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PHARMACOEPIDEMIOLOGY

Shaping the future of pharmacoepidemiology in France: Recommendations from the SFPT Pharmacoepidemiology Working Group

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Summary The drug authorization process is shifting towards a policy aimed at shortening time-to-market. While this policy facilitates early access to new treatments, it can also result in potentially insufficient knowledge of both efficacy and safety at the time of marketing. The latter is particularly true for long-term outcomes or in specific populations (e.g., children and the elderly). Yet, French pharmacoepidemiology is currently not designed to address these challenges, despite recognized expertise. In this context, we aim: (i) to define a strategy for strengthening pharmacoepidemiology in France; and (ii) to identify the associated human, technical, and financial requirements to ensure its success. In this paper, we present the French Pharmacoepidemiology Initiative (https://frenchpharmacoepi.org/), i.e. a network of independent academic teams to complement existing institutions. It will provide coordinated expertise and a workforce to meet national and regional needs for pharmacoepidemiological monitoring and drug-related decision-making. Leveraging the existing expertise of university hospital pharmacoepidemiology units would enable rapid operational deployment to inform the decisions and policies of national regulatory agencies.

Abbreviations

SFPT	French Society of Pharmacology and Therapeutics (*Société française de pharmacologie et de thérapeutique*)
SNDS	National Health Data System (*Système national des données de santé*)

Introduction

In France, over 25% of people aged 75 years and older use 5 or more drugs daily [1]. Codispensing of contraindicated drugs affects 0.6 to 2 million dispensing per year [2]. Simultaneously, the incidence of hospital admissions due to adverse drug reactions has dramatically increased over the past decade, with an estimate of 212,500 in 2018 [3]. A significant proportion of them are related to new pharmacological classes and considered preventable.

Moreover, the drug authorization process is shifting towards a policy aimed at shortening time-to-market. While this policy facilitates early access to new treatments, it can also result in potentially insufficient knowledge of both efficacy and safety at the time of marketing. The latter is particularly true for long-term outcomes or in specific populations (e.g., children and the elderly) [4,5].

This context highlights the need to enhance pharmacoepidemiology activities, which aims to monitor drug use, effectiveness, and risks in population, real-world settings [6,7]. Yet, French pharmacoepidemiology is currently not designed to address these challenges, despite recognized expertise. To improve patient care and reduce economic burden, it is crucial to integrate pharmacoepidemiology into the global framework of drug evaluation and monitoring (i.e., clinical pharmacology, pharmacovigilance, and addictovigilance). To this end, we aim: (i) to define a strategy for strengthening pharmacoepidemiology in France; and (ii) to identify the associated human, technical, and financial requirements to ensure its success.

State of pharmacoepidemiology in France

Current organization

Several reports, including some commissioned by authorities, have consistently advocated for enforcing

