Interactions between health regulation and Health Technology Assessment for coverage in health systems and comprehensive care

Interações entre regulação sanitária e Avaliação de Tecnologias em Saúde para cobertura em sistemas de saúde e a integralidade do cuidado

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Abstract

This study analyzes the interactions between regulatory and health technology assessment (HTA) processes aimed at health systems coverage. A review was carried out in five databases to identify experiences of articulation between regulatory processes and HTA processes, and 19 publications were selected. Regarding the type of process, early dialogue, scientific advice and parallel advice stood out as forms of interaction between HTA and regulation. The studies addressed the interaction between HTA and health regulation for medicines coverage policies in health systems, with scant evidence in relation to other products. Furthermore, this interaction is basically described according to the entry of new technologies into health systems. The interaction between HTA and health regulation resulted in reduced deadlines for the commercialization and incorporation of the technology into health systems. The types of interaction processes identified can benefit the entire health system, increasing coverage and comprehensiveness of care. However, despite advances, some barriers to interaction between regulatory agencies and the management of coverage systems still persist.

Keywords: Health Technology Assessment; Health Care Coordination and Monitoring, Review.

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Resumo

Este estudo analisa as interações entre os processos regulatórios e de avaliação de tecnologias de saúde (ATS) voltados para a cobertura dos sistemas de saúde. Foi realizada revisão em cinco bases de dados visando identificar experiências de articulação entre processos regulatórios e processos de ATS, sendo incluídas 19 publicações. Quanto ao tipo de processo, destacaram-se o *early dialogue, scientific advice* e *parallel advice* como forma de interação entre ATS e regulação. Os estudos abordaram a interação entre a ATS e a regulação sanitária para as políticas de cobertura de medicamentos em sistemas de saúde, sendo escassas as evidências em relação a outros produtos. Ademais, essa interação é descrita basicamente para o que se refere à entrada de novas tecnologias nos sistemas de saúde. A interação entre ATS e regulação sanitária resultou na redução de prazos para a comercialização e incorporação da tecnologia nos sistemas de saúde. Os tipos de processo de interação identificados podem apresentar benefícios para todo o sistema de saúde, aumentando a cobertura e a integralidade do cuidado, entretanto, apesar dos avanços, ainda persistem barreiras para a interação entre agências reguladoras e a gestão de sistemas de cobertura.
Palavras-chave: Avaliação de Tecnologias em Saúde; Regulação e Fiscalização em Saúde; Revisão.

Introduction

In the early 1970s, the production of knowledge in health—driven mainly by international scientific policies—demanded new strategies to improve regulatory capacity and incorporate new technologies into health systems, strategies that are processes of health technologies assessment (HTA), a multidisciplinary field of public policy analysis. Its main role is to provide information about what works and for whom regarding practical alternatives with the lowest resource demands. HTA also assists managers in making decisions about the incorporation and use of interventions used for prevention, treatment, care, including health promotion.

Technologies constitute an important part of the Brazilian National Health System (SUS), whether they are soft technologies, such as clinical protocols, or hard technologies, such as medicines. To incorporate these technologies, HTA transcends the epidemiological field, interacting with the social, cultural, ethical, and political-economic dimensions for the promotion, maintenance, or rehabilitation of health. Traditionally, the life cycle of a technology consists of the phases of innovation, diffusion, incorporation, full use, and abandonment.

During the innovation phase, characterized by the production of research and development, the regulatory discussion also begins when registrations of new health technologies are requested, which is understood as the pre-commercialization phase. During the phases of incorporation and full use of technology, effectiveness and performance in the real world of health services is monitored. Life cycle assessments involve different bodies in the health system, such as the Ministry of Health, state and municipal departments and health services, in addition to regulatory agencies, such as the *Agência Nacional de Saúde Suplementar* (ANS - National Agency of Supplementary Health) and the National Health Regulatory Agency (Anvisa).

In this context, international regulatory agencies, such as Food and Drug Administration (FDA), in the United States, the European Medicines Agency (EMA), in Europe, and Anvisa, in Brazil, play a fundamental role in decision-making in the cycle of new products. These agencies are responsible for regulating

the entry of medicines, vaccines, equipment, and medical devices into the market, authorizing or not authorizing the commercialization of technology in the country, in addition to providing information on safety, benefits, indications for use, and the price to be charged in the market (Garrison et al., 2013).

