INTERNATIONAL SOCIETY OF DRUG BULLETINS

Newsletter

Vol. 37 - Number 1 - March 2024

CONTENTS

WELCOME TO THE FIRST ISDB NEWSLETTER OF 2024

The ISDB members' part of this issue contains a "Portrait" article, from Therapeutics Initiative, Canada, on the delivery of personalized prescribing information to clinicians in British Columbia. In addition, Public Citizen, USA, mourns the passing of Dr. Sidney Wolfe, with testimonials from ISDB members.

Four topics are featured in the setion on interesting publications: the provenance and clinical benefit of medicines introduced on the French market; the origin of first-in-class drugs; Common Sense Oncology; and an FDA investigation into the safety of CAR-T cell therapies.

Last but not least, you will find an update on the ISDB Committee's activities.

NEXT ISDB GENERAL ASSEMBLY IN 2025

The next ISDB Ordinary General Assembly is scheduled for 2025. This time we would like to reconnect with an in-person meeting. We are therefore looking for a member organization willing to host that event (about 2-3 days). If you could host such an event please inform rkessler@prescrire.org

ISDB NEWSLETTER 2023, NO. 2 (OCTOBER)

The recommendation in the infographic provided by InfoFarma (Italy) concerning the use of amoxicillin + clavulanic acid for the treatment of pharyngitis and acute otitis media had been queried as other countries have other recommendations. This recommendation is basically due to the shortages of amoxicillin in Italy.

THE NEXT NEWSLETTER IS PLANNED FOR JUNE 2024

We welcome comments, suggestions, and articles. Please send them to: rkessler@prescrire.org by mid-May 2024.

News from ISDB Members

"Portrait" - Delivering personalized prescribing information to clinicians in British Columbia, Canada

University of British Columbia Therapeutics Initiative
Better Prescribing, Better Health
Ellen Reynolds

It's a similar story for family practice clinicians in many jurisdictions - working hard to provide care for patients with a wide range of healthcare needs and to keep up with an overwhelming volume of medical information. In this context, efforts to support rational and evidence-based prescribing must include user-friendly, concise, and accessible summaries of evidence provided to clinicians at the point of care.

The Therapeutics Initiative (TI) at the University of British Columbia (UBC) is a longtime member of the ISDB and our goal is to provide family clinicians with evidence-based practical information on healthcare interventions. Our independent and rigorous assessments of evidence on drug therapy also aim to counterbalance information sources sponsored by the drug industry.

One of our initiatives is a quality improvement program called *Portrait* - an intervention that provides family physicians and nurse practitioners in British Columbia with personalized snapshots or "portraits" of their prescribing (or ordering of tests) related to a specific drug or treatment regime. Portraits also include recommendations and targets with clear and direct key messages to support evidence-based prescribing, which in turn supports improved patient outcomes and more efficient use of resources. The program is sponsored by the BC Ministry of Health through a contribution agreement with the UBC Faculty of Medicine.

Portraits include a graphical display of a clinician's individual prescribing data often presented alongside a comparator (e.g., median prescribing of their peers or "optimal" prescribing based on the evidence). The accessible format is intended to catch the attention of busy clinicians looking for practical prescribing information. Several Portrait topics released to date include: long-term use of proton pump inhibitors, statins in the elderly, thiazides for hypertension, non-opioid pain medication, antibiotics for uncomplicated UTI, and most recently inhaled corticosteroids for COPD.

Portraits are delivered confidentially through a secure mailing process and website portal. A clinician's prescribing data are protected during every aspect of production and delivery and data are only made available to the individual prescriber. Also, the administrative health data used to create Portraits use encrypted patient identifiers to ensure patients cannot be identified; graphs containing fewer than 6 patients are masked to prevent possible identification due to small numbers.

Each portrait tells a story. Clinicians may be pleased to see that they are already prescribing in alignment with the evidence and/or learn something new about the evidence that may differ from current guidelines. They are able to see their own prescribing in their Portrait and to explore the topic in more detail by reading the evidence assessment in the accompanying *Therapeutics Letter*. We make it clear to clinicians that Portraits are not intended to be a performance audit but to support their practice.