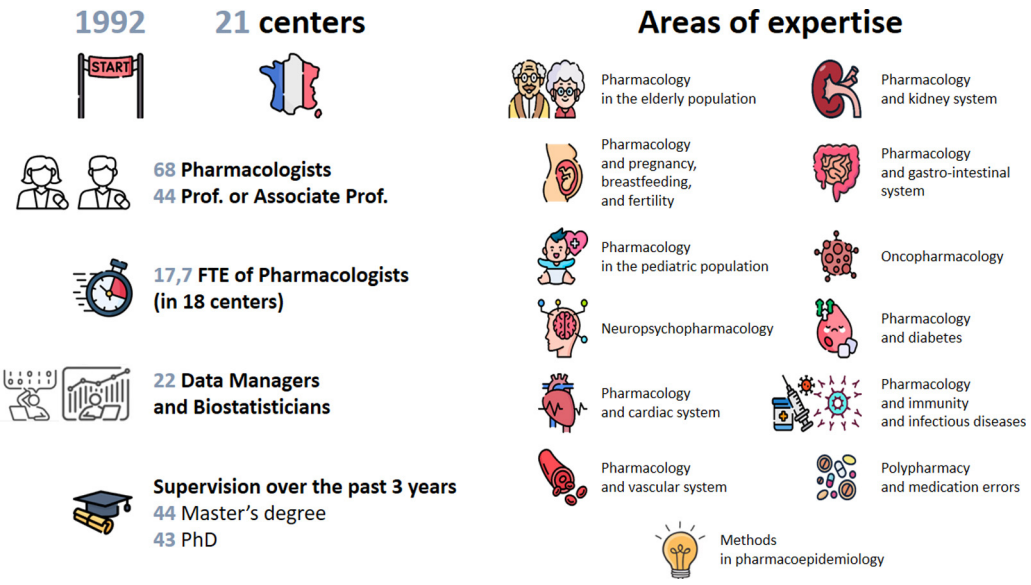

Figure 1. Current status of pharmacoepidemiology in France. Data provided by the French Society of Pharmacology and Therapeutics (*Société française de pharmacologie et de thérapeutique*) concerning its pharmacoepidemiology activities. The data are not exhaustive of all pharmacoepidemiology activities in France (e.g., three additional Inserm teams allocate part of their research to pharmacoepidemiology, some with both public and private fundings). FTE: full-time equivalent.

pharmacoepidemiology [8,9]. Despite clear recommendations from experts, the organization of pharmacoepidemiology in France lags behind that of the Nordic PharmacoEpidemiological Network [10], the Canadian Network for Observational Drug Effect Studies [11], or the USA Sentinel Initiative [12].

The current organization of pharmacoepidemiology in France involves three main types of actors. First, independent academic teams affiliated with medical pharmacology departments of university hospitals, which have derived from pharmacovigilance, addictovigilance, or clinical research centers. While this structure allows integrating pharmacological expertise into monitoring, it also significantly hinders the development of pharmacoepidemiology due to the lack of dedicated university chairs. Second, public institutions also play a critical role, particularly the Scientific Interest Group EPI-PHARE. Established in 2019 by the French Medicines Agency (*Agence nationale de sécurité du médicament et des produits de santé*) and the French Health Insurance (*Caisse nationale de l'Assurance maladie*) [13], EPI-PHARE primarily responds to drug-related safety alerts. Third, private companies, mainly Contract Research Organizations, are assigned to conduct pharmacoepidemiology studies to comply with requests from the authorities. In particular, the French Health Authority (*Haute Autorité de santé*) requires pharmaceutical companies to provide pharmacoepidemiology studies for benefit/risk balance evaluations [14].

Academic teams engaged in pharmacoepidemiology are distributed across most French regions. Areas of expertise vary among teams and cover a wide range of pharmacological fields (Fig. 1). However, the availability of technical staff trained for the real-world health data (e.g., the National Health Data System (*Système national des données de santé* [SNDS]), hospital data warehouses, and clinical databases) is inconsistent. This is due to several factors: (i) intense competition for recruitment and precarious job offers in the public sector (i.e., underpaid and short-term) despite previous recommendations [15], making it difficult to attract skilled technical staff, restricted access to data, which hampers the training of new staff, especially given the long learning curve for using the SNDS.

The establishment of the Health Data Hub in 2019 aimed to facilitate data access and address outdated data analysis tools, but these goals have not been met. The French Agency for Data Privacy (*Commission nationale de l'informatique et des libertés*) denied authorization for the Health Data Hub to host the SNDS due to its reliance on a USA-based cloud storage solution [16]. Concurrently, pre-existing solutions have deteriorated, jeopardizing research efficiency conducted using the SNDS [17]. Despite these challenges, resource allocations outside EPI-PHARE and the Health Data Hub have been minimal, although these institutions often lack the pharmacological expertise required to achieve the highest scientific standards in pharmacoepidemiology.