In this way, the first steps towards product entry are the responsibility of regulatory agencies and, subsequently, of HTA agencies—such as the National Committee for Health Technologies Incorporation in the Brazilian National Health System (Conitec)—when they refer to financing by health systems. In countries with national health systems, such as Brazil, HTA becomes increasingly necessary to support decision-making on the most efficient allocation of resources. The increase in the cost of health care, together with limited resources and the need to improve the quality and consistency of care, results in the implementation of HTA as a strategy to guide public health policies.

Although studies that evaluate the methodologies and values adopted in such HTA and health regulation assessments have been increasingly frequent, they are focused on evidence in the context of the pre-commercialization phases of new technologies, analyzing how the interaction between HTA and health regulation have contributed to the discussion about the coverage of health systems, their potential and challenges in the context of the use of real-world data, and how they have influenced risk-sharing agreements between companies and government bodies.

Incentives for regulatory interactions also came from the Health Technology Assessment International (HTAi) society, founded in 2003, whose purpose is to develop methods, strategies, and exchange of experiences in the introduction of innovations in health systems, permeating all fields of technology assessment in health, involving a multidisciplinary academic, scientific, and professional community, with the participation of public and private organizations and dedicated patients. The HTAi society has a specific interest group to study and promote greater coordination between regulation and evaluations of the incorporation of health technologies. In June 2020, this theme was incorporated into the new interest group created to promote the use of Real World Evidence for initial dialogues between the regulatory apparatus for product marketing and the standards of HTA agencies—responsible for technology evaluation and incorporation processes as a strategy for shortening the time to access technologies.

Nevertheless, the development of post-marketing effectiveness assessments using Real World Evidence is still insufficient. Also, the nature of these interactions is not known from the point of view of the context and interests involved, and neither is the convergence of evaluation dimensions used in the interactive processes between regulation and HTA.

Knowing about the interaction of HTA and health regulation is necessary to establish best practices for evaluating and incorporating new technologies into the SUS, in order to enhance the expansion of health coverage and guarantee comprehensive care. Furthermore, the institution of practices that combine HTA with health regulation in the health system has the potential to reduce the time it takes to incorporate technologies into the system, enabling new clinical and therapeutic options to reach citizens more quickly, in addition to contributing to the efficiency of resource allocation and the effectiveness and quality of services.

In this context, a review was carried out to analyze the interactions between the regulatory processes for commercialization of health technologies and those for evaluating technologies aimed at covering health systems, considering the regulatory cycles that involve entry, monitoring, and the disinvestment of health technologies.

Method

A narrative review was carried out with a view to identifying the experiences of countries that articulate regulatory processes for the commercialization of health products with HTA processes to cover health systems. The search strategy "health technology assessment" AND "regulatory" was used in the Pudmed, Embase, Cochrane Library, Scopus, Web of Science, and Scholar databases, as detailed in Annex A.

There was no publication date restriction, and studies in English, Spanish, and Portuguese were considered eligible. Primary studies that addressed the interactions between regulatory marketing processes and HTA processes aimed at health systems coverage

were included. Secondary studies, editorials, letters to the editor and articles without full text available were excluded.

To select the included articles, selection was carried out first by title and abstract. For articles classified as eligible, a complete reading was carried out. In cases of doubt regarding the inclusion or not of the article, a decision was made between the authors to reach consensus on its inclusion. For data extraction, a table was used with the general description of the studies. For analysis purposes, we considered the location of the experience, period, function within the regulatory cycle and types of interaction process between HTA and health regulation used within the regulation cycle.

The regulatory function comprises prior commercialization analyses, the development of regulations, public consultation or hearing, the authority's decision, implementation, inspection, monitoring, evaluation, and review of Regulatory Impact Analysis. The evaluation phases involve technical-scientific assessments of clinical benefits, economic, legal, and ethical aspects considering the technology cycle—innovation (research and development phase), initial diffusion (when analyses for commercialization of the country begin), incorporation (assessments for publicly funded coverage), full utilization (analysis of effectiveness and real-life performance of health services), and abandonment (withdrawal or disinvestment phase).

