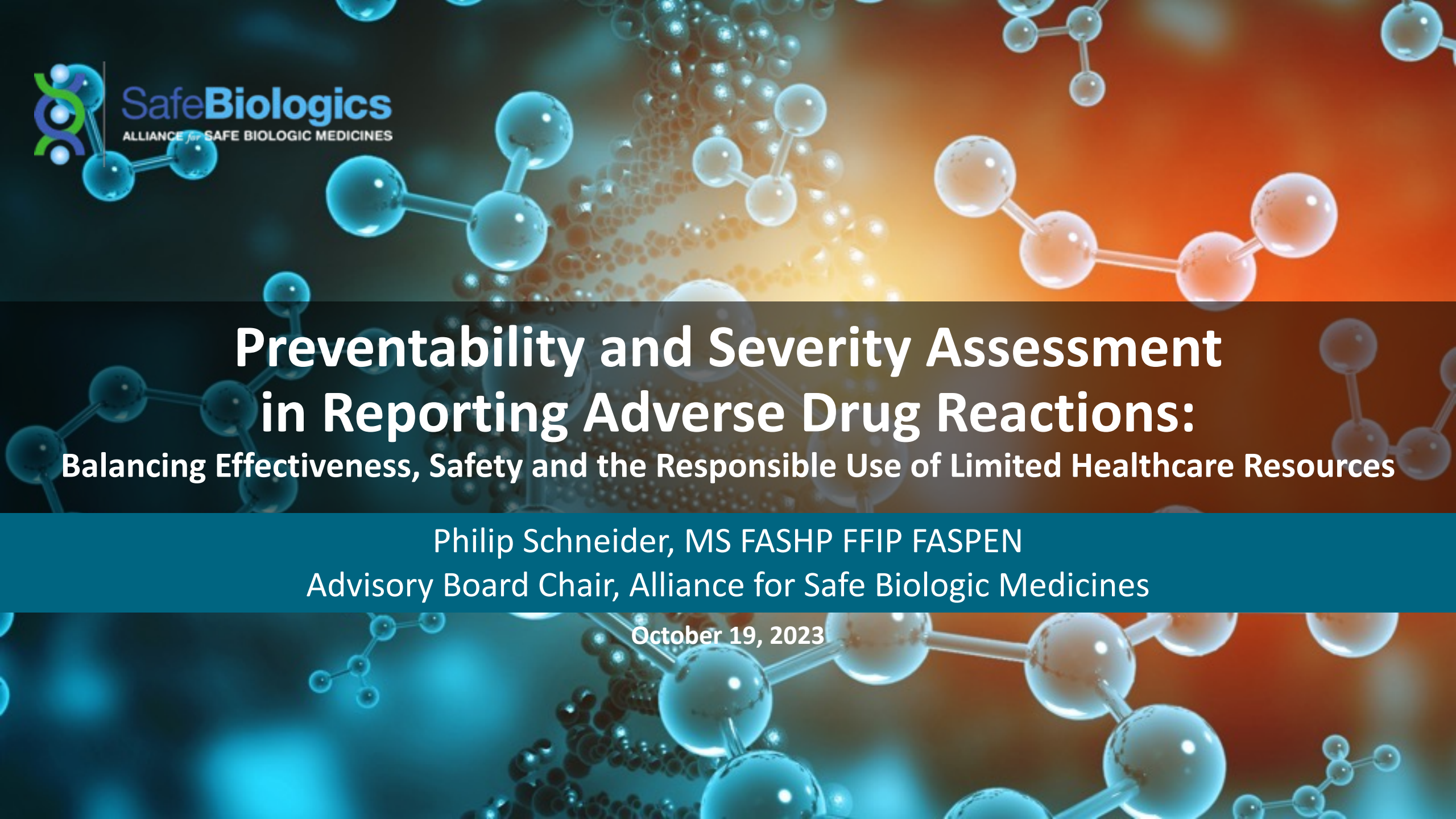


Preventability and Severity Assessment in Reporting Adverse Drug Reactions:

Balancing Effectiveness, Safety and the Responsible Use of Limited Healthcare Resources

Philip Schneider, MS FASHP FFIP FASPEN
Advisory Board Chair, Alliance for Safe Biologic Medicines

October 19, 2023

Philip Schneider, MS, FASHP, FFIP, FASPEN

- Advisory Board Chair, Alliance for Safe Biologic Medicines
- Past Vice President, International Pharmaceutical Federation (FIP)
- Past-President, American Society of Health-system Pharmacists
- Professor of Pharmacy, Ohio State University

Adverse Event Reports:

Clinicians and patients have a duty and accountability to do what is right for each clinical situation.

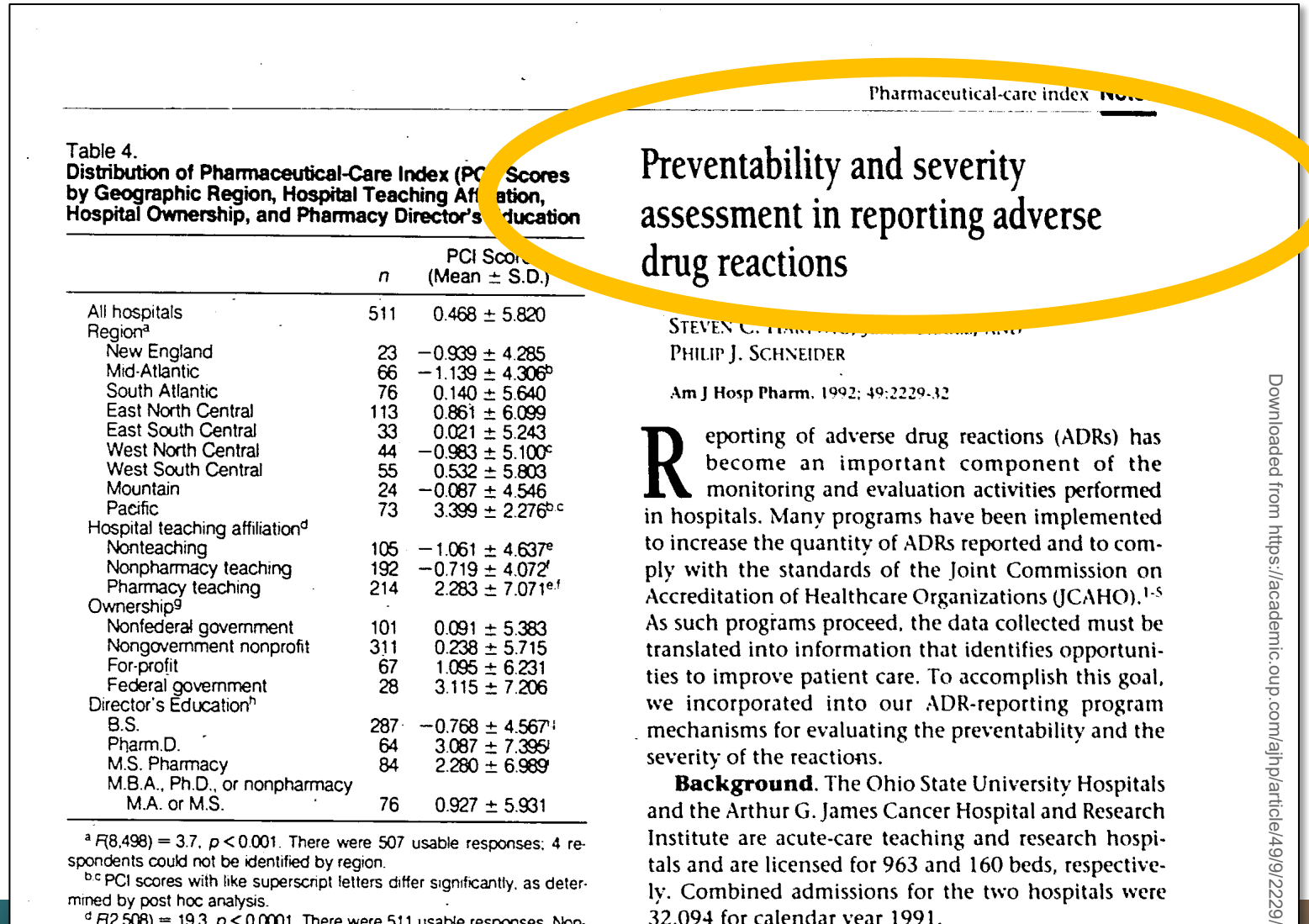
We have traditionally focused on **EFFECTIVNESS** and **SAFETY** for a long time and these are the central source of information about the patient's response to a drug.