Current process for data access

While rapid data access is a major challenge in pharmacoepidemiology, the average time to access SNDS data typically ranged from 10 to 12 months, due to regulatory requirements and the time required for data extraction by the French Health Insurance [17]. This delay has hindered French academic teams from participating in calls for applications from European bodies (e.g. calls for applications issued by the European Medicines Agency, which often require results within a year). This has long been a major threat to French expertise, its contribution to European drug decision-making, and the positioning of French research in the field. The involvement of the French Medicines Agency, the French Health Insurance, and EPI-PHARE has not fully filled this gap, as their reports may struggle to convince

foreign regulators who typically rely on academic work. However, a legal decree in 2021 granted permanent access to the SNDS for academic researchers, including those in university hospitals, allowing pharmacoepidemiology teams to shorten data access times [18].

Additionally, linking SNDS with external datasets, such as clinical cohorts and hospital data warehouses, is urgently needed due to the critical lack of clinical data in the SNDS. This is crucial to answer questions requiring in-depth clinical information or regarding in-hospital use of drugs. Combined use of these data seems now feasible in a short time, provided the political will that accompanied the creation of the Health Data Hub is maintained. This also requires France to intensify its efforts to participate in international projects aimed at defining methodological standards for linking datasets (e.g., common data models and the European Dataspace Use case) [19].

Proposition for a French pharmacoepidemiology initiative

Network structuring, positioning and functioning

To address all previously discussed needs of pharmacoepidemiology in France, we present the French Pharmacoepidemiology Initiative (https://frenchpharmacoepi.org/), i.e. a network of independent academic teams to complement existing institutions (Table 1). It will provide coordinated expertise and a workforce to meet national and regional needs for pharmacoepidemiological monitoring and drug-related decision-making. This initiative follows and extends the Pharmacoepidemiology Working Group of the French Society of Pharmacology and Therapeutics (*Société française de pharmacologie et de thérapeutique* [SFPT]) [20]. Importantly, it is extensively based on the experience of the aforementioned teams in conducting pharmacoepidemiological studies on the SNDS [21], clinical cohorts [22—25], and hospital data warehouses. In parallel, it is also based on several years of reflections to improve the standards of evidence of pharmacoepidemiological studies in France [26—29].

To ensure complementary expertise within the network, it should be open to anyone from the pharmacological community, or those with strong interactions with it, and involved in public research on drug evaluation in real-world settings (e.g., pharmacologists, epidemiologists, clinicians, biostatisticians, medical informatics engineers).

To fully benefit from access to the SNDS and to hospital data warehouses, the French Pharmacoepidemiology Initiative leverages academic research in pharmacoepidemiology, primarily based within university hospitals. The ultimate goal is for each center to contribute to the network with at least one expert in pharmacoepidemiology, or a pair comprising one expert in pharmacology and one expert in epidemiology, and a data analyst trained in the secondary use of health data (e.g., SNDS, hospital data warehouses). This territorial coverage provides the ideal configuration for collaborations with national regulatory agencies and institutions (e.g. the French Medicines Agency, the French Health Authority, EPI-PHARE, French Public Health (*Santé publique France*), and scientific societies) and Regional Health Agencies (*Agences régionales de santé*). Initially, a federated network of expertise connected by technical support nodes for practical study execution can be envisioned to reduce the risk of isolation among researchers and engineers responsible for data management and analysis.

The network has four main aims: (i) to conduct collaborative research and evaluation projects in pharmacoepidemiology, including in specific areas of expertise or under constrained timelines, by pooling pharmacological, epidemiological, methodological, and technical expertise, and data access; (ii) to facilitate experience sharing among network members through mobility and mentorship programs; (iii) to contribute to theoretical training in pharmacoepidemiology and secondary use of data for pharmacoepidemiological evaluation of drugs; and ultimately (iv) to enhance the visibility and attractiveness of academic research in pharmacoepidemiology in France. All these missions align with an open science approach, including in particular protocol and code sharing (i.e., open source code).

Importantly, we advocate for an independent academic network because public trust can only be achieved if evaluation is free of conflicts of interest with both pharmaceutical companies and national institutions. Moreover, relying heavily on private efforts would be illogical, especially when public expertise is available.