For the purposes of this review, a function in the regulation cycle is understood to be those actions that combine regulatory roles, namely: health approval and coverage in health systems, monitoring the wide dissemination of technologies involving real-life data for pharmacovigilance, surveillance in assistance devices, performance in health systems, and, to analyze effectiveness, adherence to clinical protocols and patient safety.

Results

The search in the databases resulted in the identification of 2,604 articles, with 1,219 single publications, of which nineteen articles were eligible after reading their titles and abstracts (Table 1).

Table 1 – Characterization of studies

Author (year)	Location	Institutions involved	Function in the regulation cycle	Type of interaction process
Balaisyte; Joos; Hiligsmann (2018)	European Union	EMA and HTA agencies	Reimbursement	Early dialogue
Battista et al (1999)	Canada	CETS and regulation	Incorporation	Not specified
Berntgen et al (2014)	European Union	EUnetHTA	Marketing authorizations	Early dialogue Scientific Advice
Henshall et al (2011)	European Union	Not shown	Regulatory approval and coverage	Early dialogue Scientific Advice Risk sharing or managed entry
Cuche et al (2014)	European Union	EUnetHTA	Pricing and reimbursement process	Early dialogue
Facey et al (2015)	Not shown	HTAi	Not shown	Early dialogue
Forrester et al (1997)	U.S.	FDA	Marketing authorizations and post-market monitoring	Early Dialogue

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Table 1 – Continuation

Author (year)	Location	Institutions involved	Function in the regulation cycle	Type of interaction process
Frønsdal et al (2012)	Australia, Canada, European Union	HTAi and CIRS Policy Forum. Collaboration on EPAR content (EUnetHTA and EMA)	Regulatory approval and coverage	Scientific advice Parallel submissions Information sharing Parallel advice Parallel review of medical devices
Henshall et al (2014)	UK	HTAi	Not shown	Early dialogue
Cox; de Pouvourville (2015)	European Union	EMA and HTA agencies	Reimbursement	Real world evidence Risk sharing or managed entry
Drummond (2015)	Sweden	EUNetHTA	Regulatory approval and coverage	Early dialogue Parallel advice
Maignen et al (2017)	European Union	NICE and EMA	Not shown	Parallel advice Scientific advice
McAuslane; Liberti; Connelly (2019)	U.S.	CIRS	Not shown	Flexible access and reimbursement pathways Early dialogue
Tafuri et al (2018)	European Union	EUnetHTA /EMA	Not shown	Scientific advice
Tafuri et al (2016)	European Union	EMA and HTA agencies	Not shown	Scientific advice
Tsoi (2013)	Canada	CADTH, HQO, INESSS, Alberta Health and Wellness	Regulatory approval and coverage	Harmonization of HTA-reimbursement and regulatory activities
Vella Bonanno et al (2019)	European Union	EUnetHTA	Pricing and reimbursement process	Real world evidence Scientific advice
Wang et al (2018)	European Union	TLV, NICE, OSTEBA, EMA, IMB, MEB and MPA	Pricing and reimbursement process	Scientific advice Information sharing
Wonder et al (2013)	Australia	TGA and PBAC	Pricing and reimbursement process	Early dialogue

Acronyms: Ema - European Medicines Agency; ATS - Avaliação de Tecnologias em Saúde; CETS - Quebec Health Technology Assessment Council; CIRS - Centro de Inovação em Ciência Regulatória; HTAi - Health Technology Assessment international; EPAR - European public assessment report; EUnetHTA - European Network for Health Technology Assessment; NICE - National Institute for Health and Care Excellence; CADTH - Canadian Agency for Drugs and Technologies in Health; HQO - Health Quality Ontario; INESSS - Institut national d'excellence en santé et en services sociaux; TLV - Tandvårds-Och Läkemedelsförmånsverket; OSTEBA - Basque Office for Health Technology Assessment; IMB - Irish Medicines Board; MEB - Medicines Evaluation Board; MPA - Medical Products Agency; TGA - Therapeutic Goods Administration; PBAC - Pharmaceutical Benefits Advisory Committee

Most of these studies reported the experience of interaction between health regulation and the technology assessment body that supports European Union health systems. Canadian experiences also stood out in the interaction between regulation and technology coverage in health systems. Most of these

studies reported experiences from 2010 onwards, due to the maturity of the application of HTA for coverage of health services, requiring discussions even in the product registration and commercialization phase. The complete characterization of the studies is available in Appendix C.

