illustrated. Then, an overview of the design and features of the selected scheme types was provided, followed by an in-depth analysis of four of such characteristics; namely, the objectives of the scheme, the measurement of any outcome, the timing (namely, when the payment occurs with respect to the treatment: upfront vs post-treatment) and modalities of payments (namely, how the payment is made: single payments vs staggered constant payment vs staggered outcome-based payments), and the evidence generation requirements. We chose to focus on these characteristics for two main reasons: some of them emerged during the conduct of the review itself and were the characteristics most recurrently described for each scheme type; others were informed by the targeted review of existing taxonomies.

3 Results

3.1 Overview of the Selection Process

We retrieved 11,939 records from three databases. After removing 1382 duplicates, 10,557 unique records were screened in titles and abstracts. A total of 135 records were deemed eligible for full-text screening, of which 54 were included. The main reason for exclusion was the lack of sufficient information to describe the scheme characteristics or functioning. Additionally, six eligible records were included from a manual search of references of full-text screened records (i.e., snowballing). We also identified 14 records from the gray literature (i.e., White papers, reports), of which six were included after a full text read. Overall, 68

Table 1 Overview of existing taxonomies of pricing and payment schemes

Source	Focus	Description
Carlson et al. [19]	Performance-based reimbursement schemes	The taxonomy categorizes the schemes in terms of timing, execution, and health outcomes, distinguishing health outcome vs non-health outcome schemes
Towse et al. [14]	CED	The taxonomy distinguished between outcome based and non-outcome based and also between those with agreements that specified how evidence would be translated into revisions of price, revenues, and/or use vs those that instead specify an evidence review point where renegotiation would occur
Walker et al. [18]	Coverage options at large	The taxonomy distinguishes between schemes requiring evidence generation vs schemes aiming at reducing price levels
Garrison et al. [20]	PBRSA	The taxonomy separates two types of PBRSA: CED and performance-linked reimbursement schemes
Ferrario et al. [21]	MEAs	The taxonomy classifies MEAs based on their objective, perimeter of monitoring, instruments used, and expected impact
Ferrario et al. [22]	MEAs	Conceptual framework developed around the key reasons for using MEAs: improving access, reducing uncertainty and prices, improving cost effectiveness, and personalizing treatment
Launois et al. [23]	MEAs	Payer-friendly taxonomy for MEAs, classifying the schemes based on their conceptual design (pay for performance vs pay for demonstrated effect) and on their methodological design (type of study backing the scheme)
Hertzman et al. [24]	Financial and outcome-based schemes	Categorizes the different types of financial and performance-based schemes in terms of the extent to which they address uncertainty in budget impact and cost effectiveness/value, and level of administrative complexity
Koleva-Kolarova et al. [25]	Reimbursement models for personalized medicine	Reimbursement models are clustered based on two dimensions, the presence of risk sharing (yes vs no), vs the presence of outcome dimensions (outcome based vs financial based)
Horrow and Kesselheim, 2023 [10]	Payment models for gene therapies	Payment models are clustered first based on the addressed problems (i.e., high budgetary impact vs clinical uncertainty), then based on approaches (i.e., amortization vs risk spreading vs performance-based payment) and strategies (e.g., divide payments over time vs share costs with other payers)

CED coverage with evidence development, *MEAs* managed entry agreements, *PBRSA* performance-based risk sharing agreement

records were selected for data synthesis. Figure 1 provides an overview of the selection process.

3.2 Descriptive Characteristics of Selected Papers

The body of literature illustrating pricing and payment schemes of health technologies has gained momentum within the timeframe under consideration, with half of the selected papers published from 2020 onwards (34/68, 50%). Based on the main affiliation of the corresponding author, most of the scientific papers were conducted in the USA (18/62, 29%) and the UK (14/62, 23%). The studies considered were mostly original research articles (31/68, 46%), followed by review articles (14/68, 21%), editorials, opinion and commentaries (13/68, 19%), reports and White papers (6/68, 9%), or other (4/68, 6%). In terms of media outlets, the journals more frequently encountered were *Applied Health Economics and Health Policy* (7/62, 11%), *Value in Health* (6/62, 10%), and *Expert Review of Pharmacoeconomics & Outcomes Research* (4/62, 6%). The detailed characteristics of the selected papers are reported in Table 3 of the ESM.