Network dimensioning and strengthening

As of March 2024, the results of 114 of the post-authorization studies requested by the French Health Authority from pharmaceutical companies are still pending (e.g., from 11 to 19 studies per year over 2020—2023) [30]. This questions the adequacy of the means devoted to conduct these studies. Additionally, Regional Health Agencies will likely require several studies each year to monitor drug concerns specific to their territories and fulfill the commitments of their Regional Health Project (*projet régional de santé*) and Goals and Resources Contract (*contrat pluriannuel d'objectifs et de moyens*). Of all the studies that are or will be requested, some might be conducted by private entities with limited potential impact relating to conflicts of interest (e.g., some drug utilization studies). Conversely for others, independent expertise could appear crucial (e.g., benefit/risk balance evaluations).

The average completion time of pharmacoepidemiology studies using the SNDS is about 12 person-months, excluding time for data access, when conducted by experienced staff. This includes the time required for researchers (i.e., conception, supervision, interpretation, code review, report writing, and valorization) and staff (i.e., data management, data analysis, and contribution to interpretation, report writing, and valorization). An additional two person-months should be considered for the efforts of scientific committee members.

In summary, the workforce required to meet the above needs in pharmacoepidemiology studies is estimated at 280 person-months per year (i.e., around 20 studies per year, each requiring 14 person-months).

Table 1 Shaping the future of pharmacoepidemiology in France: expected needs, identified obstacles, proposed solutions, and expected benefits for stakeholders.

Expected needs	Identified obstacles	Proposed solutions	Expected benefits for stakeholders
Growing need for pharmacoepidemiology studies: — To monitor drug use and misuse in the population — To monitor benefit/risk balance of drugs in real-world settings and in vulnerable populations — To complete clinical evaluation of drugs	— Lack of organization of pharmacoepidemiology — Scattered pharmacological expertise — Lack of trained pharmacoepidemiologist and data analyst — No protocol and code sharing	— Create a pharmacoepidemiology network with permanent funding — Increase the pharmacoepidemiology workforce	— Meet national and regional needs for pharmacoepidemiological monitoring and drug-related decision-making — Produce results free of conflicts of interest with pharmaceutical companies — Cost savings through a more rational use of drugs and a decrease in adverse drug reactions-related costs
Need to shorten data access and data analysis times to allow providing results more rapidly	— Average time to access SNDS data typically ranged from 10 to 12 months — Outdated data analysis tools (both software and hardware)	— Improve the training of pharmacoepidemiologist and data analyst with permanent access to the SNDS — Update software and hardware used for data analysis	Participation to calls for applications from European bodies, including in specific areas of expertise or under constrained timelines
Need for more clinical, biological, and imaging data in the SNDS	Need for data standardization according to common data models	— Participation in international projects aimed at defining methodological standards for linking datasets — Develop research and training that will enable linking SNDS with external datasets, such as clinical cohorts and hospital data warehouses	Answering questions requiring in-depth clinical information or regarding in-hospital use of drugs
Methodological research and training in new methods in statistics and informatics	Lack of trained pharmacoepidemiologist and data analyst	Methodological research and training	Intellectual property-related incomes for drug repurposing

SNDS: National Health Data System (*Système national des données de santé*).

Network funding and stabilizing

Permanent funding is crucial to stabilize the federated network, as the needs are permanent and require specific skills and experience. We propose to allocate a percentage of drug expenses to fund their pharmacoepidemiological monitoring. Drug prices could be reduced by 0.05% (e.g., the price of a drug costing 1,000.00 euros per box would be lowered to 999.50 euros). The corresponding amount could be converted into a specific tax to fund pharmacoepidemiology activities, including those required by institutions. The budget would be defined each year based on expenses from the previous year. Any unused funds at the end of the year would be either returned to the funder or invested in structural actions, allowing the network to develop and adapt. Under this system, if the network is tasked with conducting independent studies, no additional cost would be requested from the concerned pharmaceutical companies.