Regarding the role in the regulatory cycle, the majority mention working with health approval and technology coverage for the population and in the pricing and reimbursement process. Regarding the type of process, a variety of interactions were identified, whose characteristics are shown in Table 2. Most interactions reported experiences on early dialogue, one that is focused on dialogue between industry, regulatory agency, and HTA agency in the phase of clinical studies of medicines and health products.

Also noteworthy is the scientific advice process type, in which companies meet with the regulatory or HTA body to establish a better understanding of the recommended assessment methodologies (Berntgen et al., 2014; Frønsdal et al., 2012; Henshall et al., 2014; Maignen et al., 2017; Tafuri et al., 2016; 2018; Vella Bonanno et al., 2019; Wang et al., 2018).

Parallel advice, a process to fill gaps between the evidence requirements for regulation and incorporation of technology in health systems, was a point described on the reported experiences (Drummond, 2015; Frønsdal et al., 2012; Maignen et al., 2017).

Table 2 – Types of interaction between HTA and health regulation

Type of process	Definition
Early dialogue	Early dialogue is characterized as an initial dialogue between the industry and HTA and health regulatory agencies. It occurs in the pre-clinical phase, more specifically between phases II and III. It can facilitate the development of new technologies by clarifying the needs, expectations, and requirements for specific patient populations, comparators, and endpoints, as well as raising discussions about unmet needs in clinical practice, products in progress, expected indications, potential market size, benefits envisaged, regulatory approach and forms of evidence that are likely to be required (Balaisyte; Joos; Hiligsmann, 2018; Facey et al., 2015). Technology developers often present their proposed clinical trial designs to regulators in order to obtain recommendations and receive suggestions for improvement (Drummond, 2015).
Scientific advice	Scientific advice is a voluntary and early dialogue, in which companies request advice from a regulatory body and/or HTA on their clinical development plans (population and comparison used and expected results) and economic models (Maignen, et al., 2017). The aim is to answer questions from the pharmaceutical industry, as well as improve interactions and understanding of methodologies between the two agencies (Frønsdal et al., 2012).
Parallel advice	Similar to scientific advice, parallel advice aims to bridge the gap between evidence requirements for different decision makers and can be initiated at any point in the technology development life cycle, although it is often requested before the development program reaches the crucial phase (Tafuri, et al., 2016, 2018).
Real world evidence	Real-world evidence is that collected from medical records and the pharmacovigilance system. Increasingly being preferred over surrogate data, they can contribute to the evidence base needed for coverage and reimbursement decisions, such as demonstrating how a medicine works in populations or under conditions not covered by the study or concerning another medicine not included in the study (Cox; de Pouvourville, 2015; Kanavos; Angelis; Drummond, 2019).
Risk sharing or managed entry	These are agreements between agencies and industry that occur when evidence of effectiveness and safety is not clear enough. Sometimes these agreements are designed to facilitate the generation of key evidence while using technology in the healthcare system (Henshall et al., 2014).