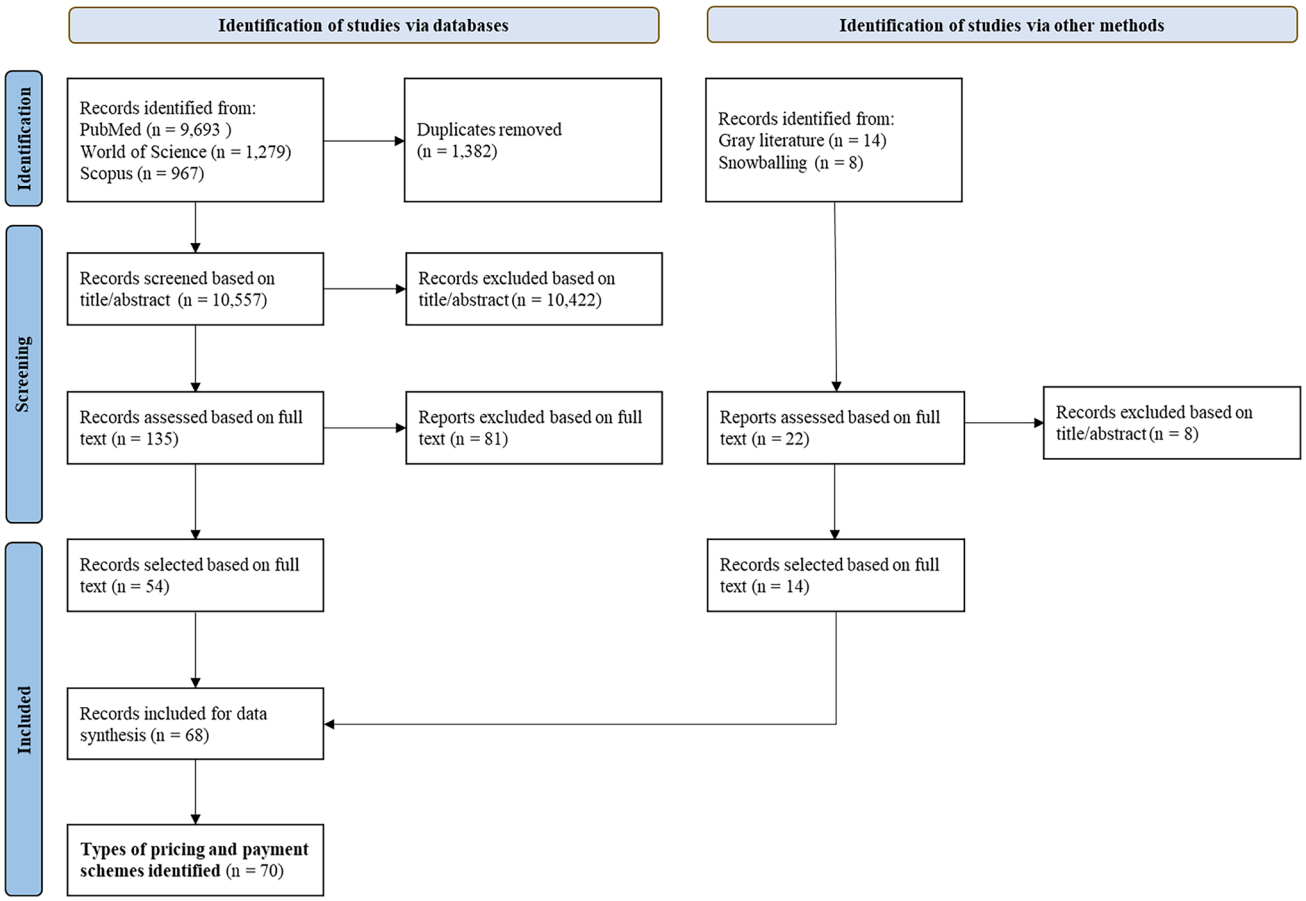

Fig. 1 Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) diagram

3.3 Types of Pricing and Payment Schemes

A total of 70 types of pricing and payment schemes were identified. The full list of types of pricing and payment schemes is reported in Table 2, with references to examples given for each type. Twenty-three (33%) were theoretical schemes only specified in principle, whereas 47 (67%) were, or had been, implemented in practice. Of these, 28 (40%) were mainly focused on pricing, and 42 (60%) focused on payment and were mainly proposed by payers. However, there were some schemes, particularly the theoretical schemes, that were hard to classify. The identified schemes could be designed for drugs (34/70, 49%), vaccines (3/70, 4%), devices (2/70, 3%), or other categories (4/70, 6%), such as drug-device combinations, apps, artificial intelligence tools, and innovative pathway-approved technologies (each 1/70, 1%), whilst 32 (46%) schemes did not refer to a specific technology. In the case of schemes proposed or used for drugs, the great majority could be used with any drug (23/34, 68%), while a minority was designed specifically for generics (5/34, 15%), antibiotics (4/34, 12%), patent-protected molecules (1/34, 3%), or biosimilars (1/34, 3%). Many of the retrieved schemes were not designed for a specific therapeutic area (55/70, 79%), while others were proposed specifically for orphan or ultra-rare diseases (5/70, 7%), targeted conditions such as cancer or multiple sclerosis (6/70, 9%), and genetic conditions and ATMPs (4/70, 6%).

The remaining part of the paragraph analyzes in depth four distinctive characteristics of each type of schemes: the objectives, the presence of an outcome component, the timing and modalities of payments, and the evidence collection requirements.

3.3.1 Objectives of the Schemes

Pricing and payment schemes can be chosen to pursue different objectives. In Towse and Garrison for instance, the agreements were categorized according to either efficiency objectives (i.e., cost effectiveness) or financial objectives (e.g., managing budget constraints or granting discounts) [14]. Other researchers classified the schemes looking at the type of uncertainty, financial or clinical, they sought to mitigate. We synthetized prior contributions and categorized

Table 2 Types of pricing and payment schemes

ID	Scheme type, source	Scheme type description	Illustrative examples
1	Cost-plus pricing [29]	A fixed price that covers the costs of producing and distributing a therapy while allowing for some profit. The price can include R&D costs, and the profit margin can be tied to the therapy's value	Common in Japan [30]
2	Combination-based pricing [31, 32]	Combination-based pricing addresses the challenge that the value of products used in combination does not equal the added value of the medicines used separately. It is used to assign value and negotiate prices when different manufacturers hold marketing rights for each drug to be used in combinations. The company selling the main product, A, may support the combination's coverage if it boosts the sales of A, possibly agreeing to a lower price for A in that indication if it does not affect the price of A in other indications. However, if A's price is affected in all cases, the manufacturer may be reluctant to accept lower price levels not fully offset by increased sales from the combination of A+B	Cases in France, UK, and Switzerland [32]
3	Reference pricing (RP) [33, 34]	This approach involves grouping drugs based on certain equivalence criteria and setting a reference price for each group. Drugs can be categorized by their chemical, pharmacological, or therapeutic equivalence. There are different types of RP: *generic RP* for off-patent generic drugs, and *therapeutic RP* for drugs that are therapeutically equivalent. The latter uses the prices of identical (ATC 5 level) or similar medicines (ATC 4) to establish a RP. If a consumer buys a drug priced at or below the RP, it is reimbursed up to that amount. However, if the drug purchased above the RP, the consumer may have to pay the difference	Therapeutic RP is applied to specific clusters in Canada (e.g., calcium channel blockers) [33]
4	External (or international) reference pricing (ERP) [35–37]	The approach involves using the price of a medicine in one or more countries to establish a benchmark or reference price for setting or negotiating the product's price in a given country. ERP determines prices based on a selected group of reference countries, chosen according to criteria such as geographic proximity, similar GDP, comparable socioeconomic conditions, or other specific factors. ERP can be used as the main method to directly set prices, or as one of the factors to guide pricing and reimbursement decisions. It is mainly applied to regulate price for new products, while it is less commonly used in off-patent products	Used in Switzerland (the number of countries used as benchmark has been revised to put downward pressure on prices) [35, 36]
5	Internal reference pricing (IRP) [34, 38]	The approach involves payers creating groups of interchangeable drugs, and setting a reimbursement price for all drugs within each group. These groups consist of either drugs with the same active ingredient or with different active ingredients deemed to have comparable efficacy and safety. IRP typically applies only to off-patent drugs. The specific mechanisms can vary between countries, such as using the average or lowest of equivalent treatments, weighted for multiple indications, and measuring costs per cycle, month or year	Germany includes on-patent drugs with no additional benefit to existing therapies in IRP groups [38]
6	Generic or biosimilar price linked to the originator product [35, 38]	Mandatory price reductions are applied to generics and biosimilars, calculated as a percentage of the originator price. These discounts can be negotiated and may differ between drugs. For biosimilars, the required price difference from the originator is typically smaller than that for generics.	Generic outpatient prescription drugs in Estonia [38]

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
7	Indication-based pricing (IBP) [31, 39, 32, 40, 41]	The drug price is determined by its value across different indications, recognizing that a drug used for multiple indications may provide varying benefits to different patient groups, resulting in different values for each indication. Using distinct brand names for different indications is termed "pure IBP". Several pricing strategies for multi-indication drugs include: (1) *weighted pricing:* the drug price is renegotiated when a new indication is introduced, with the weighted average price based on the volume and value of each indication, either estimated beforehand or adjusted later through rebates (used in France, Germany, Spain, Belgium, and Canada); (2) *differential discounting*: separate discount rates are negotiated for each indication (used in England and Switzerland); (3) *single list price of highest value indication, combined with mandatory price discounts*: the price is set at the highest value indication, with mandatory discounts (often through MEAs) based on the expanded patient population from new indications, leading to different net prices (used in Italy); (4) *anchoring by the first indication:* pricing is based on the first indication approved for reimbursement (used in Turkey); and (5) *free pricing*: there are no restriction on drug pricing (used in the USA)	Aflibercept, with different brand names in the USA: (1) Eylea® for ophthalmology; (2) Zaltrap® for colorectal cancer [42]
8	Indication-based pricing (IBP) with outcomes guarantee [43]	Outcomes guarantees can be used to establish indication-based pricing that reflects the real-world value of a drug. With this approach, uncertainties about a drug's effectiveness for different indications are addressed by assessing the actual clinical and economic outcomes of patients within the payer's covered population. The net price is thus aligned with the actual value that the drug provides for each indication in real-world use. This differs from traditional IBP, which relied on pre-launch data such as pivotal trials, rather than RWD from the payer's experience	Theoretical scheme
9	Prices for orphan drugs set using an adjusted cost-effectiveness threshold [44]	A model proposed for orphan drugs, that builds on the proposition that the expected return of investment for developing these drugs should align with the industry average. The method involves adjusting the payer's standard cost-effectiveness threshold for non-orphan drugs, considering the R&D and expected revenues of the orphan drug, to ensure that manufacturers achieve a return consistent with the industry-wide rate	Theoretical scheme
10	Value-based pricing (also, "cost effectiveness-based" or "pharma economic" pricing) [34, 35]	Value-based assessment involves setting prices for new drugs or determining their reimbursement based on the therapeutic value they provide, typically evaluated through a health technology assessment. The VBP of a new treatment is the price at which its ICER is equal to the cost-effectiveness threshold, or alternatively, the price at which the incremental net monetary benefit for the new treatment is zero, based on a specific cost-effectiveness threshold	Common approach in the UK and Sweden [34, 35]
11	Value-based pricing adjusted to account for a technology net present value [45]	In this model, payers consider the acquisition of a new health technology as an investment and calculate its present value similarly to how the NPV function is used in finance. The present value is determined by adding up the discounted incremental costs and the quality-adjusted life-years produced over the technology's entire lifespan, akin to how the NPV function totals future cash inflows and outflows	Theoretical scheme