Network generated incomes and cost savings for the public funder

The risks of the network not being cost-effective are minimal. Anticipated savings far exceed the network costs, primarily through the reduction of public expenses.

Outpatient drug-related expenses amounted to about 33 billion euros in 2022, with an average increase of about 700 million euros per year in France [31]. This is likely to keep growing with the aging population. The economic burden of hospital admissions due to adverse drug reactions is estimated to be at least 420 million euros per year [3]. Esti-

mates of the economic burden of drug misuse, from the cost of unnecessary drugs to the cost of complications, suggest it exceeds 10 billion euros a year [8]. Slowing this increase by only a few percent would result in significant savings.

In addition to the anticipated cost savings through a more rational use of drugs and a decrease in adverse drug reactions-related costs, the network could generate direct incomes by contributing to drug repurposing. Intellectual property-related incomes could be partially attributed to the public funder.

Prospects

In the coming years, methods used in pharmacoepidemiology are expected to evolve as a consequence of several factors, including standards of evidence, data characteristics, changes in missions, and advances in statistics and informatics.

First, the next standard in drug clinical evaluation will increasingly rely on pharmacoepidemiology to address the limitations of traditional clinical trials. For diseases with a poor short-term prognosis (e.g., cancer) and orphan diseases, the drug authorization process is shifting towards a policy aimed at shortening time-to-market. This involves brief clinical evaluations on small numbers of patients, often based on surrogate endpoints with uncertain long-term clinical significance. While this policy facilitates early access to new treatments, it can also result in potentially insufficient knowledge of both efficacy and safety at the time of marketing. The latter is particularly true for long-term outcomes or in specific populations (e.g., children and the elderly) [4,5]. These promising but poorly developed drugs may achieve a favorable benefit/risk balance primarily due to the high mortality rates in the indicated conditions. Uncertainty about the benefit/risk balance of drugs also stems from the differences in patterns of use (e.g., drug misuse) and characteristics of patients between clinical trials and in real-world settings (e.g., extension of indications). Importantly, when dealing with drugs intended for widespread use, any loss in efficacy or safety will have a significant impact on public health, also resulting in economic burden. In this context, real-word evidence, especially from emulated trials, can supplement clinical trials, assess effectiveness, and clarify the place of drugs in therapeutic strategies [32].

Second, access to data with more clinical information is critical for pharmacoepidemiology. Many European countries have successfully linked medico-administrative data with clinical, biological, and imaging data, allowing: (i) to improve confidence regarding the characteristics of the studied populations and thus, generalizability of results; and (ii) to reduce the need for statistics to ensure the comparability of the studied population for important characteristics. As linked data are not systematically provided in a structured format, new methods tailored to the data format should be employed (e.g., Natural Language Processing for unstructured text from medical reports).

Third, a new mission for pharmacoepidemiology will be to bridge preclinical knowledge and data from real-world evaluation. Along with drug development and preclinical evaluation evolving, there is a shift from animal testing to receptor, cellular, or organoid studies. New translational methods are required to cover the need for drug evaluation owing to the repositioning of preclinical and post-marketing information. Modeling techniques will be necessary to combine preclinical knowledge with e.g. post-marketing data from other drugs [33]. Similar methods will be needed for drug repurposing before conducting studies that align with the new standards in clinical evaluation. Developing the corresponding research and training to enable effective implementation is crucial.

Finally, advances in statistics and informatics may shift focus towards artificial intelligence methods, especially for large datasets like the SNDS. Methodological research and training will also need to determine the circumstances under which artificial intelligence models provide added value compared to conventional models in pharmacoepidemiology.

Conclusion

France is currently facing a paradox of having recognized pharmacoepidemiological expertise while having unaddressed needs in pharmacoepidemiological monitoring. To date, no political strategy has been deployed to take advantage of this expertise despite the importance of pharmacoepidemiology for public health. Structuring a pharmacoepidemiology network, highlighted as a critical need in a report to the Ministry of Health 10 years ago [8], is now an urgent priority. If properly implemented, this network will contribute to monitor drug safety and effectiveness, to improve the quality of care, and ultimately to reduce drug-associated costs. Leveraging the existing expertise of university hospital pharmacoepidemiology units would enable rapid operational deployment to inform the decisions and policies of national regulatory agencies.