The program began in 2020 and builds on previous TI initiatives, including the Better Prescribing Project in the 1990s and the Education for Quality Improvement in Patient Care (EQIP) program from 2006 to 2012. Evaluations of both previous programs found significant improvements in prescribing outcomes following the interventions (1,2). Also, literature on similar audit and feedback interventions shows that this kind of prescriber education can be effective especially when interventions are targeted, tailored, include clear messaging with reminders, and when feedback is coupled with other educational activities (3).

The potential of this program for quality improvement continues to be demonstrated through our ongoing evaluations of Portraits. For each Portrait topic, approximately 7,000 BC physicians are randomly divided into groups that receive the Portrait at different times. This "designed delay" allows us to evaluate the impact of Portraits on prescribing at an aggregate level across BC. Evaluations are always population level, and never look at individual physician prescribing.

We produce 2 or 3 Portraits per year and the evaluation process begins after each delayed release -- 6 to 9 months following the early Portrait. We have moved away from mailing paper Portraits toward online access, which has been available since March 2022. We are also in the process of

developing an interactive digital Portrait that will allow clinicians to view and compare their data more easily and in different ways, and to seamlessly link to continuing medical education credits.

The Portrait sample included below contains fictional data on to the topic of prescribing for uncomplicated urinary tract infection and was accompanied by *Therapeutics Letter* #135: "Empiric Antibiotic Therapy for Uncomplicated Lower Urinary Tract Infections." To date this is the most popular of our 7 fully released Portraits. Produced in collaboration with the BC Centre for Disease Control, the Portrait was sent the early group in September 2021 and the delayed group in March 2022. An evaluation of the impact of this Portrait has been completed and results are pending publication.

The most recent release in December 2023 is the Portrait, "How do you prescribe ICS to COPD patients?" with the associated Letter, "Minimizing inhaled corticosteroids for COPD." A full list of references from evidence reviews is published with each Therapeutics Letter and available on the TI website.

As we continue to work on improving and enhancing the Portrait program, we welcome feedback from other ISDB members regarding this intervention, and would like to hear about similar initiatives in other jurisdictions. Email us at portrait@ti.ubc.ca or visit www.ti.ubc.ca/portrait . If you want to be informed when the UTI Portrait evaluation results are published, you can subscribe to the TI email list.

References

1- Herbert CP, Wright JM, Maclure M, et al. Better Prescribing Project: a randomized controlled trial of the impact of case-based educational modules and personal prescribing feedback on prescribing for hypertension in primary care. Family Practice 2004; 21(5):575-81. DOI: 10.1093/fampra/cmh515

2- Dormuth CR, Carney G, Taylor S et al. A randomized trial assessing the impact of a personal printed feedback portrait on statin prescribing in primary care. Journal of Continuing Education in the Health Professions 2012; 32(3):153-62. DOI: 10.1002/chp.21140

3- Ivers N, Jamtvedt G, Flottorp S et al. Audit and feedback: effects on professional practice and healthcare outcomes. Cochrane Database of Systematic Reviews 2012; Issue 6. Art. No.: CD000259. DOI: 10.1002/14651858.CD000259.pub3

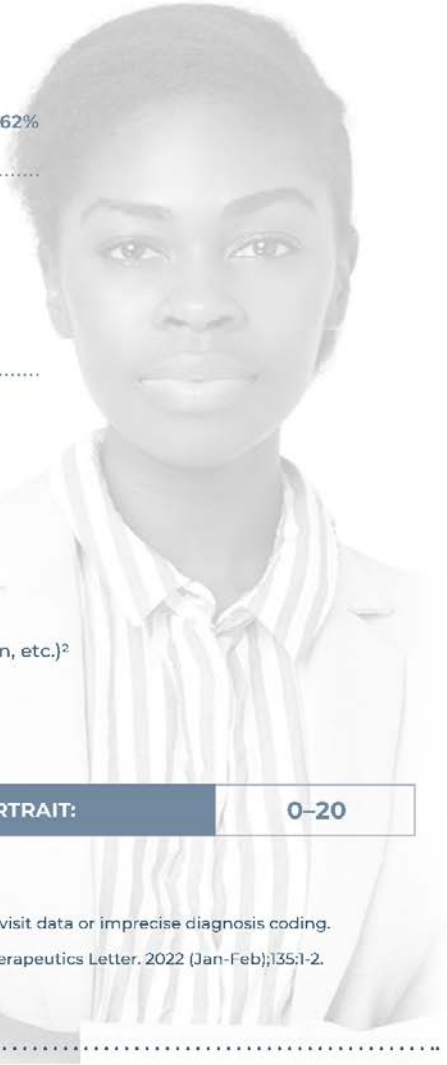
Therapeutics Initiative | THE UNIVERSITY OF BRITISH COLUMBIA

Portrait ID: **SAMPLE (FICTIONAL DATA)**

What is your first-line choice for uncomplicated UTI?