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
12	Nationwide budget thresholds for individual innovative agents [46]	A model proposed to set national budget thresholds for individual innovative drugs, where a fixed percentage of historical pharmaceutical spending sets the maximum budget for a new treatment. Under this model, as many patients as possible are treated provided the total spending does not exceed the pre-established budget limit. This approach was originally developed to price PCSK9 inhibitors at their launch in the USA, based on the principle that the total budget for these drugs should not exceeded "*the amount of net cost increase per individual new intervention that would contribute to growth in overall health care spending greater than the anticipated growth in national GDP + 1%*"	Theoretical scheme
13	Drug pricing index [47]	A model proposed for cancer drugs based on a global pricing index that considers both the drug's performance and value thresholds, while accounting for a country's wealth (using GDP and Gini coefficient). The model uses cost and utility data to generate cost-effectiveness pricing outputs, estimating price points for specific survival increments, with the target value threshold set at three times the per capita GDP of each country. A multivariable analysis was then conducted on these price points to assess how survival benefits, per capita GDP, and income inequality influence the final price estimate. The results were used to create a pricing index that can determine a value-based price for a new drug	Theoretical scheme
14	Price-volume agreement [29, 48]	Drug prices decrease gradually as more patients are treated. The pricing may be influenced by value assessments, such as health technology assessments or other methods, but revenue for specific uses is determined by sales volume and associated discounts. In this common approach, payers use formulary tiers that prioritize branded drugs while incorporating manufacturer discounts based on the volume of sales. Preferred formulary placement may also require prior authorization and utilization reviews	Commonly used in France [15]
15	Price-volume agreement with nationwide exponential decays [46]	A scheme that involves an exponential reduction in price as the number of treated patients increases. The key parameter is the "price halving population", where the treatment price is reduced by half each time the count of treated patients doubles. Variations of this approach include a continuous price decay function, or a series of discrete progressive price reductions.	Ranibizumab in Italy [46]
16	Price–volume agreement under asymmetric information about the mean total demand [2]	Model designed for creating price-volume agreements in situations with information asymmetry (where the payer is uncertain about the average demand) and market uncertainty (where both the payer and manufacturer are uncertain about the actual demand). The optimal contract has the following characteristics: an incentive-compatible agreement is always achievable; the optimal price decreases as the expected market size grows, while rebates may vary based on the expected market size. Furthermore, a manufacturer with the highest possible demand would ideally receive no rebate, and, if the average reservation profit does not decrease with a larger expected market size, no rebates would be included for any manufacturer	Theoretical scheme

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
17	Price linked to patients' willingness to pay [49]	Model proposed to integrate patients' WTP into value-based pricing using discrete choice experiments, which evaluate the WTP for various product attributes. It was proposed to estimate prices for interferon-beta in a sample of patients with multiple sclerosis	Theoretical scheme
18	Rate of return pricing [50]	A scheme that guarantees a pre-determined rate of return to manufacturers after covering development and marketing costs. A similar concept is seen in the UK's Pharmaceutical Price Regulation Scheme, which limits manufacturer profits by a 'claw-back' of excess revenues above an agreed level	Theoretical scheme
19	Payer license agreement (PLA) (subscription-based pricing model) [51]	The scheme introduces three changes to traditional pharmaceutical pricing: (1) pricing is based on the entire population served by the payer, rather than individual patients or treatments; (2) the drug's price is directly linked to the savings it creates by avoiding additional costs; and (3) payments is spread over a period of 5 or more years	Hepatitis C treatment in Australia [51]
20	Tendering/negotiations [30, 35]	A process whereby the government invites manufacturers to submit bids for a specific contract, often through competitive bidding, to lower drug prices in markets with existing competition, such as for generics. This process also serves as a procurement strategy to determine supplier and quantities for certain drugs and typically involves negotiation. Tendering can be centralized at the national level or decentralized at the regional level	Commonly used in the Asia Pacific region [30]
21	Generics: blind tenders and sole supply contracts [52]	Sole supply tender involves an exclusive supply tender process for generic drugs conducted at regular intervals (e.g., annually). The process is "blind," with payers requesting annual bids without negotiation, allowing suppliers to set their price points. Penalty clauses are usually included for failure to supply	Used in New Zealand [52]
22	Two-part pricing [24]	The scheme includes an "entry fee (EF)" for the right to use a product, and a "usage price (UP)", charged every per purchase. The scheme allows differentiation among healthcare payers: high-volume payers could be offered a higher EF with a lower UP, while low-volume payers may prefer a lower EF with a higher UP. High-volume payers would benefit form a lower average cost per use despite the higher EF	Theoretical scheme
23	Three-part pricing (TPP) [53]	Tiered pricing approach over fixed time intervals during a drug's exclusivity period, which consists in three phases: Phase 1, Evaluation: prices are set low to encourage adoption and generate real-world evidence; Phase 2, Reward: prices reflect the effectiveness determined in the Evaluation phase, rewarding innovation. Phase 3, Access: prices are reduced to enable widespread adoption	Theoretical scheme
24	Value informed, affordable pricing ("VIA pricing") [54]	The model adjusts societal thresholds for WTP based on the disease severity and the innovative drug's budget impact. Different thresholds are set based on trade-offs among cost per QALY, disease severity, and budget impact, as determined by decision makers	Theoretical scheme