We have looked for "**SAFETY SIGNALS**" to find problems with the use of medications.

The Goal: Preventability

As we learn more from experience, clinicians have directed their attention to **PREVENTING adverse drug events** (including problems with effectiveness and safety).

Subject of my 1992 Article.



Pharmaceutical-care index

Table 4.
Distribution of Pharmaceutical-Care Index (PC Scores by Geographic Region, Hospital Teaching Aff ation, Hospital Ownership, and Pharmacy Director's ducation

	n	PCI Scor (Mean ± S.D.)
All hospitals	511	0.468 ± 5.820
Region[a]		
New England	23	−0.939 ± 4.285
Mid-Atlantic	66	−1.139 ± 4.306[b]
South Atlantic	76	0.140 ± 5.640
East North Central	113	0.861 ± 6.099
East South Central	33	0.021 ± 5.243
West North Central	44	−0.983 ± 5.100[c]
West South Central	55	0.532 ± 5.803
Mountain	24	−0.087 ± 4.546
Pacific	73	3.399 ± 2.276[b,c]
Hospital teaching affiliation[d]		
Nonteaching	105	−1.061 ± 4.637[e]
Nonpharmacy teaching	192	−0.719 ± 4.072[f]
Pharmacy teaching	214	2.283 ± 7.071[e,f]
Ownership[g]		
Nonfederal government	101	0.091 ± 5.383
Nongovernment nonprofit	311	0.238 ± 5.715
For-profit	67	1.095 ± 6.231
Federal government	28	3.115 ± 7.206
Director's Education[h]		
B.S.	287	−0.768 ± 4.567[i]
Pharm.D.	64	3.087 ± 7.395[j]
M.S. Pharmacy	84	2.280 ± 6.989[i]
M.B.A., Ph.D., or nonpharmacy M.A. or M.S.	76	0.927 ± 5.931

[a] $F(8,498) = 3.7$, $p < 0.001$. There were 507 usable responses; 4 respondents could not be identified by region.
[b,c] PCI scores with like superscript letters differ significantly, as determined by post hoc analysis.
[d] $F(2,508) = 19.3$, $p < 0.0001$. There were 511 usable responses. Non-

Preventability and severity assessment in reporting adverse drug reactions

STEVEN C. [illegible]
PHILIP J. SCHNEIDER

Am J Hosp Pharm. 1992; 49:2229-32

Reporting of adverse drug reactions (ADRs) has become an important component of the monitoring and evaluation activities performed in hospitals. Many programs have been implemented to increase the quantity of ADRs reported and to comply with the standards of the Joint Commission on Accreditation of Healthcare Organizations (JCAHO).[1-5] As such programs proceed, the data collected must be translated into information that identifies opportunities to improve patient care. To accomplish this goal, we incorporated into our ADR-reporting program mechanisms for evaluating the preventability and the severity of the reactions.

Background. The Ohio State University Hospitals and the Arthur G. James Cancer Hospital and Research Institute are acute-care teaching and research hospitals and are licensed for 963 and 160 beds, respectively. Combined admissions for the two hospitals were 32,094 for calendar year 1991.

Downloaded from https://academic.oup.com/ajhp/article/49/9/2229/

Preventability and ADR Severity Assessments

Preventability Assessment

1.	Was the drug involved in the ADR appropriate for the patient's clinical condition?	YES	NO
2.	Were the dose, route, and frequency of administration appropriate for the patient's age, weight, organ function, and disease state?	YES	NO
3.	If the reaction was due to a drug allergy, was this allergy previously documented..; A. In the admitting orders?	YES	NO
	B. In the patient's computer profile?	YES	NO
4.	Were appropriate therapeutic drug monitoring or other laboratory tests performed which may have predicted this reaction?	YES	NO