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Table 2 – Continuation

Type of process	Definition
Information sharing	Sharing information reduces duplication of work between HTA and health regulation, making access to technology faster for the patient (Frønsdal et al., 2012; Wang et al., 2018). However, information sharing may face legal limitations, as some agencies have strict legislation on data confidentiality (Frønsdal et al., 2012).
Flexible access and reimbursement pathways (FRP)	They provide options to manage the introduction of new medicines, to reduce the uncertainty present at the time of accelerated regulatory approval. This process occurs through the evaluation of a robust practical experience database. They can address regulatory data limitations and provide opportunities for managed divestment if products do not meet initial clinical expectations (Mcauslane; Liberti; Connelly, 2019).
Harmonization of HTA - reimbursement and regulatory activities	Harmonization involves the rationalization of regulatory processes, in addition to the alignment of evidentiary requirements These initiatives can have positive implications across and within the healthcare system in terms of patient care, innovation, and system sustainability, creating economies of scale in clinical data generation, promoting good interactions, defining the boundaries of governance and leadership and ensuring organizational security (Tsoi et al., 2013).
Parallel review of medical devices	It is the enhanced sharing of information between agencies used in the regulation of medical devices (Frønsdal et al., 2012).
Parallel submissions	It concerns the submission of the product's preparation proposal to HTA and health regulatory agencies at different times. However, it must be noted that due to this time variation in the evaluation process, it is necessary to add some restrictions to these parallel submissions, such as the recommendations, publication, or authorization of one agency cannot be publicized before the other agency gives its decision (Frønsdal, et al., 2012).

It was observed that the interaction processes described in Table 2 need to be better developed to avoid duplicate analyses and facilitate access to new health technologies (Balaisyte; Joos; Hiligsmann, 2018; Drummond, 2015; Facey et al., 2015; Frønsdal et al., 2012; Mcauslane; Liberti; Connelly, 2019). Furthermore, the role of the industry at the moment of discussion and methodological alignments in the pre-market phase is highlighted. This triad–industry, regulatory body, and incorporation body in the health system–brings benefits to those involved. For the industry, investment in studies that are unlikely to be useful can be avoided; for the regulatory body, internal alignment around the clinical development of a product is further facilitated; and, for the health system coverage body, the possibility of obtaining real-world data to understand the benefits and risks of a technology is created (Cuche et al., 2014).

For cases where the evidence is still uncertain, risk sharing agreements have been an alternative for mitigating the risks caused by technology. Such agreements are generally made between industry and governments, with predetermined deadlines.

Some studies have highlighted the need to align work processes between HTA agencies and regulatory agencies. Most of the evidence generated by the industry met regulatory requirements; however, they did not fully meet the HTA evidentiary requirements to support decision-making in the scope of health system coverage (Berntgen et al., 2014; Cox; Pouvourville, 2015; Cuche et al., 2014; Frønsdal et al., 2012; Tafuri et al., 2016; 2018; Wang et al., 2018; Wonder; Backhouse; Hornby, 2013), for example, in regulatory agencies placebos are accepted, but in health systems coverage institutions, technologies already incorporated into health systems are preferred. The choice of primary and surrogate outcomes (Cox; Pouvourville , 2015; Tafuri et al., 2018; Wang et al., 2018) also differs between the requirements because for the coverage institution, outcomes that impact patients' clinical conditions are preferred, leaving laboratory outcomes in the background. In relation to the population and population subgroups (Berntgen et al., 2014; Cox; Pouvourville, 2015; Wonder; Backhouse; Hornby, 2013), the criteria of

the entities that finance coverage are concerned with the magnitude and transcendence of the disease. Insufficient efficacy data was another critical point identified in the studies (Cox; Pouvourville, 2015; Facey et al., 2015; Forrester et al., 1997; Frønsdal et al., 2012; Mcauslane; Liberti; Connelly, 2019; Wang et al., 2018), because for regulatory agencies, phase I and II studies are accepted, while entities that decide on coverage prefer phase III studies because they address a larger number of research subjects.

Another issue identified in the findings was the communication gap between HTA and health regulation. There is evidence that when communication and coordination between agencies is improved, review processes can be improved and possibly reduce differences in work processes (Frønsdal et al., 2012). However, it has been observed that agencies' communication with health professionals and users is incipient, with little participation of organized civil society in the health regulation process (Facey et al., 2015).

Table 3 presents the barriers to interactions between HTA and health regulation identified by the studies included in this review. Based on the analysis, three dimensions were defined to categorize barriers: (1) organizational barriers; (2) work process barriers; and (3) regulatory cycle barriers.