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
25	Pricing anchored to RCT performance [47]	Model proposed to link drug pricing to performance as demonstrated in later phases of RCTs, starting from phase III. It involves a series of specific performance benchmarks that allow for incremental price adjustments within pre-negotiated ranges based on evidence from trials. After proving safety in phase II, an initial price is negotiated to cover operating expenses and production costs. Price are adjusted as certain milestones, such as improved clinical efficacy, are achieved. The maximum price is reached if all performance milestones are met, while the lowest price applies if only one early-phase milestone is met	Theoretical scheme
26	Limit pricing model (for patent-protected drugs) [55]	Model proposed for drugs with patent protection that provides a threshold above which a net increase in health spending is triggered. The limit pricing identifies the maximum viable price that will not necessitate extra funding, although the final price remains negotiable. Limit pricing helps determine if a requested drug price will increase the overall budget. Unlike an ICER analysis, which assesses the drug's benefits from an individual perspective, limit pricing considers the broader impact on healthcare budgets. Exceeding the budget could mean cutting other services. Limit prices are set equal based on reduced use of related healthcare services either by eliminating redundant services or enhancing outcomes to avoid costs	Theoretical scheme
27	Portfolio package [56]	A combined product package for first-line and second-line treatments is offered at an reduced price	See "combination-based pricing"
28	Benefit-Based Advance Market Commitment (BBAMC) [57]	Model proposed for vaccines that offers value-based AMCs to manufacturers that meet a minimum effectiveness standard, leading to a country-specific process for securing guaranteed volumes. The product that aligns best with the payer's preferred characteristics receives both a higher price and a larger share of the revenue commitment. The value-based price is paid for a specific portion of the guaranteed commitment up to a maximum volume or time; beyond that, a discounted "tail-price" similar to off-patent generic pricing applies. Poor countries would pay only the tail price from the start	Theoretical scheme
29	DRG add-on payments: high-priced drugs and MDs [58]	Add-on payments to the DRG tariff to cover high-cost drugs, MDs, or combinations. Hospital payments follow national tariffs set per DRG, covering the costs of drugs/MDs. However, innovative treatments with expensive drugs and MDs can lead to significant cost variations within a DRG, which might cause hospitals limit access to these technologies. A short-term solution often involves using such add-on payments	Inpatient drugs and MDs in France [58]
30	DRG add-on payments: new technology add-on payment [59]	Temporary payment added to the existing DRG, giving payers time to collect cost data to set future DRG payment rates (typically updated every 2–3 years). To qualify, technologies must meet certain innovation criteria. The scheme suits AI algorithms or technologies licensed with "innovativeness pathways" (e.g., FDA breakthrough device designation)	AI stroke triage tool in the USA [59]

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
31	Advance market commitment (AMC) [57, 60]	Governments or purchasing groups commit to buying a set quantity of a drug at a mutually agreed price before it is available. Prices are usually tied to R&D costs with an assumed profit margin. AMCs are a "pull" mechanism, ensuring a market for products that meet predefined specifications, fostering competition without binding to a specific manufacturer or product. They are often used to finance vaccines development, production, and distribution	Late-stage pneumococcal vaccine in low-income countries [57]
32	Annuity-style payment model [61]	Model that spreads the cost of extremely high-priced therapies over a specified period. Payments may be tied to continued proof of clinical efficacy, forming a risk-sharing agreement between the payer and the manufacturer. This scheme is suitable for ultra-rare genetic diseases	Strimvelis in Italy (autologous CD34+ enriched cell) [62]
33	Performance-based instalment payment model for ATMPs [63]	Model proposed for ATMPs that integrates outcome-based instalment payments with pay-for-performance and annuity payment features. Payments for ATMPs are made in instalments due upon achieving specified pre-agreed goals. A fund may be necessary for cases where the therapy's success probability is low to prevent cases with uncertain outcome from being rejected due to the risk of uncovered costs. This would require combining performance-based reimbursement with a risk-pool model to ensure access to ATMPs for challenging cases	Luxturna® (voretigen neparvovec) in Denmark [64]
34	"Insurance-type" model for antibiotics [65]	Model proposed for antibiotics involving a global flat annual fee, shared among all healthcare systems, combined with a per-unit price paid by healthcare providers to the manufacturer. Most of the manufacturer's revenues is detached from the volumes of drug usage. The structure provides insurance as follows: (1) the manufacturer is protected from the commercial risk of low pricing and variable usage; (2) healthcare systems are assured of the availability of antibiotics for patients, promoting the development of new antibiotics; and (3) financial obligations of healthcare systems are capped, safeguarding against the financial impact of a resistant infection outbreak under a premium pricing model	Theoretical scheme
35	ATMP funds [64]	Establishment of dedicated "ATMP funds" to cover high-cost ATMPs, similar to the Cancer Drug Fund in the UK or the specialized fund for "expensive innovative drugs" in Italy	First attempts in UK, Italy, and Germany [64]
36	Bundled pricing/payment (bundling) [52, 56]	Drug bundling involves negotiating agreements that combine multiple individual pharmaceutical agreements from various clinical areas into a single deal. Bundling may also include additional patient services provided by manufacturers alongside the product	On-patent drugs in New Zealand [52]
37	Marginal value-based reimbursement (MVBR) [66]	When multiple medicines are used in combination therapy, it is challenging to determine the value contribution of each medicine. Current reimbursement practices may not fully reward an add-on drug based on its marginal economic value within a combination therapy. This issue arises because: (a) infusions are reimbursed per vial at a constant price and (b) the per-vial price does not change based on the indication. In the MVBR scheme, the total cost (i.e., the 'reward') should adjust depending on the specific indication if the marginal value differs. The original therapy does not share the marginal value of combination therapy and is not reimbursed at a fixed per-vial price	Theoretical scheme

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
38	Combination of national value-based + regional cost-plus pricing [67]	Scheme where the cost of drugs is divided between regional and national payers. The scheme involves: (1) regional funding for drug volumes at cost-plus pricing; (2) regional responsibility for the drug budget, but only for cost-plus-priced drugs; and (3) national responsibility for funding the value of innovations using VBP	Theoretical scheme
39	Conditional treatment continuation: patient level [23, 68, 69]	Coverage for treatment continues only for patients who show a predefined response. Typically, continued coverage depends on achieving short-term goals (e.g., tumor response or lower cholesterol levels). For patients who do not respond, manufacturers may provide products for free or at a discount	Alzheimer's disease drugs in Italy [68]
40	Coverage with evidence development (CED) [18, 23, 68–71]	A MEA for new health technologies that allows temporary reimbursement with the requirement of collecting further evidence. Data collection can occur either at the patient or population level. CED can be designed around two options: (a) coverage with study participation ("only in research"), limiting coverage to patients in clinical trials or registries and (b) coverage with appropriateness determination ("only with research"), granting coverage to all patients, provided additional evidence is collected	Acomplia® in Sweden for the treatment of obesity from 2006 to 2008 [72]
41	Diagnosis confirmation model (DCM) [73]	Model proposed for antibiotics with a dual reimbursement structure based on whether the novel therapy is continued. (1) Empiric use price: if the decision is made to stop the novel therapy within a specified period (usually before microbiological results are available), a lower "empiric use" price is charged, lower than the full price, but higher than other cheaper yet effective antibiotics. The difference discourages overuse of the novel therapy and encourages a shift to cost-effective drugs. (2) full price: If the novel therapy is continued, indicating necessary for treatment, a full price reflecting the antibiotic's value is charged for the entire course. Patient-level data collection is crucial to enable payment calculations and monitor adherence to clinical guidelines	Theoretical scheme
42	Discounts or rebates (confidential) [68, 70]	An unconditional discount off the list price is agreed upon confidentially, either as an upfront discount or an ex-post rebate refunded by the manufacturer	Kisplyx® (lenvatinib) in England and Wales [15]
43	Early temporary authorization/reimbursement (ETA/ETR) [74]	An innovative drug that is awaiting central authorization or is not available through conventional reimbursement can be provided to patients with critical medical need. The manufacturer must be in the process of seeking market authorization or conducting clinical trials with preliminary evidence. An ETA license is requested by the manufacturer. Depending on prior authorization, either a medical need program or a compassionate use program can be initiated. If monetary compensation is requested, it is defined as early temporary reimbursement (ETR)	Compassionate use in Belgium [74]
44	Expenditure capping: patient level [15]	A patient-level cap is set on the treatment cost (based on the number of products, dosage, or duration), and the manufacturer provides any products exceeding the cap for free	Revlimid® (lenalidomide) in England and Wales [68]
45	Expenditure capping: population level [15]	An aggregate spending cap is agreed upon for a defined number of patients, and the manufacturer provides products beyond this cap free of charge	Firazyr® (icatibant) in Belgium until November 2013 [75]
46	Free initial treatment/free doses: patient level [15, 22]	The manufacturer supplies initial treatment units free of charge up to a predetermined level for each patient. Beyond this, additional units are purchased at an agreed price	Cimzia® (certolizumab pegol) in England and Wales [68]