Disclosure of interests

The authors declare that they have no competing interest.

Références

[1] Guillot J, Maumus-Robert S, Pariente A, Bezin J. Chronic polypharmacy at all age: a population-based drug utilization study. Fundam Clin Pharmcol 2022;36:405—13.
[2] Létinier L, Cossin S, Mansiaux Y, Arnaud M, Salvo F, Bezin J, et al. Risk of drug-drug interactions in out-hospital drug dispensings in France: results from the drug-drug interaction prevalence study. Front Pharmacol 2019;10:265.
[3] Laroche M, Gautier S, Polard E, Rabier M, Chouchana L, Lebrun-Vignes B, et al. Incidence and preventability of hospital admissions for adverse drug reactions in France: a prospective observational study (IATROSTAT). Br J Clin Pharmacol 2023;89:390—400.
[4] SFPT — GT méthodologie. Livre blanc SFPT : de la nécessité de la méthodologie dans l'évaluation des médicaments. 2022. https://sfpt-fr.org/livreblancmethodo/index.htm [Accessed 9 December 2024].
[5] Downing NS, Shah ND, Aminawung JA, Pease AM, Zeitoun JD, Krumholz HM, et al. Postmarket safety events among novel therapeutics approved by the US Food and Drug Administration between 2001 and 2010. JAMA 2017;317:1854.