This Portrait details your 2019–2020 first-line prescribing patterns for oral antibiotics used to treat uncomplicated lower urinary tract infections (UTI) and the current recommendations for BC[1].

How you prescribed | How BC family doctors prescribed



NITROFURANTOIN

should be the number one antibiotic prescribed as empiric therapy

50%
62%

FOSFOMYCIN

should be reserved as first-line therapy for patients who cannot take nitrofurantoin due to allergy or creatinine clearance < 30 mL/min

7%
6%

CIPROFLOXACIN, TRIMETHOPRIM-SULFAMETHOXAZOLE & OTHER ANTIBIOTICS

should not be used as first-line empiric therapy due to bacterial resistance rates in BC

Ciprofloxacin
10%
11%

Trimethoprim-sulfamethoxazole
13%
7%

Other (e.g. amoxicillin, cephalexin, etc.)[2]
20%
11%

NUMBER OF PATIENTS INCLUDED IN YOUR PRESCRIBING PORTRAIT: 0–20

PLEASE NOTE:
Inaccuracy in your personal prescribing portrait may arise from incomplete patient visit data or imprecise diagnosis coding.

[1] Therapeutics Initiative. *Empiric antibiotic therapy for uncomplicated lower UTI*. Therapeutics Letter. 2022 (Jan-Feb);135:1-2.
[2] A list of antibiotics included can be found at www.ti.ubc.ca/portrait-UTI.

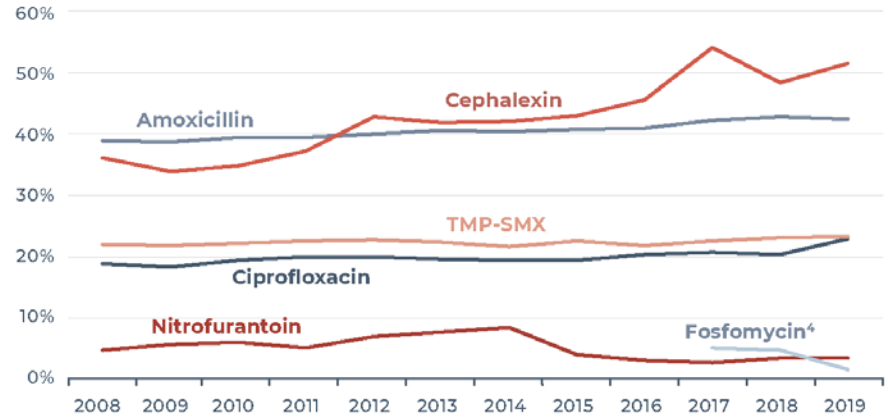
In partnership with: antibiotic wise.ca | DO BUGS NEED DRUGS?

See reverse for data, definitions, and references

Why is nitrofurantoin recommended for empiric treatment of uncomplicated UTI?

Because various antibiotics achieve similar symptom resolution for uncomplicated UTI, treatment choice should reflect local bacterial resistance patterns. *E. coli* is responsible for the majority of uncomplicated UTIs. *E. coli* resistance to nitrofurantoin has remained low in BC, despite increasing utilization. Overuse of fluoroquinolones, TMP-SMX, and other antibiotics is contributing to resistance in *E. coli* and other enteric Gram-negative organisms.

Percent of *E.coli* isolates resistant (2008–2019)[3]



[3] BC data from the BC Centre for Disease Control Antimicrobial Resistance Dashboard; 99% of *E. coli* isolates are from urine samples.

[4] Fosfomycin resistance rates may not be accurate; current available susceptibility methods do not detect all mechanisms of resistance.