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
47	Financial/utilization arrangements (FU) [69]	Reimbursement is linked to financial or utilization outcomes, rather than explicit clinical outcomes	Increasing adoption of FU arrangements in the UK NHS [69]
48	Generic or biosimilar price linked to originator product [35, 38]	Specific price reductions are mandated for generic and biosimilar drugs, typically calculated as a percentage of the originator price. The discount can vary depending on the drug. For biosimilars, the required price form the originator is generally smaller than for generics	Generic outpatient prescription drugs in Estonia [38]
49	Individual funding request [61]	A high-cost treatment is provided through individual funding requests on a patient-by-patient basis, typically applicable to extremely expensive gene therapies	Alipogene tiparvovec available in the UK on a patient-by-patient basis [61]
50	IP-based payment: monetary prizes [60, 61]	Monetary prizes can be used to encourage innovation. Such prizes model might be used to promote the development of new antibiotics, treatments for rare diseases, drugs needed in low-income countries, or essential therapies, vaccines, and diagnostics for potential pandemics. Prizes could involve the government purchasing the therapy, offering the manufacturer a significant sum for full control over production and distribution	Prize of $5 million offered by the XPRIZE Foundation to develop COVID-19 rapid tests [60]
51	IP-based payment: out licensing of technology rights [61]	Option to license production and distribution rights to public or private payers while the manufacturer retains IP rights	Theoretical scheme
52	IP-based payment: prolonged patent rights [61]	Extension of IP rights, granting prolonged market exclusivity. The duration of the extension varies by treatment type (e.g., longer for gene therapies compared to orphan drugs)	The EU can grant Supplementary Protection Certificates
53	Priority review voucher program [60, 76]	Manufacturers who develop treatments for neglected or rare diseases receive a bonus voucher for priority review of a future drug	Voucher for United Therapeutics. for their drug Unituxin® (pediatric neuroblastoma) [77]
54	Outcome guarantees [23]	The manufacturer offers rebates, refunds, or price adjustments based on treatment failure, measured by clinical or intermediate endpoints. This approach is a subset of patient-level payment-by-results, that penalizes underperformance	ChondroCelect® (TiGenix) in Spain [61]
55	Pattern/process of care agreements [19, 23]	Reimbursement depends on the patient adhering to a recommended treatment regimen. Payers reimburse the manufacturer whenever a patient complies with the suggested treatment protocol	OncotypeDx gene expression tests in the USA [19]
56	Payment at result [78]	Payment at result agreements are conditional reimbursement schemes where payment is spread over a pre-defined period, linked to achieving milestones that measure the drug's performance. Payments to the manufacturer are withheld if the therapy is ineffective	Zolgensma in Italy [78]
57	Payment by results: patient level [15]	Payment for treatment is contingent on achieving specific patient outcomes. Payers may withhold payments until results are achieved, receive refunds for non-responders, or get additional free products for subsequent patients. Manufacturers might be required to refund a proportion of the payment based on individual patient outcomes	Alglucosidase alpha for late-onset Pompe disease in Estonia [68]
58	Payment by results: population level [15]	Payment to the manufacturer depends on achieving agreed outcomes in the treated population. Payers can withhold payments until outcomes are achieved, receive refunds for a predefined share of patients not responding to treatment, or receive free additional products for subsequent patients	Interferon-beta and glatiramer acetate in England and Wales [68]
59	Performance-linked reimbursement [69, 71]	Scheme that ties the level of reimbursement for covered products to the measurement of clinical outcomes observed in the real-world settings	Oncotype DX® Breast Cancer Assay in the USA [79]

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
60	Staggered (or over-time) payments [31]	Model that allows for payers to make structured payments to manufacturers over set periods for each patient receiving the therapy	Kymriah® (tisagenlecleucel) in Italy [31]
61	Netflix/subscription model [31, 80]	The scheme decouples reimbursement from sales volume, granting manufacturers a fixed payment amount regardless of how much it is sold. It serves as a "pull incentive" based on the overall value to the health and social care system, rather than just individual patient benefits. It is particularly effective in addressing "market failures" and has been utilized to revive development in neglected therapeutic areas, such as antimicrobials	Ceftazidime-avibactam in the UK [80]
62	Netflix plus model [81]	The scheme aims to incentivise R&D and foster competition through multiple tenders involving patented therapeutic alternatives, creating a market environment similar to the off-patent generic market. Unlike the classic Netflix model, where only the tender winner of could sell their product, the Netflix plus model proposes multiple short-term tenders, encouraging future market entries and negotiating lower prices by circumventing long exclusivity periods. This scheme is especially relevant for niche markets often dominated by a single manufacturer, providing a guaranteed revenue stream to encourage ongoing development. It also incorporates a fee-for-service payment with a price-volume agreement, where larger purchases lower the overall procurement cost for the payer	Theoretical scheme
63	Benchmark-based sales-delinked payment model for antibiotics [82]	A model designed for antibiotics that proposes payments to manufacturers based on factors other than sales volume, such as value-based or milestone payments over a defined period. Payments can start with a base amount linked to the registration of a new qualifying antibiotic, with additional payments awarded for meeting specific benchmarks demonstrating the drug's effectiveness. The delinked payment model can include a mix of globally benchmarked payments, with the benchmarks reflecting the manufacturer's net profit	Theoretical scheme
64	Success fee (add on to outcome-based risk-sharing agreements) [83]	Ex-post payment scheme where manufacturers are reimbursed only for patients who benefit from the therapy. Initially, the drug is provided at no cost to the NHS. The NHS and the manufacturer set a timeframe to assess the drug's effectiveness based on the disease, clinical trial data, and treatment duration, distinguishing responders from non-responders	Esbriet (pirfenidone) in Italy [83]
65	Reimbursement for life-saving/life-extending drugs [84]	Involves reimbursement for treatments of programs that may not considered be cost effective but are considered life saving for serious and rare medical conditions	Life-Saving Drug Program in Australia [85]
66	NUB payments (German acronym for "New Diagnostic and Treatment Model") [86]	Additional funding is provided for new technologies if their cost exceeds existing DRG tariffs in inpatient care, pending updates to the DRG tariffs. The process involves two steps: (1) the hospital submits a request to the German Institute for the Hospital Remuneration System to gain 'Status 1' designation if the technology meets the innovation criteria and (2) the hospital negotiates a payment with health insurance representatives, who are not obliged to agree on the payment	Used in Germany [86]

Table 2 (continued)