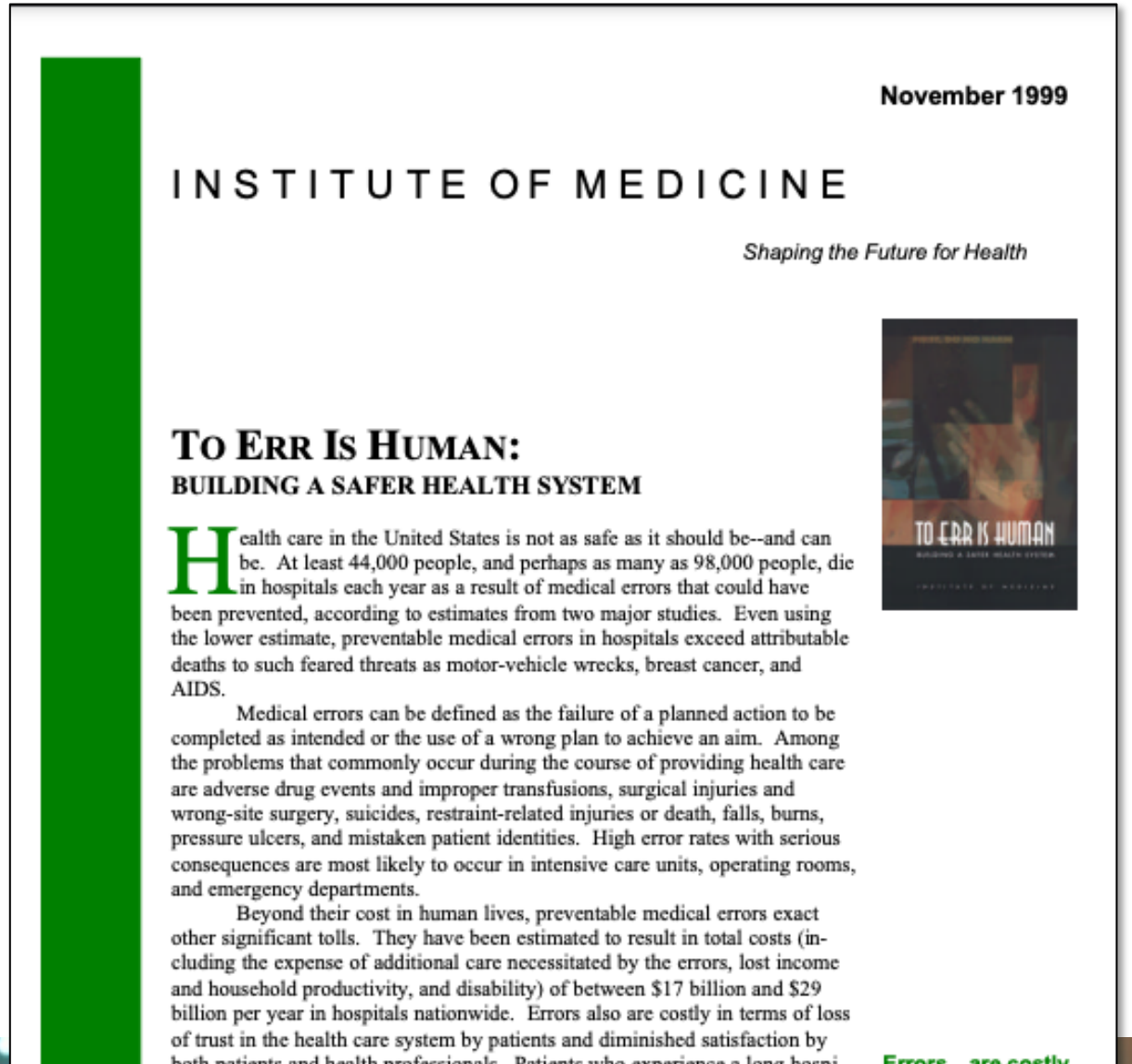
Severity Assessment

1.	Was the ADR the reason for admission?	YES	NO
2.	If not the reason for admission, did the ADR cause an increased length of stay (LOS) by at least one day?	YES	NO
3.	Did the ADR result in permanent harm to the patient? (Explain any YES responses.)	YES	NO

Prevention of Medical Errors: "To Err is Human"

"Experts estimate that as many as 98,000 people die in any given year from medical errors that occur in hospitals. That's more than die from motor vehicle accidents, breast cancer, or AIDS--three causes that receive far more public attention. Indeed, more people die annually from medication errors than from workplace injuries."

"To Err is Human; Building a Safer Health System", Institute of Medicine, 1999



November 1999

INSTITUTE OF MEDICINE

Shaping the Future for Health

TO ERR IS HUMAN:
BUILDING A SAFER HEALTH SYSTEM

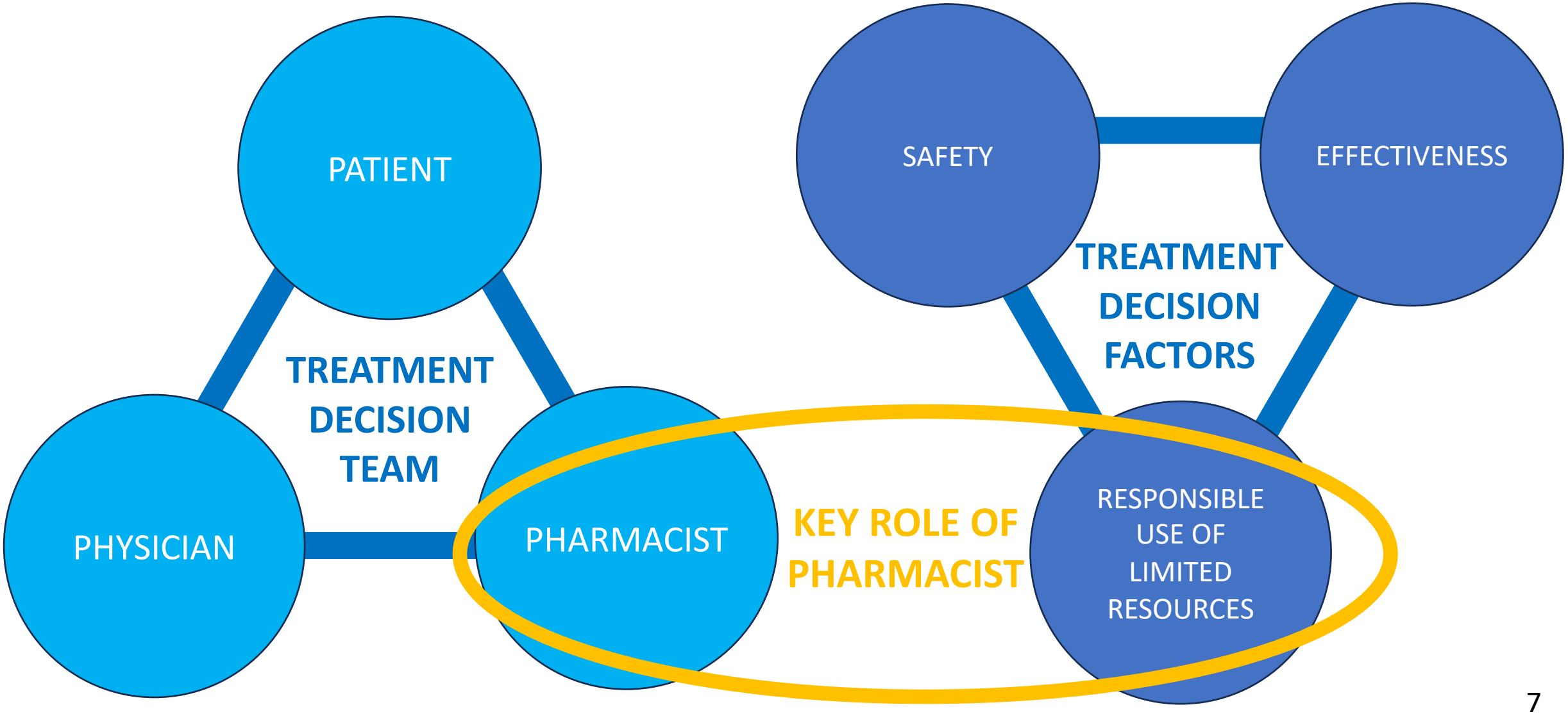
Health care in the United States is not as safe as it should be--and can be. At least 44,000 people, and perhaps as many as 98,000 people, die in hospitals each year as a result of medical errors that could have been prevented, according to estimates from two major studies. Even using the lower estimate, preventable medical errors in hospitals exceed attributable deaths to such feared threats as motor-vehicle wrecks, breast cancer, and AIDS.

Medical errors can be defined as the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim. Among the problems that commonly occur during the course of providing health care are adverse drug events and improper transfusions, surgical injuries and wrong-site surgery, suicides, restraint-related injuries or death, falls, burns, pressure ulcers, and mistaken patient identities. High error rates with serious consequences are most likely to occur in intensive care units, operating rooms, and emergency departments.