[6] Faillie JL, Montastruc F, Montastruc JL, Pariente A. Pharmacoepidemiology and its input to pharmacovigilance. Therapie 2016;71:211—6.
[7] Montastruc JL, Benevent J, Montastruc F, Bagheri H, Despas F, Lapeyre-Mestre M, et al. What is pharmacoepidemiology? Definition, methods, interest and clinical applications. Therapie 2019;74:169—74.
[8] Bégaud B, Costagliola D. Rapport sur la surveillance et la promotion du bon usage du médicament en France. 2013. https://www.vie-publique.fr/rapport/33483-rapport-sur-la-surveillance-et-la-promotion-du-bon-usage-du-medicament-e [Accessed 9 December 2024].
[9] Bégaud B, Polton D, Von Lennep F. Les données de vie réelle, un enjeu majeur pour la qualité des soins et la régulation du système de santé : l'exemple du médicament. 2017. https://www.vie-publique.fr/rapport/37068-les-donnees-de-vie-reelle-enjeu-majeur-pour-la-qualite-des-soins [Accessed 9 December 2024].
[10] NorPEN. Nordic Pharmacoepidemiological Network. NorPEN homepage. 2024. https://www.norpen.org/ [Accessed 9 December 2024].
[11] CNODES. Canadian Network for Observational Drug Effect Studies. CNODES homepage. 2024. https://www.cnodes.ca/ [Accessed 9 December 2024].
[12] Sentinel Initiative. Sentinel Initiative homepage. 2024. https://www.sentinelinitiative.org/ [Accessed 9 December 2024].
[13] Zureik M, Cuenot F, Bégaud B. Pharmacoepidemiology and public decision. Therapie 2023;78:549—51.
[14] Berdaï D, Thomas-Delecourt F, Szwarcensztein K, d'Andon A, Collignon C, Comet D, et al. Requests for post-registration studies (PRS), patients follow-up in actual practice: changes in the role of databases. Therapie 2018;73:13—24.
[15] Ministère de la transformation et de la fonction publiques. Le référentiel de rémunération des métiers du numérique est mis à jour. 2024. https://www.fonction-publique.gouv.fr/toutes-les-actualites/le-referentiel-de-remuneration-des-metiers-du-numerique-est-mis-jour [Accessed 9 December 2024].
[16] Cour des comptes. Rapport sur l'application des lois financement de la sécurité sociale. 2024. https://www.vie-publique.fr/rapport/294422-rapport-sur-lapplication-des-lois-de-financement-de-la-securite-sociale [Accessed 9 December 2024].
[17] Marchand-Arvier J, Allassonnière S, Hoang A, Jannot AS. Fédérer les acteurs de l'écosystème pour libérer l'utilisation secondaire des données de santé. 2024. https://igas.gouv.fr/federer-les-acteurs [Accessed 9 December 2024].
[18] Légifrance. Décret nº 2021-848 du 29 juin 2021 relatif au traitement de données à caractère personnel dénommé « système national des données de santé ». 29 juin 2021. https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000043715694 [Accessed 9 December 2024].
[19] European Commission. European Health Data Space. 2024. https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en [Accessed 9 December 2024].
[20] SFPT. Société française de pharmacologie et de thérapeutique. 2024. https://sfpt-fr.org/ [Accessed 9 December 2024].
[21] Maillard O, Bun R, Laanani M, Verga-Gérard A, Leroy T, Gault N, et al. Use of the French National Health Data System (SNDS) in pharmacoepidemiology: a systematic review in its maturation phase. Therapie 2024;79:659—69.
[22] Liabeuf S, Lambert O, Metzger M, Hamroun A, Laville M, Laville SM, et al. Adverse outcomes of proton pump inhibitors in patients with chronic kidney disease: the CKD-REIN cohort study. Br J Clin Pharmacol 2021;87:2967—76.
[23] Benevent J, Araujo M, Beau AB, Sicard D, Sommet A, Hurault-Delarue C, et al. First trimester pregnancy exposure to fosfomycin and risk of major congenital anomaly: a comparative study in the EFEMERIS database. Infection 2023;51:137—46.
[24] Laville SM, Couchoud C, Bauwens M, Vacher-Coponat H, Choukroun G, Liabeuf S, et al. Efficacy and safety of direct oral anticoagulants versus vitamin K antagonists in patients on chronic dialysis. Nephrol Dial Transplant 2024;39:1662—71.
[25] Dubucs C, Caillet A, Frémont F, Delteil L, N'Go V, Neville AJ, et al. Prevalence of congenital ocular anomalies in 15 countries of Europe: results from the Medikeye study. Birth Defects Res 2024;116:e2414.
[26] Dupui M, Micallef J, Lapeyre-Mestre M. Interest of large electronic health care databases in addictovigilance: lessons from 15 years of pharmacoepidemiological contribution. Therapie 2019;74:307—14.
[27] Conte C, Vaysse C, Bosco P, Noize P, Fourrier-Reglat A, Despas F, et al. The value of a health insurance database to conduct pharmacoepidemiological studies in oncology. Therapie 2019;74:279—88.
[28] Benevent J, Araujo M, Hurault-Delarue C, Montastruc JL, Sommet A, Lacroix I, et al. Pharmacoepidemiology in pregnancy. Therapie 2019;74:289—300.
[29] Kaguelidou F, Durrieu G, Clavenna A. Pharmacoepidemiological research for the development and evaluation of drugs in pediatrics. Therapie 2019;74:315—24.
[30] Haute Autorité de santé. HAS Les études post-inscription pour les médicaments. 2019. https://www.has-sante.fr/jcms/p_3113800/fr/les-etudes-post-inscription-pour-les-medicaments [Accessed 9 December 2024].
[31] DREES. Les dépenses de santé en 2022 : résultats des comptes de la santé. 2023. https://drees.solidarites-sante.gouv.fr/publications-communique-de-presse-documents-de-reference/panoramas-de-la-drees/les-depenses-de [Accessed 9 December 2024].
[32] Corrigan-Curay J, Sacks L, Woodcock J. Real-world evidence and real-world data for evaluating drug safety and effectiveness. JAMA 2018;320:867—8.
[33] Wong F, Zheng EJ, Valeri JA, Donghia NM, Anahtar MN, Omori S, et al. Discovery of a structural class of antibiotics with explainable deep learning. Nature 2024;626:177—85.