ID	Scheme type, source	Scheme type description	Illustrative examples
67	Technology leasing reimbursement strategy (TLRS) [87]	The scheme involves regular cost-effectiveness assessments. Once a technology cost-effectiveness price is determined, the "lease" payment for each period of delivered health is calculated based on a series of payments over the technology's expected lifespan, equivalent to the net present value. Payment streams may vary, considering inflation adjustments, fixed payment periods, and measures of effectiveness. Payments are made based on the observed mean effectiveness compared to expected outcomes, with adjustments if the technology underperforms or overperforms in delivering health benefits	Theoretical scheme
68	Tiered-pricing framework (TPF) [2]	The reimbursement price decreases as more generic firms enter the market. The maximum allowable reimbursement price starts high and progressively lowers with each new generic entrant supplying the market. In Canada, when a generic manufacturer enters the market, the generic drug price must decline to the next tier (i.e., from 75%/85% to 50% to 25%)	Generics policy in Canada [88]
69	Prize (reward) system based on societal willingness to pay for health benefits [89]	Model proposed to reward innovation by setting a price based on the cumulative health benefits achieved over time, particularly total population health gains. The approach a maximum WTP for research based on WTP for health improvements. If prices exceed societal WTP, further research may be incentivized, but the resultant discoveries may not be economically viable; conversely, lowering prices below societal WTP, may stifle research and inhibit valuable discoveries. The proposed prize system incentivizes investments in R&D by compensating innovators for the social value of their drug innovation	Theoretical scheme
70	DiGA model ("Digitale Gesundheitsanwendungen") [90, 91]	The pricing of DiGA (German for: Digital Health Applications) is governed by §134 of the Social Code Book V. In the first year, manufacturers set their price freely but must consider fixed reference price groups based on the application's indication and the category of its positive healthcare effect. Starting from the 13th month, prices are negotiated between the manufacturer and the National Association of Statutory Health Insurance Funds (i.e., GKV-Spitzenverband)	Apps reimbursed in Germany available in the DiGa Directory [92]

ATC Anatomical Therapeutic Chemical Classification, *ATMP* advanced therapy medicinal product, *DRG* diagnosis related group, *EU* European Union, *FDA* Food and Drug Administration, *GDP* gross domestic product, *ICER* incremental cost-effectiveness ratio, *IP* intellectual property, *MD* medical device, *MEA* managed entry agreement, *NHS* national health system, *NPV* net present value, *QALY* quality-adjusted life-years, *RCT* randomized controlled trial, *R&D* research and development, *RWD* real-world data, *VBP* value-based pricing, *WTP* willingness to pay

Note: Schemes 1–28 are labeled as pricing schemes; schemes 29–70 are labeled as payment schemes

the retrieved schemes in four clusters, indicative of possible rationales for choosing a scheme: *handling financial affordability* (e.g., reducing financial uncertainty and managing budget impact) [37/70, 53%], *providing market incentives* (e.g., rewarding innovation and stimulating further R&D) [15/70, 21%], *ensuring industry profitability* (e.g., maximizing revenues, entering new markets, or growing the market share in existing markets) [14/70, 20%], and *mitigating clinical uncertainty* (e.g., generating real-world clinical evidence) [13/70, 19%]. These objectives are not mutually exclusive. When a scheme type could not be assigned to any of the above, its objective was generically labeled as *fostering patient access* (e.g., addressing unmet needs and enlarging patient access) (5/70, 7%).

3.3.2 Measurement of an Outcome

Among the 70 scheme types, around one quarter (15/70, 21%) involved the measurement of clinical outcomes, at the patient level (9/70, 13%), population level (3/70, 4%), or both (3/70, 4%). In three scheme types (3/70, 4%), the outcome measurement was optional. Some schemes conditioned reimbursement on meeting specific process outcomes (as opposed to clinical outcomes), including pre-specified patient adherence targets [23] or measures of utilization outcomes [69]. For some schemes, such as the performance-linked reimbursement arrangements, it is not the *reimbursement status*, but rather the *reimbursement level* that is tied to real-world clinical outcome measures [69, 71].

3.3.3 Timing and Modalities of Payments

Payments could be made as single lump sums, or could be split over time, either in the form of staggered constant payments or staggered performance-based payments. In our sample, staggered payments were observed in eight schemes (11%), as constant payments (5/8, 63%), performance-based payments (2/8, 25%), or both (1/8, 13%). The two-part pricing scheme proposes a payment format that combines an entry fee to be paid upfront, with a usage fee, charged every time there is a purchase [24]. As for the other schemes, detailed information on the timing of payments is missing, although it can be inferred that in most of the agreements, payments happen in lump sums either upfront or upon reaching certain outcome targets.

Furthermore, some schemes involve a financial adjustment upon verification of the specified outcome component being measured. Such adjustments can be either *prospective* (i.e., payments are made only if the treatment works) or *retrospective* (i.e., refunds are received if the treatment does not work). Among the schemes that involved the measurement of an outcome identified in this review, eight (11%) involved explicitly *prospective adjustments*, for instance in the case of ex-post payment of success fees only for patients receiving a real benefit from therapy [83], or annuity-style payment agreements with payments contingent on continuous demonstration of treatment success [61, 63]. Agreements with outcome guarantees referred explicitly to *retrospective adjustments* in the form of rebates, refunds, or other adjustments following treatment failures (1, 1%) [23]. However, some schemes could entail *either prospective or retrospective adjustments*, be it in the form of treatment response conditioned payments or of full/partial refunds, depending on the specificities of the negotiations. In several cases, the timing of payments, modality of payments, or both, could not be univocally defined for a scheme type.

3.3.4 Evidence Collection Requirements

Pricing and payment schemes could be characterized by varying types and levels of uncertainties. Size of the treated population, treatment duration, or treatment effectiveness were mentioned as the most common sources of uncertainty in MEAs by Andersson and colleagues [93]. Clinical evidence can be collected in different ways, leveraging ad hoc clinical studies, ongoing clinical studies, or real-world data, either based on newly established registries or other available routine sources (e.g., hospital data). More recently, Horrow and Kesselheim also referred to the clinical relevance of the outcome measures used in clinical trials as an additional relevant source of uncertainty for gene therapies [10]. Following the approach in Towse and Garrison [14], this study leveraged the value of information (VOI) framework to investigate the evidence collection requirements in pricing and payment agreements.

Among the retrieved schemes, in 33 (47%) cases a given technology was adopted without requiring additional evidence collection, in 18 (26%) it was adopted but additional evidence was required, by linking the evidence collection to manufacturer prices or revenues, sometimes through a specific follow-on study. In 19 cases (27%), the general description of the scheme did not allow us to distinguish whether and how further evidence had to be collected, or this dimension was not relevant. The data collection requirements, the stakeholders involved in this process, and the link between the real-world evidence and the agreement price/payment levels are also indicative of the efforts associated with its implementation, and/or of the feasibility of its implementation in each context. Table 3 summarizes the defining elements of pricing and payment schemes observed in the 70 scheme types retrieved, while Table 4 of the ESM provides such information for each scheme of the list.

4 Discussion

The purpose of this work, conducted as part of the larger Horizon Europe project HI-PRIX (Health Innovation Next Generation Payment & Pricing Models), was to build an inventory of the types of pricing and payment schemes, either used or proposed, for new health technologies. Overall, 70 unique types of pricing and payments schemes have been identified, both theoretical formulations and schemes applied in the real world. Some clusters of schemes designed or theorized for therapeutic areas that pose specific challenges could be identified (e.g., antibiotics, vaccines, rare/orphan, gene therapies). Fewer types of schemes seem to address other equally important challenges, such as the already high (and likely rising) cost of long-term care associated with the aging population, or the reimbursement of digital health technologies. Furthermore, this analysis shows that most of the scheme types are not designed for specific technologies, and could in principle be applied to drugs, devices, or their combinations.