Beyond their cost in human lives, preventable medical errors exact other significant tolls. They have been estimated to result in total costs (including the expense of additional care necessitated by the errors, lost income and household productivity, and disability) of between $17 billion and $29 billion per year in hospitals nationwide. Errors also are costly in terms of loss of trust in the health care system by patients and diminished satisfaction by

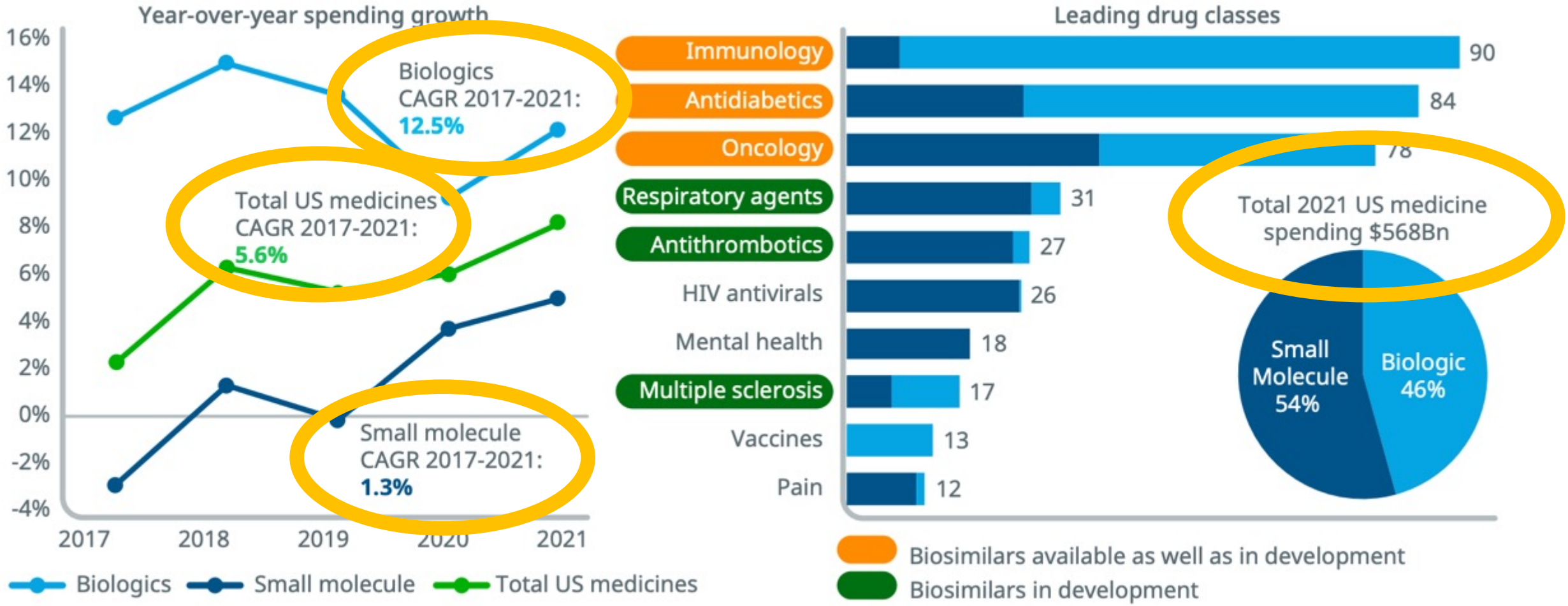
Errors...are costly

In Addition to Safety and Efficacy, Pharmacists Consider Cost…



Cost is A Major Concern with Biologics

Exhibit 1: Total U.S. invoice spending growth by type and leading therapy areas by 2021 spending, US$Bn



Source: IQVIA MIDAS, Dec 2021; IQVIA Institute, Nov 2022.

Biosimilars Help Make More Effective Use of Resources, Expand Access

Biosimilars- achieving cost savings to the health system through competition: freeing up money for other health spending.

- Adalimumab biosimilars (2023) created downward pressure on originator adalimumab product.
- Biosimilars range from 5% to 85% discount over reference product.
- **American Journal of Managed Care study estimates biosimilar savings from 2021 to 2025 will be $38.4 billion.** "Greater savings may be feasible if managed care and other settings increase biosimilar utilization and promote competition."

AJMC

Projected US Savings From Biosimilars, 2021-2025

Jan 3, 2022

Andrew Mulcahy, PhD, MPP

Christine Buttorff, PhD

View All

The American Journal of Managed Care

July 2022

Volume 28 Issue 7

Projected savings from biosimilars from 2021 to 2025 were $38.4 billion vs conditions as of quarter 4 of 2020 and were driven by new biosimilar entry. Savings were $124.5 billion under an upper-bound scenario.

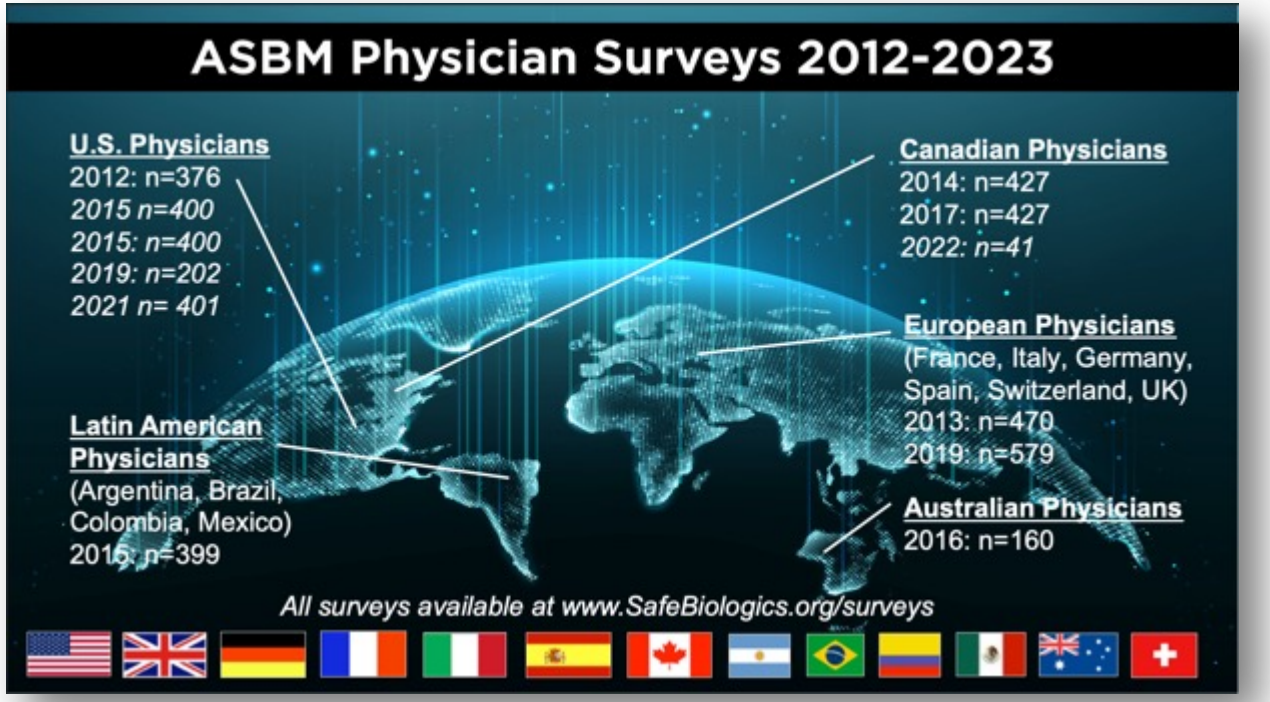
ABSTRACT

Objectives: Biologics account for an increasing share of US prescription drug spending. Biosimilars could lower biologic prices through competition, but barriers to increasing both supply and uptake remain. We projected US biosimilar savings from 2021 to 2025 under different scenarios.