Table 3 – Barriers identified for interaction between HTA and health regulation

Dimension	Barriers
Organizational	- HTA and regulatory agencies linked to different entities; - Difference between agencies' mission; - Different legal structures; - Limitation on sharing information between regulatory and HTA institutions due to secrecy legislation; - HTA and regulatory agency operating at different levels of centralization; - Possible lack of resources to adopt and/or continue with interaction initiatives
Work process	- Use of different evaluation methodologies, including population and population subgroups, comparators, and endpoints; - Overlapping activities; - Lack of communication between agencies; - Different vocabulary between HTA and health regulation agencies
Regulatory cycles	- Little evidence of effectiveness presented for the entry of technology into the health system; - Lack of monitoring over the use of technology; - Inefficient technology divestment process; - Low participation of healthcare professionals and patients in discussions about regulatory cycles and processes

It was observed that the articles would refer to interaction processes between HTA and health regulation in the context of medicines, with little or no reference to analyses of other technologies. Another issue observed was the focus on the entry of new technologies into the health system, with little reference by the authors to an interactive process when monitoring the wide dissemination and use of technologies (Cox; Pouvourville , 2015; Henshall et al., 2014). Finally, no study was identified that addressed the interaction between HTA and health regulation for the withdrawal or disinvestment of health technologies.

Discussion

The interaction between regulatory commercialization processes and technology assessment processes aimed at health systems coverage has proven to be effective for the entry of technologies—especially medicines—into health systems, reducing registration, and incorporation deadlines, contributing for expanding equity and access to health services. However, incipient interaction was observed in the processes of monitoring the use and performance of technologies already commercialized or incorporated.

The purpose of HTA is to ensure an adequate balance between patient access and rationality, considering the impact on budget/price within the jurisdictions of a country, thus playing a fundamental role in improving the production of evidence and ensuring that the health service is ready to adopt effective technologies (Facey et al., 2015; Vreman et al., 2020). Furthermore, HTA is considered a tool to inform decision makers of the best evidence regarding the entry of new medicines, medical devices, and other technologies into health systems, being an effective way to achieve universal health coverage (Gonçalves, 2020; Wasir et al., 2019).

Furthermore, there is a beneficial effect of the interaction between HTA and health regulation for the industry, which invests in studies more likely to be positively evaluated in the technology registration and incorporation phase, as they adequately meet the requirements, allowing new clinical options and therapies to reach the citizen. Also, interaction between agencies helps to align methodologies and work processes, reducing unnecessary differences in assessment requirements, in addition to defining governance limits between organizational aspects of agencies (Frønsdal et al., 2012; Tsoi et al. , 2013).

This time, a fundamental role of HTA in mitigating the risk of health inequities is observed, investigating the extent to which a new technology is relevant for the health system of interest, considering the local ethical, social, and economic contexts (Fontrier; Visintin; Kanavos, 2022). At the macropolitical level, technologies must be inserted into the health system to reduce rather than exacerbate inequities.

In this sense, it is highlighted that HTA can become more responsive with the inclusion of other actors in the evaluation process, more transparency, inclusion, and reflection from different perspectives in the incorporation of technologies, improving citizens' access to more appropriate interventions and improving efficiency in the development of new technologies (Henshall et al., 2011). Therefore, HTAi recommends that HTA approaches other actors for regulatory approval and coverage of health systems to promote comprehensiveness and equity in health. In addition to regulators, the participation of social control, patients, organized civil society, and the general public (users or not of public health systems) is necessary (Cowie et al., 2022; Henshall et al., 2011). This will almost certainly require deliberative methods and localized decision-making (Chalkidou et al., 2013). Deliberative processes are expanded instances inserted in the technology assessment structure, being an important step for HTA agencies to improve and legitimize decisions and the definition of priorities (Novaes; Soárez, 2020).

Nevertheless, the involvement of key actors in these processes often does not occur, hindering planned and practice-oriented decision-making, even though the importance of the institutionalized role of HTA in the continuous development of health actions is known. This contributes significantly to identifying strengths and weaknesses in the internal environment, as well as opportunities and threats in the external environment (Colpani et al., 2020). On the other hand, when health technology evaluators work in isolation from regulators, some problems may arise, such as the alignment of mandatory requirements that meet both requests: HTA and health regulation (Blüher et al., 2019).