Data & Definitions

Patients included: Nonpregnant women age ≥ 15 enrolled in MSP who received an oral antibiotic from a BC community pharmacy in 2019-2020 within 5 days of UTI diagnosis coded in an MSP claim without systemic antibiotic use in the prior 3 months. A woman is assigned to your Portrait if you diagnosed her UTI and she filled a prescription with your prescribing number. Prescribing data shown for visits coded as cystitis (ICD-9 595, 595.0, 595.3-595.9), UTI site not specified (599, 599.0, 599.8, 599.9), symptoms involving urinary system or dysuria (788, 788.9, 788.1), other disorders of bladder (596.X), hematuria (599.7), or nonspecific findings on examination of urine (791.X).
Patients excluded: Patients with complicated UTI were excluded. Complicated UTI was based on recurrent UTI or recent discharge from hospital, concomitant STI or pyelonephritis, dialysis, chronic kidney disease, visits to a nephrologist, indwelling catheter, or a structural or functional abnormality of the urinary tract. Patients in palliative and long-term care (PharmaCare plans P or B) were excluded.

FOR REFERENCES AND DETAILED DEFINITIONS SEE: WWW.TI.UBC.CA/PORTRAIT-UTI

PORTRAIT@TI.UBC.CA | P 604.822.4887 | F 604.822.0701

Public Citizen Mourns Passing of Dr. Sidney Wolfe, A Towering Public Health Leader

Dr. Sidney Wolfe passed away on January 1, 2024. He was one of the founders of Public Citizens. He was 86 years old.

Statement from Robert Weissman, President, Public Citizen

"Dr. Sidney Wolfe founded the Health Research Group in 1971 with Ralph Nader, part of the enterprise that launched as Public Citizen that same year. Sid invented a new approach of 'research-based advocacy' to get dangerous drugs and devices off the market, win new protections for worker health and safety, address doctor misconduct, challenge the Food and Drug Administration (FDA) to do its job, and hold pharmaceutical companies accountable."

"Under Sid's guidance, Public Citizen:

- Helped to force 28 dangerous medications off the market, limiting the use of 10 more and adding strong warnings to dozens of others.
- Pushed the Occupational Safety and Health Administration to set more than a dozen worker-protective health standards.
- Testified before hundreds of FDA advisory committees urging against approval of dangerous drugs and devices, and for limited use or strong warning labels of others, with substantial influence over countless decisions. He helped prevent many dangerous products from ever making it to market.
- Won a ban of Red Dye No. 2, obtained warning labels about Reye's syndrome on the side of aspirin bottles, and helped impose restrictions on silicone breast implants.
- Sold 2.5 million copies of Worst Pills, Best Pills.
- Documented weakening standards at the FDA following passage of the first Prescription Drug User Fee Act, which made drug companies a major revenue source for FDA.
- Won earlier public access to safety and efficacy information for products being considered for approval by the FDA, enabling more effective advocacy by consumer advocates.
- Advocated for decades against drug company marketing of dangerous opioids and demanded accountability for the drug companies and the corporate CEOs who fueled the deadly opioid addiction epidemic."

https://www.citizen.org/news/public-citizen-mourns-passing-of-dr-sidney-wolfe-a-towering-public-health-leader/
see also Remembering Dr. Sidney M. Wolfe, Public Citizen https://www.citizen.org/remembering-sidney-wolfe/

Member Testimonials

ISDB lost a good friend and highly committed public health leader. He devoted his life to get dangerous drugs and devices off the market. In September 2023, he was quoted in a ProPublica article on the Philips scandal relating secrecy on complaints about dangerous breathing machines: "*It's one of the two or three worst things I have ever seen*,"..."*It was unacceptable to sell these machines.*" For many years, Sidney played an active role within ISDB. He participated recently in the discussions on conflicts of interest and financing of independent drug bulletins during the last online General Assembly (GA) in November 2022. In 2019, at the GA in Paris, he made a presentation on the topic of "*Breaking through Corporate/ Government Duopoly of Power*". ISDB members will miss him.
Rita Kessler, ISDB President

All of us at DTB are deeply saddened by news of the death of our friend and colleague Sid Wolfe. We have many happy memories of meeting Sid at ISDB events and he was always very good company at the ISDB social events and dinners. He was an inspirational person and any conversation or interaction with him was always a joy. He took great interest in people, both professionally and personally, and he was always keen to hear about our work. We collaborated with Sid for an article for the 60th anniversary issue of DTB (Wolfe S. Mandatory disclosure of all pharmaceutical and medical device companies' payments to healthcare providers: learning from the USA. Drug and Therapeutics Bulletin 2022;60:52-55). I corresponded and spoke to Sid several times over the last couple of years and he continued to encourage and support DTB in its work and mission. I will miss his friendship and wise counsel.
David Phizackerley, DTB

Dr. Fugh-Berman, PharmedOut was quoted in "Sidney Wolfe: public health leader who campaigned for reform across the US health system" in BMJ. She said "When Sid walked into the room at an FDA meeting, industry representatives would shudder... He was very effective."