Am J Manag Care. 2022;28(7):329-335. https://doi.org/10.37765/ajmc.2022.88809

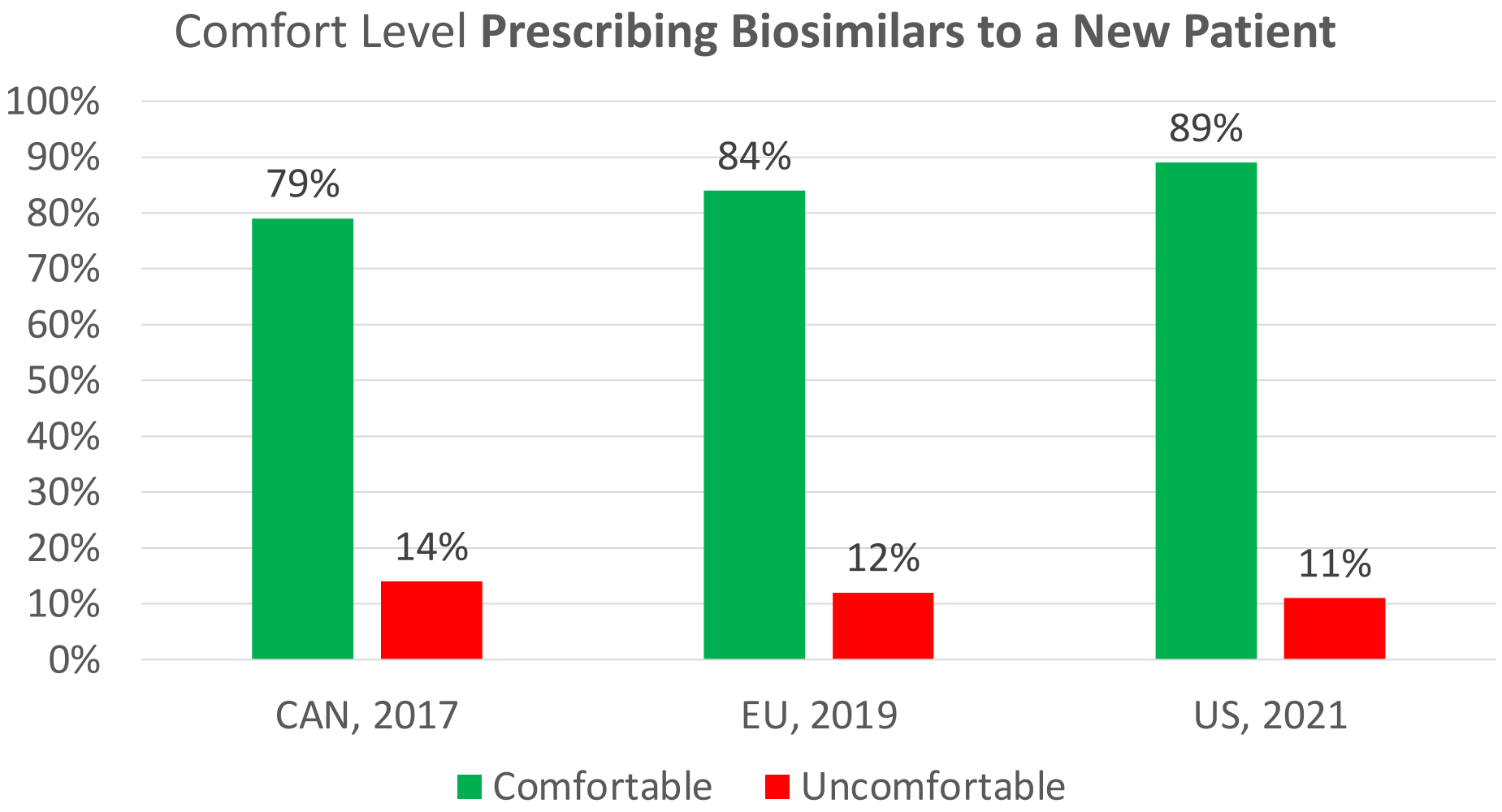
Physician Views of Biosimilars. What does Data Show?

- **Clinicians understand the potential of biosimilars to save money…if safety and efficacy are not compromised**
- They resent having treatment decisions imposed on them and their patients solely for economic reasons.
- **They have confidence in biosimilars,** especially if they are making the treatment decision to use them.



- **Confidence is improved by additional data demonstrating safety/efficacy – especially with regard to switching stable patients.**