4.1 Flexible Use of the Database to Identify Relevant Pricing and Payment Schemes

The second objective of this study was to classify the totality of types of pricing and payment schemes retrieved, with the ambition of helping interested individuals — from different stakeholder groups — search for, and find, the schemes relevant to their specific purposes. At first, we sought to generate a new or updated taxonomy for the schemes. However, this proved more difficult to achieve than expected, and developing a taxonomy that meets this need was deemed not viable, owing to the intertwined characteristics that define each scheme. Therefore, our proposal is that it is better to define pricing and payment schemes by the combination of their key characteristics, rather than clustering them based on a pre-defined set of labels that may be vague. The outcome of this endeavor was therefore that the best way to categorize available types of pricing and payment schemes is to allow a flexible use of the entire repository of schemes, and to subordinate any further classification to the specific purposes or uses that different stakeholders might have.

4.2 Practical Examples of How the Database of Schemes Can Be Used

This paragraph illustrates possible practical applications of the database of types of pricing and payment schemes (Table 4 of the ESM), and includes the information and insights it can provide. In the following examples, the main search driver is the objective for choosing a scheme, that fulfills a predefined goal.

Example 1 Schemes to manage the budget impact of high-priced drugs.

> A payer is interested in exploring possible solutions that could be employed for the coverage of expensive therapies, like cell or gene therapies, and wants to find more information about available types of pricing and payment schemes in this area.

A first keyword search with relevant terms such as "expensive," "high-priced," "high costs," or combinations of similar words would preliminarily identify very different scheme types: annuity-style payment model, which spreads the costs over a certain period of time [61], including with performance-based payments conditioned to treatment efficacy [63]; add-on payments topped up to standard Diagnosis Related Groups tariffs for innovative high-priced therapies as short-term tailored solutions for the reimbursement of costly drugs and MDs (and avoid denied patient access at the hospital level) [58]; dedicated funds (e.g., ATMP funds), which grant reimbursement drawing upon a pre-defined pool of resources [64]; and issuing of individual funding requests, on a patient-by-patient basis [61]. While all are suitable for expensive treatments, each type of scheme addresses specific challenges and could be employed by diverse actors in different circumstances. For instance, to create an ATMP fund, institutional commitment from the Ministry of Health might be necessary. Another viable approach would be to search the schemes whose primary objective includes "handling financial affordability," identifying 37 possible scheme types. One could then refine the search by adding additional design features, based on specific needs. For instance, compared to prior taxonomies that plainly distinguished between outcome-based and financial-based schemes, anyone interested in understanding how to leverage split payments to address the challenge of high costs could identify instalment/annuity-style models [61, 63, 87] (e.g., reimbursement of

Luxturna® [voretigen neparvovec] in Denmark since 2020), or subscription-style models [51, 80, 81] (e.g., fixed amount paid for ceftazidime-avibactam in the UK regardless of the amount of antimicrobials used via a 3-year extendable contract), as well as scheme types that, by design, do not have univocally defined payment timing or modalities, like the combination of different lines of treatments in a portfolio package [56] (e.g., several cases in France, Switzerland, or the UK) or the tiered-pricing framework [2] (e.g., generics in Canada [88]).

Example 2 Schemes to drive continuous innovation.

> The scientific committee of an observatory focussing on antibiotic resistance seeks to develop a model to pay for antibiotics prescribed following antimicrobial stewardships guidelines and needs to explore available payment schemes in use in that area, as well as any pull incentive that act as an actionable tool to reward and incentivize innovation.

In that area, the database allows the retrieval of types of schemes designed to address specific antibiotic challenges, collecting both applied and theoretical types of schemes. Applied schemes include the subscription models that offer manufacturers fixed monetary sums irrespective of actual antibiotic sales volumes [80, 94] (e.g., we already cited the example of antimicrobials in the UK), or the advanced market commitments, under which large purchasing bodies, like governments, make formal commitments to buying a given amount of drugs at an agreed price [57, 60] (e.g., documented for pneumococcal vaccines in low-income countries [57]). Theoretical schemes include the "insurance-type" model, which aims at insuring the producers (against the commercial risk of low prices and unpredictable usage), the healthcare providers (against the risk of scarcity of antibiotics) and the healthcare systems (against the financial risk of facing infection outbreaks under high prices) [65], or the benchmark-based sales-delinked payment model, which propose a baseline payment when a new qualifying antibiotic is registered, followed by marginal benchmark-based payments when specific performance milestones are reached [82]. These proposals by the scientific community seem to suggest that antibiotic-specific challenges are still unresolved, and that the further development of practical tools such as dedicated pricing and payment schemes is needed.

Example 3 Schemes to generate revenues from digital health technologies.

> A software developer is interested in exploring payment schemes for digital health technologies, with a specific focus on the prescription apps that are used directly by patients with no mediation nor interaction with clinicians (such as digital therapeutics or DTx).

The database can be searched for terms such as "digital health," "digital therapeutics," and "mHealth". The German DiGA ("Digitale Gesundheitsanwendungen") model for low-risk prescription apps is identified [90], under which the manufacturer sets the price independently for the first 12 months; then, starting from the 13th month, the price is determined through joint negotiations between the German National Association of Statutory Health Insurance Funds (GKV-SV) and the manufacturer. This agreement must be in place for at least 12 months and may include components based on performance [90]. The full list of reimbursable apps are available in a public DiGA directory [92]. More recently, France has introduced a reimbursement scheme for DTx and digital MDs (including telemonitoring), the PECAN model ("Prise en charge anticipée des dispositifs médicaux numériques"). This scheme guarantees an initial flat rate for a period of 3 months, and a maximum yearly reimbursement per patient [95].

In the area of digital health technologies, the database also reports examples of payment schemes that could be used for AI-based decision support systems used by clinicians, such as the Diagnosis Related Group add-on payment model for new technologies (NTAP) [59]. To be covered under the NTAP, technologies need to meet specific innovativeness criteria, which makes the model well suited for AI-based applications. Some applications in the USA are available, where the Centers for Medicare and Medicaid Services applied it to an AI-based stroke triage algorithm that detects and supports the treatment of patients with stroke. Tellingly, the NTAP is similar to the German NUB (German acronym for "New Diagnostic and Treatment Model"), which grants additional funding for innovative technologies in the inpatient setting, when their price is above existing Diagnosis Related Group tariffs, while waiting for the tariffs' update [86].

Example 4 Schemes to reduce the clinical uncertainty around medical devices.

A governmental body would like to grant access to new devices, but the evidence of their effectiveness is uncertain.