Sidney was a personal friend of mine, remembered with warm feelings.
Frits Rosendaal, Ge-Bu

His legacy within ISDB will remain viable. He will always be remembered for his contribution.
Lara Magro, Focus Farmacovigilanza

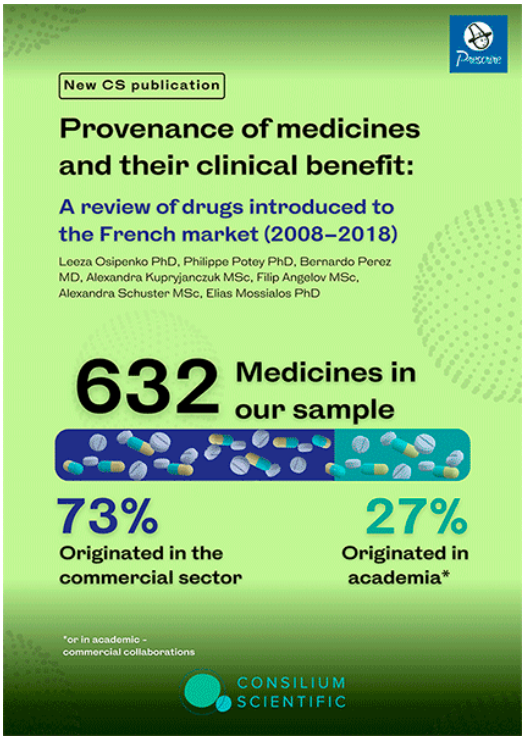
Interesting Publications

Provenance and Clinical Benefit of Medicines Introduced to the French Market, 2008 to 2018

By Leeza Osipenko, Philippe Potey, Bernardo Perez, Alexandra Kupryjanczuk, Filip Angelov, Alexandra Schuster, Elias Mossialos
JAMA Intern Med. 2024;184(1):46-52. doi:10.1001/jamainternmed.2023.6249

Both the commercial sector and academia play a vital role in medicine development. Ongoing debates exist on their contribution and the value of medicinal products entering the market. In this work we identify the provenance and clinical benefit of medicines that entered the French market between 2008 and 2018. Of the 632 medicines that entered the French market between 2008 and 2018, 73% originated in the commercial sector, and 27% originated in the academic setting or in collaboration with commercial enterprises. Prescrire graded psychotropic agents (93%; 13/14), while HAS graded respiratory agents (96%; 24/25) as the highest percentage of medicines that provided no added benefit. Prescrire graded 77.6% of medicines that originated in the industry and 64.3% that originated in the academic setting (p=0.001) to have no added clinical benefit. HAS assigned such grading to 71.3% (industry) vs 61.9% (academia) (p=0.024). Based on the Prescrire grading, academia invented more medicines delivering some added benefit 33.9% vs 21.12% invented by industry (p=0.001). HAS grading on some added benefit 30.4% (academia) vs 26.1% (industry) did not reach statistical significance (p=0.29). However, HAS grading on substantial added clinical benefit reached statistical significance in favour of academia 7.7% vs 2.6% in the industry (p=0.003), while Prescrire grading did not (1.8% academia vs 1.3% industry p=0.64). Over 70% of medicines that entered the French market during the 10-year period originated in the commercial sector. Although the majority of medicines were not graded as providing clinical benefit, medicines originating in the academic setting were more likely to be graded as conferring clinical benefit than those originating in the commercial setting.

Read on



JAMA Intern Med. 2024;184(1):52-53. doi:10.1001/jamainternmed.2023.6256

Editorial comment by Joel Lexchin
Therapeutic Benefit From New Drugs From Pharmaceutical Companies

In *JAMA Internal Medicine*, Osipenko and colleagues expand our knowledge about the role of the public sector in both contributing to the development of new drugs and the therapeutic gains from those drugs. They found that 27% of the 632 new drugs introduced to the French market between 2008 and 2018 originated either in the academic setting alone or in collaboration with the commercial sector. The authors also evaluated therapeutic value, applying rating scales from the French independent drug bulletin Prescrire and the Haute Autorité de Santé, the French agency that provides a scientific opinion concerning the usefulness and appropriate use of new drugs. Based on the Prescrire ratings, academia invented more medicines delivering some added benefit than industry (33.9% vs 21.1%; P < .001). Using the Haute Autorité de Santé scoring system, 7.7% of academia drugs had a substantial added clinical benefit compared with just 2.6% of industry ones (P = .003).