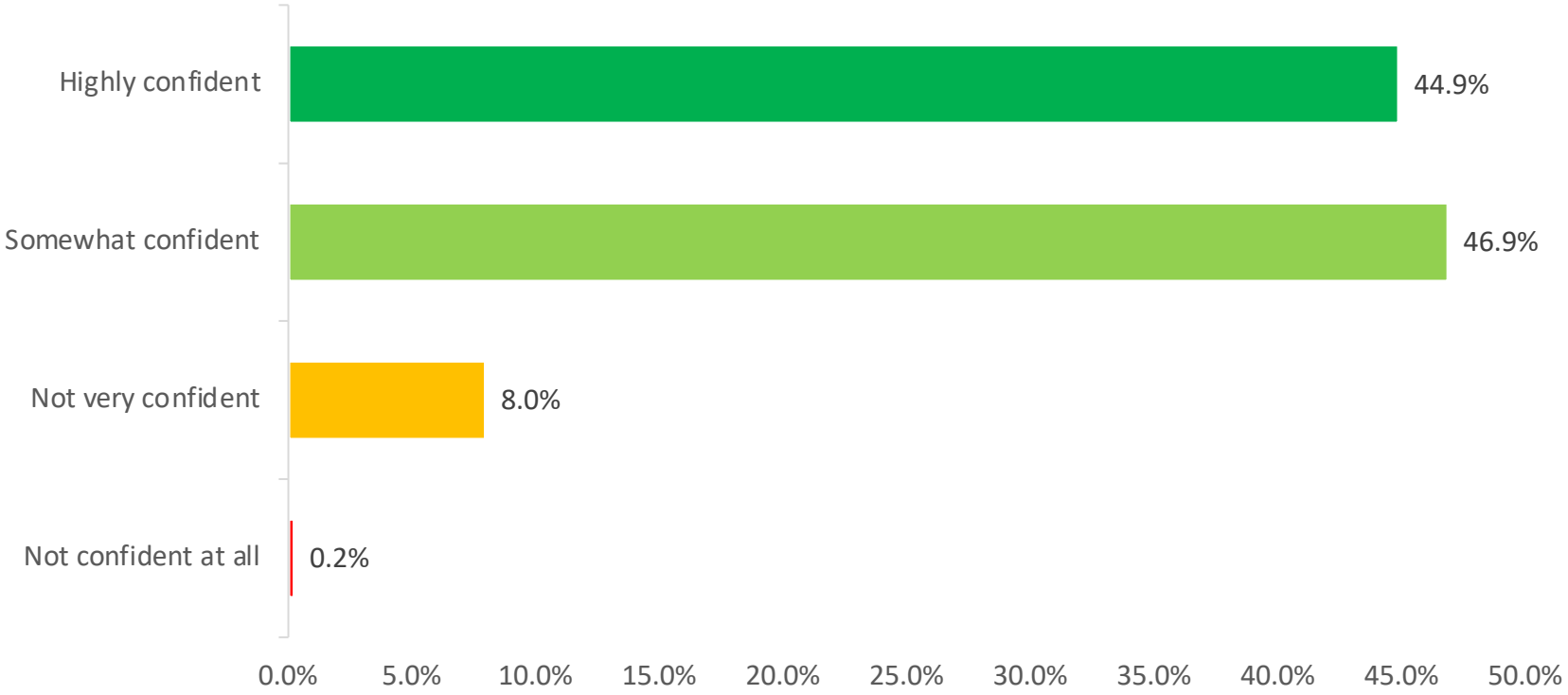
Physicians Are Very Comfortable Prescribing Biosimilars to New Patients…



Physician confidence in and comfort with biosimilars is high- the vast majorities of physicians have no concerns with prescribing biosimilars- to new patients.

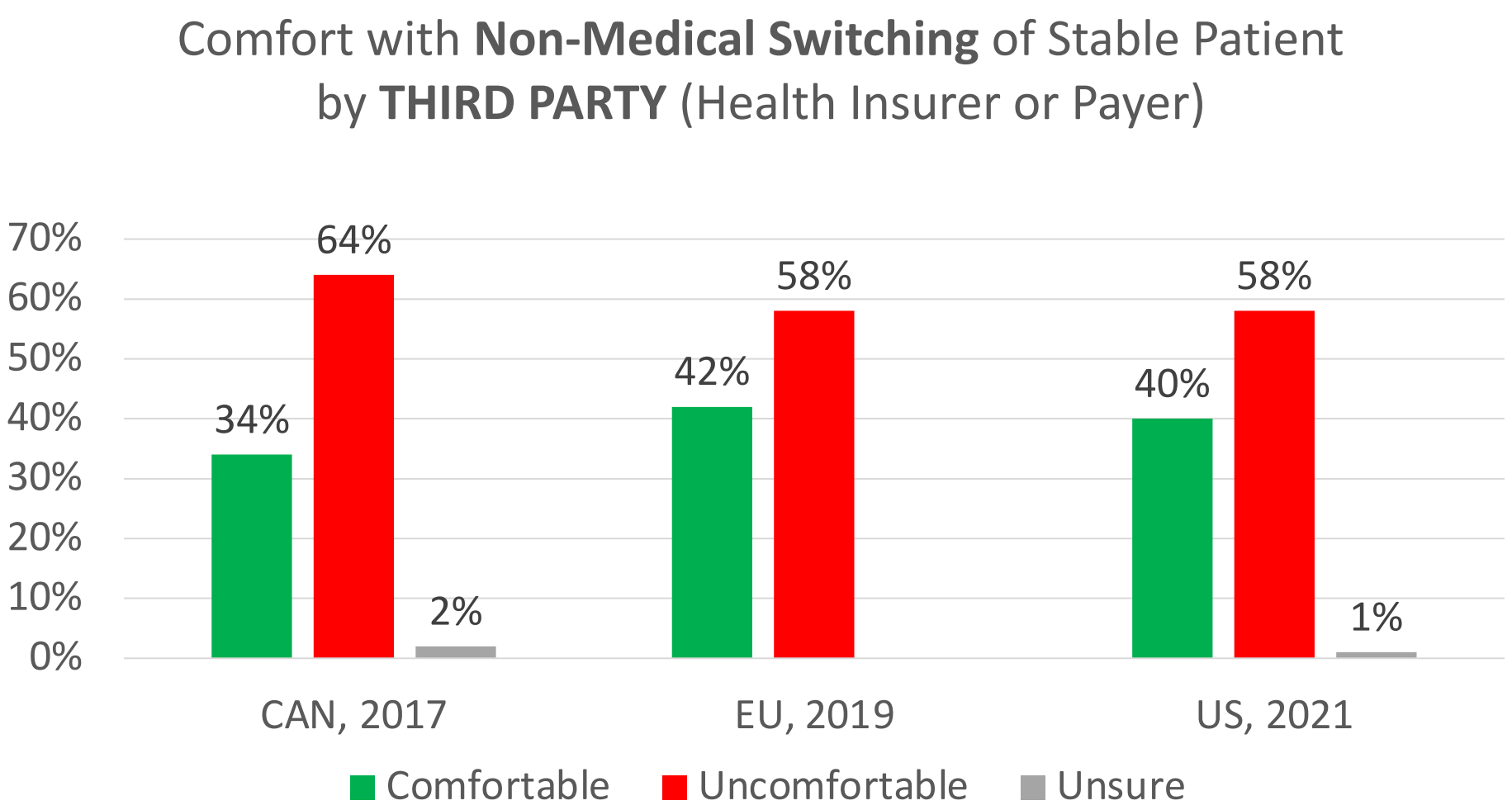
U.S. Physicians Are Confident in the Safety of Efficacy of Biosimilars…

- **Q1. How would you describe your personal confidence level in the safety and efficacy of biosimilars? (n=401)**