It is worth noting that, within companies, HTA has strong credibility and reputation for producing evidence that proves the quality of use of medicines or other supplies. However, the institutional arrangement of industries has biases regarding the acceptability or incorporation of drug or vaccine technologies. The global economic order is clearly based on aspects of efficiency with the inclusion of cost-effective technologies aimed at new medicines/vaccines, among other supplies, especially when it comes to public health systems.

One study pointed out that while the focus of the evaluation for the commercialization of medicines and medical care equipment is the quality of the study and the safety of the product, the clinical evaluation carried out by public agents who carry out HTA in European agencies focused on the evaluation of comparative effectiveness in relation to the existing therapeutic alternative in the health system, concerning itself with the population that will have access to this technology (Gonçalves, 2020). This methodological divergence was evident in the studies identified in this review, whether in the definition of population, comparator or outcomes, constituting a barrier to interaction between agencies (Berntgen et al., 2014; Cox; Pouvourville, 2015; Cuche et al., 2014;

Facey et al., 2015; Forrester et al., 1997; Frønsdal et al., 2012; Mcauslane; Liberti; Connelly, 2019; Tafuri et al., 2016; 2018; Wang et al., 2018; Wonder; Backhouse; Hornby, 2013).

We reinforce that differences in work processes impact the interaction between these agents. The organizational structure of HTA and regulatory agencies can generate important noise in the context of health systems coverage and comprehensive care. In Brazil, HTA operates within the Ministry of Health via Conitec, responsible for covering technologies to be financed by the SUS, while Anvisa is responsible for marketing authorization within the Brazilian market. Despite both being administratively linked to the ministry, there are tensions in the application of regulations, producing barriers, such as the incipient inter-institutional communication for the implementation of normative requirements for evaluating effectiveness (Blüher et al., 2019). It is necessary to develop permanent and inter-institutional flows to support dialogue throughout the life cycle of health technologies, mindful of limited resources, operating across jurisdictions and drawing lessons from other countries' experiences (Facey et al., 2015). Improved communication between regulators, HTA and other actors can improve the efficiency of review processes and reduce the overall burden of evidence requirements throughout the product lifecycle and thus enable faster citizen access to useful products (Henshall et al., 2011).

We also observed that the divergence in the agencies' evaluation process allows limitations in other stages of the technology cycle. Notably, health technology assessors and regulators have different experiences, roles, and approaches, which can affect the interpretation of clinical evidence (Jaksa et al., 2022). For evaluation and monitoring processes to converge, public agents must be considered as social beings, with primacy in the institutional dynamics of decision-making for health system coverage. In this sense, the need for ongoing education actions is highlighted to bring the decision-making process closer to the daily implementation of public health policies.

Bringing HTA closer to health regulation is an action that requires the adoption of clearly defined processes and strategies, such as those identified in this study. However, despite the contributions that this review can bring to decision-making, some limitations should be mentioned, such as studies being mostly from developed countries, far from the Brazilian reality, studies mainly focused on medicines as opposed to other types of health technology, such as diagnostic tests, vaccines, or hospital equipment. Despite the considerable relevance of medicines to public health, alignment between agencies also needs to include other health technologies, such as medical devices and equipment.

Final Considerations

The types of processes identified reflect the interaction between the entities responsible for HTA and health regulation, to expand coverage in health systems and comprehensive care. The processes identified in this review (early dialogues, scientific advice, parallel advice, real-world evidence, risk sharing) demonstrated benefits for coverage in health systems and comprehensive care, such as the adequacy of clinical effectiveness requirements and the reduction of deadlines for commercialization and coverage processes in the incorporation of health technologies.

Several barriers were also identified, such as the difference between the requirements demanded and the gaps in flows and communication, which are necessary to strengthen interactive decision-making processes. It is worth noting the need to adopt strategies to mitigate these barriers, such as including other players in the evaluation and regulation processes (industry, organized civil society and social control), aligning work processes, and encouraging ongoing education for all parties involved.

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Authors' contribution

Ramos was responsible for collecting, analyzing, and interpreting the data, and preparation and review of the manuscript. Oliveira, Andrade, and Silva were responsible for reviewing the manuscript. Elias was responsible for the design and planning of the study and review of the manuscript.

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