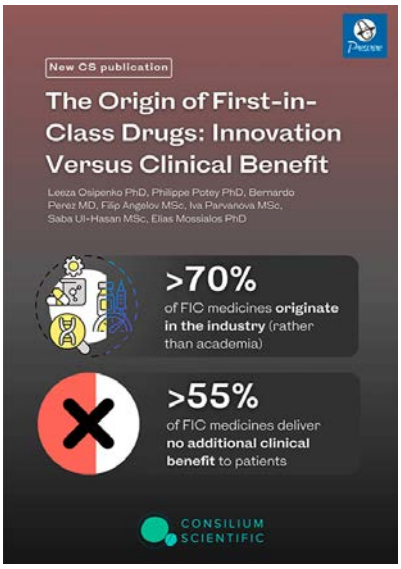
These findings challenge 2 tropes that are central to how the pharmaceutical industry would like the world see it. The first is that the pharmaceutical industry is responsible for all the new medicines that appear on the market. The second is that while all new drugs may not be breakthroughs, they are all advances because they give patients more therapeutic choices. Both are false.

When new drugs appear on the market, clinicians and patients have little to no information about where these medications fit into the therapeutic armamentarium.

One other important question is how to structure public policy to better align pharmaceutical companies R&D activities with public health needs. Joel Lexchin points out several approaches.

Read on

The Origin of First-in-Class Drugs: Innovation Versus Clinical Benefit



(Clin Pharmacology & Therapeutics, 2023)

By Leeza Osipenko, Philippe Potey, Bernardo Perez, Filip Angelov, Iva Parvanova, Saba Ul-Hasan, Elias Mossialos

https://doi.org/10.1002/cpt.3110

Abstract

First-in-class (FIC) designation became a hallmark of innovation, however, even at the marketing authorization stage, little is known about the clinical benefits these products deliver. We identified the provenance of the FIC drugs that entered the French market from 2008 to 2018 and matched these medicines to the clinical benefit grading by Haute Autorité de Santé (HAS) and Prescrire. Analyses were performed using descriptive statistics to present our findings by drug origin and therapeutic area and to establish the degree of concordance between HAS and Prescrire. Of the 135 FIC drugs identified, 71.1% (n = 96) originated from the industry, 16.3% (n = 22) from academia, and 12.6% (n = 17) from joint partnerships. Three therapeutic areas accounted for most FIC medications: antineoplastic (25.9%, N = 35), anti-infective (14.1%, N = 19), and metabolic (11.1%, N = 15) agents. HAS and Prescrire agreed on 60.74% of clinical benefit gradings. According to HAS, only 5% of all FIC drugs had substantial added benefit, and only 3%, according to Prescrire. HAS and Prescrire graded 45.9% and 68.2%, respectively, of FIC drugs as no clinical benefit and 48.9% and 28.9%, respectively, as some clinical benefit. FIC-designated drugs are primarily of industry (> 70%) rather than academic origin. We found that 55% of FIC medicines that entered the French market over the 10-year period deliver no additional clinical benefit. Whereas FIC medicines may represent important scientific advancements in drug development, in > 50% of cases, the new mode of action does not translate into additional clinical benefits for patients.

Read on

Common Sense Oncology : outcomes that matter

Booth CM, Sengar M, Goodman A, et al. Common Sense Oncology: outcomes that matter.
Lancet Oncol. 2023; 24: 833-835

https://doi.org/10.1016/S1470-2045(23)00319-4

The Common Sense Oncology (CSO) initiative's core mission is to ensure that cancer care and innovation is focused on outcomes that matter to patients rather than the commercial bottom line.

For CSO, oncology needs a recalibrated approach that is more patient-centered and delivers equitable cancer care. An approach that prioritizes:

- patients' needs with treatments that improve survival and quality-of-life
- patient informed decision making
- making treatments accessible to all patients

Patients deserve better information and better care. To achieve this, paradigm shifts will be needed in education research design and investment, policy, media and communication, and delivery of care.