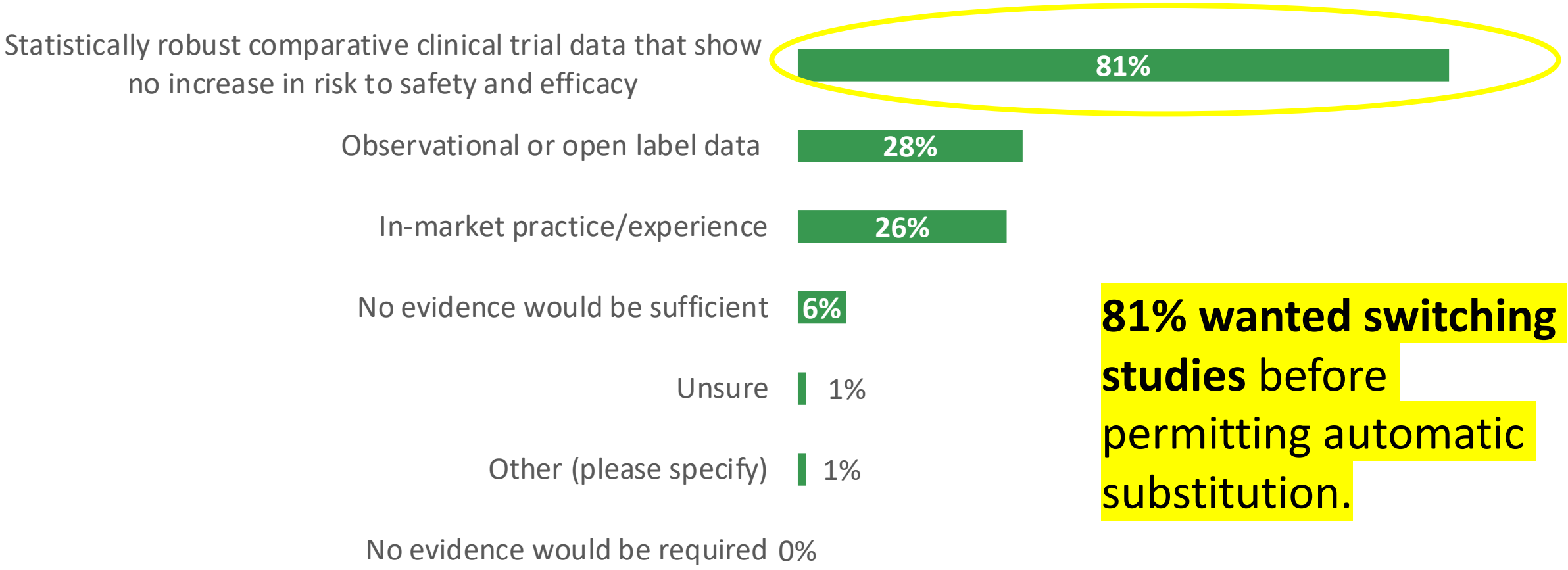
92% of U.S. physicians have confidence in the safety and efficacy of biosimilars

Most Physicians Are Not Comfortable with Third Party Non-Medical Switching



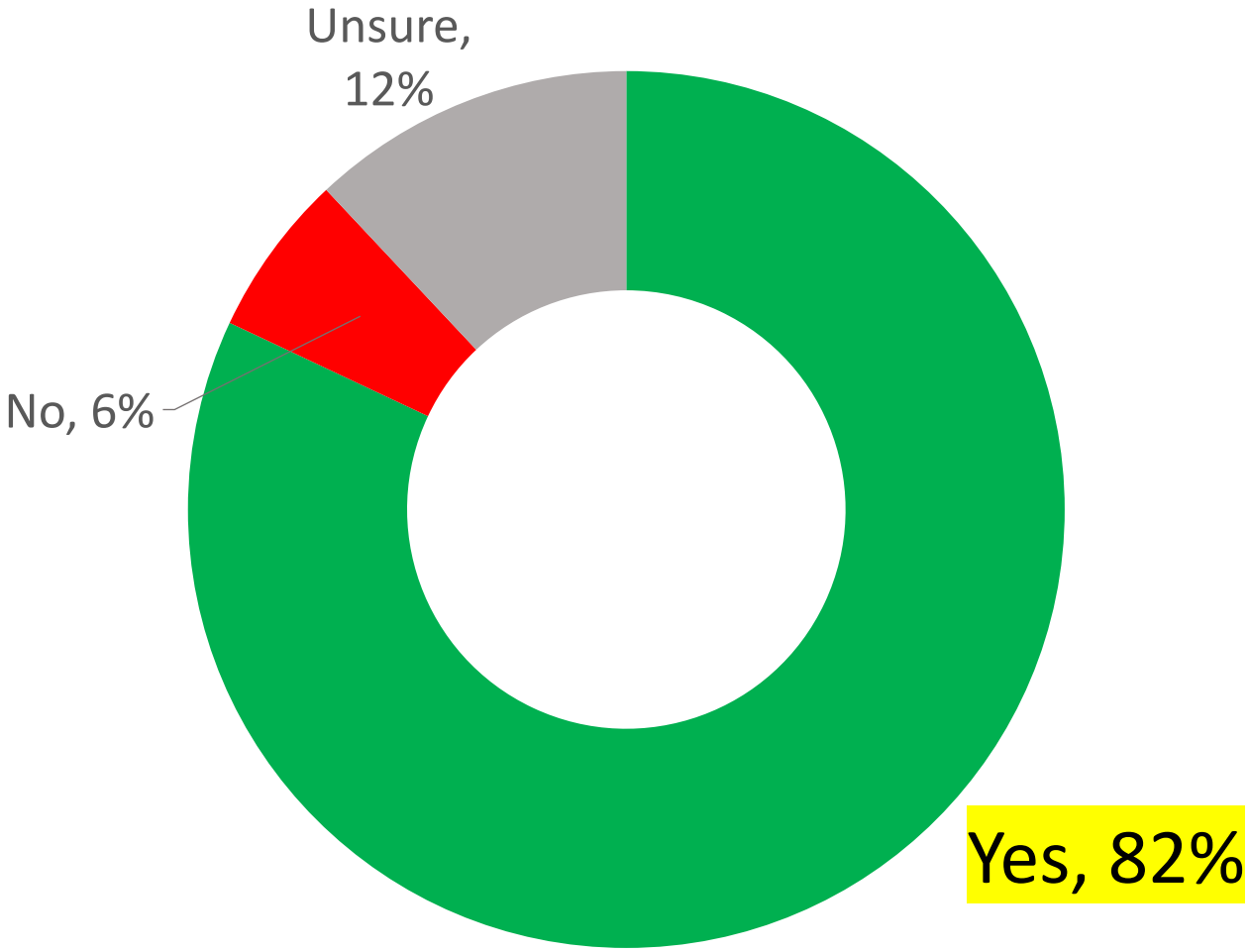
The majority, about 60% are NOT comfortable with Third Party Non-Medical Switching.

Australian Physicians Want Switching Studies Before Automatic Substitution is Permitted



81% wanted switching studies before permitting automatic substitution.