The database allows filtering for schemes whose primary objective is to reduce the clinical uncertainty by collecting new evidence over the technology lifecycle. Though not limited to MDs, evidence collection can be mandated under schemes that subordinate payments to the presentation of further evidence. Compared to the simple distinction between outcome-based and non-outcome-based schemes, the database allows the identification of multiple pricing and payment schemes, and cases of application where available, each with its own unique features and mechanisms, as described by their unique relevant dimensions (above). Payers can opt for withholding full or partial payments until a pre-agreed outcome is achieved, may receive refunds, partially or entirely, when patients/populations do not meet the expected response, or can obtain free additional units to treat future patients. For instance, conditional treatment coverage continuation to the achievement of a pre-agreed response at the patient level [15, 23, 69]; outcome guarantees can be used to penalize underperformance [23]. For instance, some Alzheimer's disease drugs in Italy are provided for free by the manufacturers for the first 3 months, after which, if successful, treatment is continued under national reimbursement [68]. Similarly, a vast number of coverage with evidence development schemes, applied to MDs and diagnostics, designed around alternative coverage options (i.e., only in research, only with research) and implemented in different countries (Austria, Belgium, England, France, Germany, Switzerland, USA), can be explored. Payment by results, either at the patient or population level, links payments to actual responses [15, 79].

4.3 Contribution to the Literature

This work adds to the available body of research that investigates pricing and payment schemes of health technologies. As for the first objective, this work had the ambition to become the first comprehensive repository of any type of pricing and payment scheme for health technologies (medicinal products, devices, and drug-device combinations; theoretical and applied schemes). Other databases exist, including the dataset of coverage with evidence development schemes for devices implemented from 2015 to 2020 in Europe, produced as part of the Horizon 2020 project COMED (Pushing the Boundaries of Cost and Outcome Analysis of Medical Technologies) [96], as well as the Performance Based Risk Sharing Database, produced by the University of Washington [97]. While leveraging these prior examples, our work intended to be more comprehensive in its scope, and to be a freely accessible tool. Regarding the scope, our database extensively covers any type of pricing and payment schemes proposed or used, not only the outcome-based schemes, or not only those with real-world implementations. Regarding the accessibility, the complete list of scheme types, including their distinctive features identified through this review, has been made publicly available through the Pay-for-Innovation Observatory. The Observatory is accessible online through the HI-PRIX website (https://p4i.hiprixhorizon.eu/) and will be periodically updated to continuously include both new types of schemes, and practical applications of the already available scheme types. Yearly updates will be done throughout the project duration both by employing ASReview, a machine learning tool that assists researchers in the conduct of literature reviews, as well as with ad hoc consultations of relevant

stakeholders (e.g., health technology assessment bodies) involved in the HI-PRIX project [28].

As for the second objective, given the comprehensive nature of our work, we concluded that a unifying taxonomy to categorize the high variety, and complexity, of the retrieved types of schemes was not easily achievable. Not only are various types of pricing and payment schemes characterized by many distinctive features, but these may also be differently relevant across different stakeholders or specific purposes. Tellingly, whether designed to incorporate the unique features of a given technology, or to address specific challenges, the schemes have been classified in different ways.

Prior taxonomies [14, 19, 22] are useful at a general descriptive level (e.g., distinguishing outcome-based vs financial-based schemes), but are less useful at a more detailed level (e.g., distinguishing between the vast number of available types of schemes given certain objectives or requirements), as they typically account for only a handful of relevant dimensions. While some searches are rather obvious (e.g., by country or by types of technology), if someone has specific objectives in mind for a search, existing taxonomies may be poorly informative. Therefore, we proposed a new approach that overcomes the shortcomings of prior taxonomies. Instead of trying to fit the full list of scheme types into a rigid taxonomy, built around arbitrary fixed dimensions, we suggest a flexible use of our database, driven by the specific objective that one might have, and that allows leveraging of the key characteristics of each type of scheme. This allows each individual user to select the dimensions that are most relevant for their specific purposes. To that end, the best taxonomy might result in being essentially no fixed taxonomy.

4.4 Limitations

This study has some limitations. First, our analysis comments on the available types of pricing and payment schemes without considering their relative frequency of observation. For instance, scheme types that are described in single sources (e.g., "insurance-type" model for antibiotics) receive the same attention as scheme types that are commonly used (e.g., CED). While the frequency of observation could provide insights into trends and practices, our primary focus was to shed light on the distinctive design features of any type of scheme, being proposed or used. Second, this study only considered records published in English, therefore excluding sources in other national languages. This limitation was mitigated by the search of the gray literature that included multi-country evidence from international organizations.

Table 3 Design and features of pricing and payment schemes

Design and features of pricing and payment schemes	*N*	%
Pricing vs payment		
Pricing	28	40%
Payment	42	60%
Theoretical vs applied		
Applied	47	67%
Theoretical	23	33%
Target health technology		
Any technology	32	46%
Drugs	34	49%
Drugs in general	23	68%
Generics	5	15%
Antibiotics	4	12%
Patent-protected drugs	1	3%
Biosimilars	1	3%
Vaccines	3	4%
Devices	2	3%
Other (digital apps, drug-device combinations, AI)	4	6%
Target therapeutic area		
Any therapeutic area	55	79%
Orphan/ultra-rare diseases	5	7%
Disease-specific conditions	6	9%
Genetic conditions and ATMPs	4	6%
Objectives		
Handling financial affordability	37	53%
Providing market incentives	15	21%
Ensuring industry profitability	14	20%
Mitigating clinical uncertainty	13	19%
Other (fostering patient access)	5	7%
Measurement of an outcome		
No	52	74%
Optional	3	4%
Yes	15	21%
Patient level	9	13%
Population level	3	4%
Both levels	3	4%
Timing and modalities of payments		
Single payment	5	7%
Staggered payments: constant	6	9%
Staggered payments: outcome based	3	4%
Entry fee + usage fee	2	3%
Retrospective adjustments	8	11%
Prospective adjustments	1	1%
Only modality of payments not univocally defined	9	13%
Only timing of payments not univocally defined	3	4%
Both timing and modality of payments not univocally defined	50	71%
Not relevant/applicable	2	3%
Evidence collection requirements		
Adopt with no additional evidence collection	33	47%
Adopt but seek/require further evidence	18	26%
Not relevant/available	19	27%

AI artificial intelligence, *ATMP* advanced therapy medicinal product

Note: percentages do not always add to 100% because one scheme type may be designed for multiple uses (e.g., more than one technology, therapeutic area, or objective)

5 Conclusions

As tensions between manufacturers (who legitimately aim to recoup remarkably high R&D investments), healthcare providers (who want to guarantee widespread patient access to novel technologies), and payers (who are responsible for the sustainability of the healthcare systems) continue to mount, pricing and payment schemes have the potential to offer a comprehensive toolkit to those interested in pricing, reimbursement, and access decisions, highlighting that it is not the scheme per se that is innovative, but rather its application or use in a given context or for a given challenge. This work attempted to elaborate a new comprehensive approach to classify available types of pricing and payment schemes of health technologies. The next consecutive steps of the research focus on the analysis of the specific details of each scheme negotiated in a given real-life context, retrieved as part of this review.

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Declarations

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Conflicts of Interest/Competing Interests There are no direct conflict of interests to declare relating to this work. Outside the conduct of this work, Oriana Ciani has received consulting fees from Lumanity and participated in advisory boards sponsored by MSD. Michael Drummond has provided consulting services to several pharmaceutical companies and has advised several governments on issues relating to the pricing and reimbursement of pharmaceuticals.

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Availability of Data and Material Part of the data used as part of the current study are available through the Pay-for-Innovation Observatory of the HI-PRIX project website. Further details of the data used are available from the corresponding author on reasonable request.

Code Availability Not applicable.

Authors' Contributions All authors contributed to the study conception and design. VA performed the literature search and data analysis, and prepared the original draft; OC and MD critically revised the work. All authors read and approved the final manuscript.

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