Panel: Common Sense Oncology: outcomes that matter

Mission

To ensure that cancer care focuses on outcomes that matter to patients

Vision

Patients have access to cancer treatments that provide meaningful improvements in outcomes that matter, irrespective of where they live or their health system. To realise this vision, we aspire that:

- Patient outcomes that matter must be at the centre of every drug registration trial; and patient outcomes that matter should be the standard for every drug regulatory decision
- Reporting of trials is transparent and uses language that can be understood clearly by oncologists and patients
- Patients receive clear communication regarding treatment options that enables them to make informed decisions that are aligned with their personal goals and values
- The only treatments that are registered, reimbursed, and recommended are ones that meaningfully improve patients' lives
- Common Sense Oncology that is grounded in evidence-based medicine and critical appraisal becomes a core curricular component for oncology training programmes
- Health systems invest in both developing new treatments and ensuring that patients have access to and benefit from proven effective treatments

Guiding principles

1 Access to quality cancer care is a basic human right—no patient should be denied access to effective therapy or forced into financial catastrophe to access meaningful cancer care
2 Patient and societal needs should drive cancer research and delivery of care
3 Patient and public involvement is essential when making policy decisions
4 Patients should expect that recommended cancer treatments meaningfully improve their survival or quality of life
5 Shared decision making between patients and oncologists should be based on patient values and grounded in evidence-based medicine and critical appraisal
6 Cancer treatments should be fairly priced for the context in which they are used
7 Equity in access to high quality care should be prioritised as much as innovation and new treatments
8 Comprehensive patient-centred cancer care includes timely integration of psychosocial oncology, survivorship, and palliative care

CSO's Pillars of Work

1- Evidence generation: ensure that clinical trials use and report outcomes that matter to patients

2- Evidence interpretation; foster critical thinking by oncologists

3- Evidence communication: improve patient, public, and policy-maker understanding of cancer treatment options

Read on

FDA Investigating Serious Risk of T-cell Malignancy Following BCMA-Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T cell Immunotherapies (November 28, 2023)

The Food and Drug Administration (FDA) has received reports of T-cell malignancies, including chimeric antigen receptor CAR-positive lymphoma, in patients who received treatment with BCMA- or CD19-directed autologous CAR T cell immunotherapies. Reports were received from clinical trials and/or postmarketing adverse event (AE) data sources.

FDA has determined that the risk of T-cell malignancies is applicable to all currently approved BCMA-directed and CD19-directed genetically modified autologous CAR T cell immunotherapies.

Read on

Feedback on ISDB Committee activities

The ISDB Committee held two online meetings between November 2023 and February 2024. An in-person meeting, kindly hosted by the Mario Negri Institute, took place in Milan on December 11 and 12, 2023. It was the first time that the Committee had met in person since the ISDB Ordinary General Assembly in November 2022.

The first day was devoted to internal issues, in particular the ISDB website and the ongoing activities of the two working groups concerned with the ISDB Strategic Plan (one focusing on ISDB membership and the other on the ISDB's mission and activities). An online survey of our members concerning the ISDB's priorities was launched in November 2023, and the results will be shared in the upcoming weeks. On the second day, the Committee had the great pleasure of meeting with Professor Silvio Garattini, founder of the Mario Negri Institute, and three researchers from the Institute, who provided an overview on their research projects involving child health, cardiovascular prevention, and medical research & consumer involvement:

- Antonio Clavenna, Head of the Laboratory of Child Health and Development Epidemiology
- Marta Baviera, Head of the Laboratory of Cardiovascular Prevention
- Cinzia Colombo, Researcher at the Laboratory of Medical Research and Consumer Involvement
- Rita Kessler, the ISDB President (Prescrire, France), delivered a presentation on the revision of European Pharmaceutical legislation.

In December 2023, the Committee sent a letter to Australian Prescriber regarding adherence to the ISDB's rules on conflicts of interest and the use of external authors.

On 1st December 2023, Barbara Mintzes, the ISDB Secretary General (Therapeutics Initiative, Canada), gave a presentation on the importance of independent drug information, at a symposium organized by Thierry Christiaens (BCFI/CBIP) in Ghent, Belgium. As Thierry had recently retired from Ghent University, the event was an opportunity to celebrate his 35-year academic career, devoted to teaching and fighting for rational prescribing.

From left to right: Barbara Mintzes, Roberta Joppi, Nuria Homedes, Luis Carlos Saiz, Rita Kessler