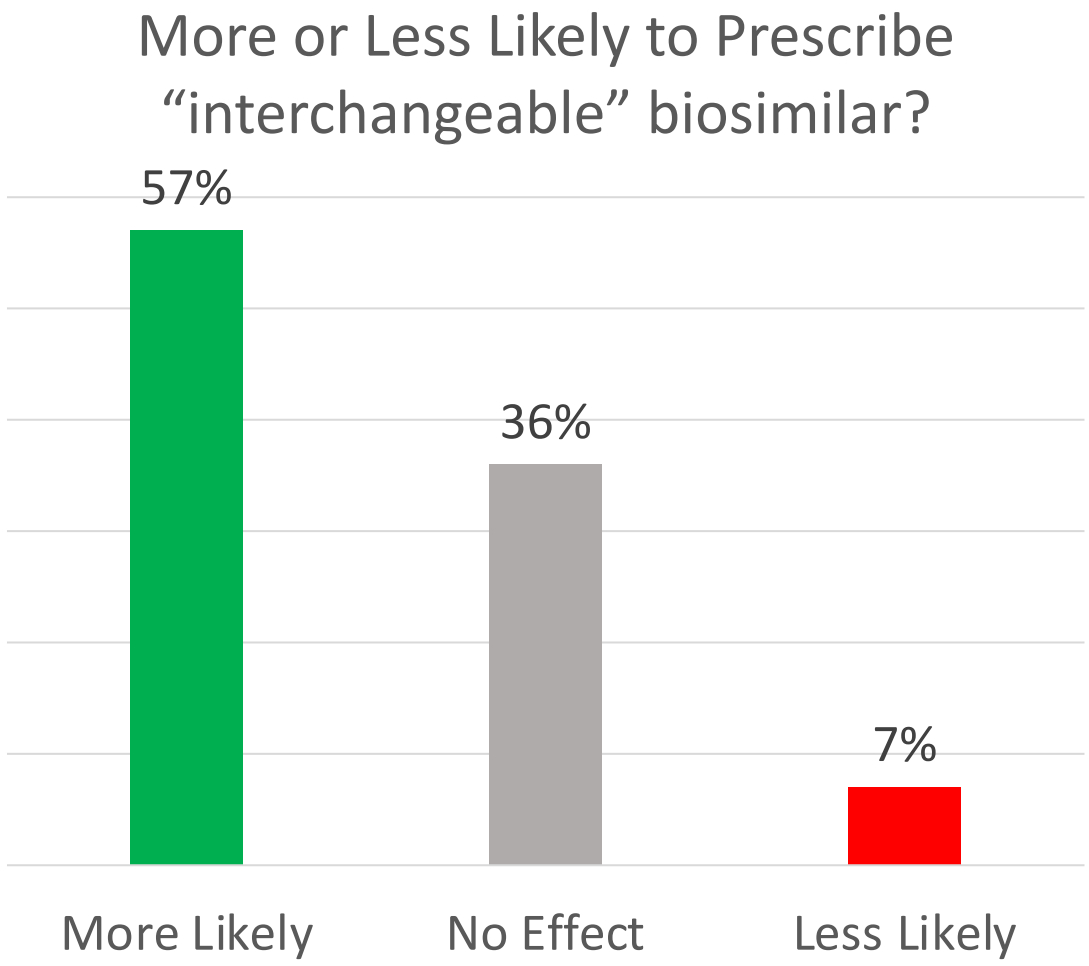
Canadian Physicians Want Switching Studies Before Automatic Substitution

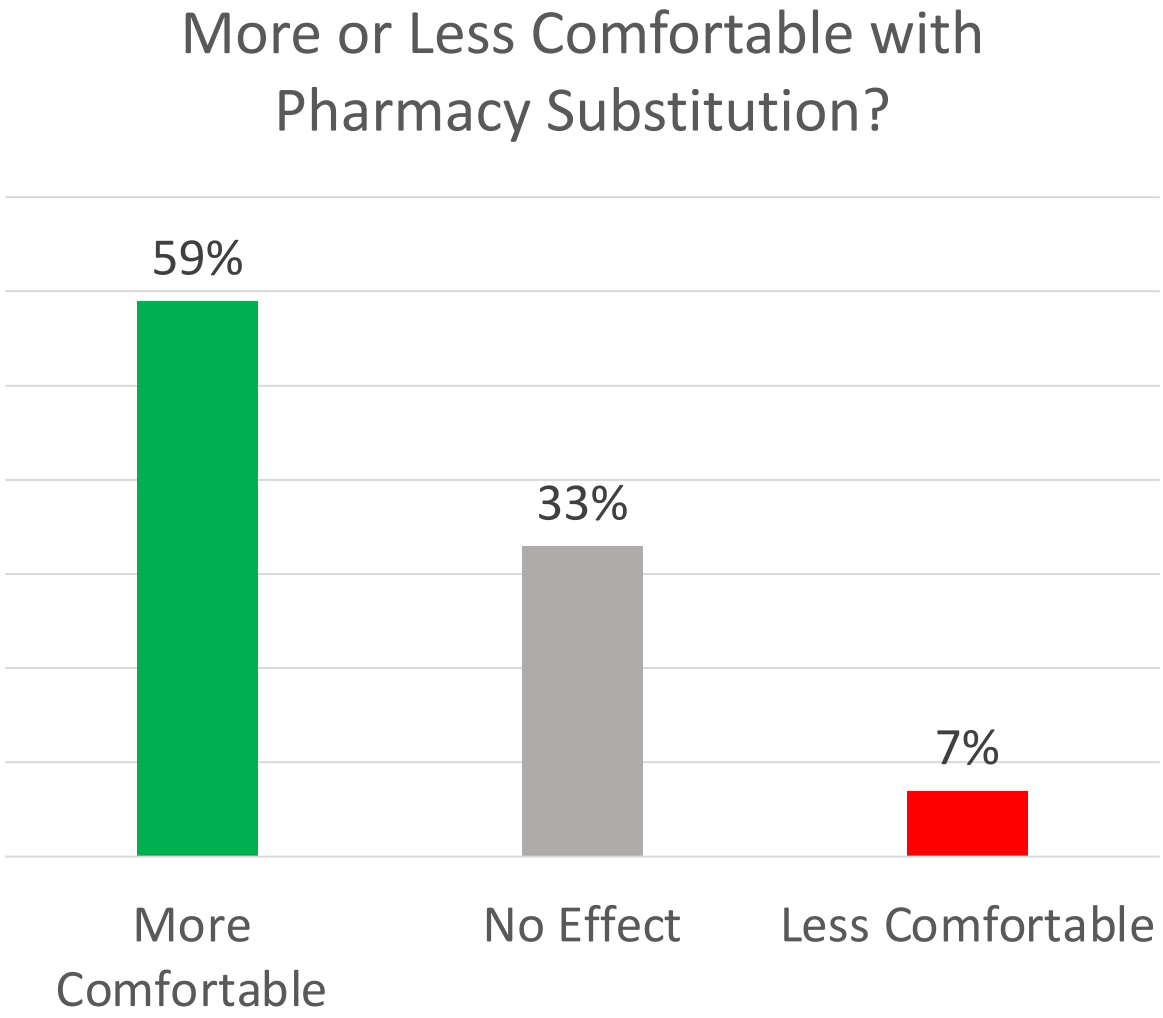


Canadian Survey, 2017 (n=403):

Prior to deciding whether automatic substitution should be allowed by a pharmacist or payer, **do you believe studies should be conducted that measure the effects of switching on patient safety and product efficacy?**”

US Survey: Additional Data/Switching Studies Makes Most Physicians More Comfortable With Prescribing, Substitution of "Interchangeable" Biosimilars





Pharmacovigilance: Pre- and Post- Market

- However, studies like a double blind, randomized, controlled trial (RCT) are expensive and time consuming.
- They are also based on a narrow spectrum of patients.
- **As a result, strong post-market pharmacovigilance programs are critical to building confidence.**
- This is especially true for products with abbreviated approval pathways that emphasize analytics over clinical trials (biosimilars).
  - **Robust Post-Marketing Surveillance and Real World Evidence are Key**

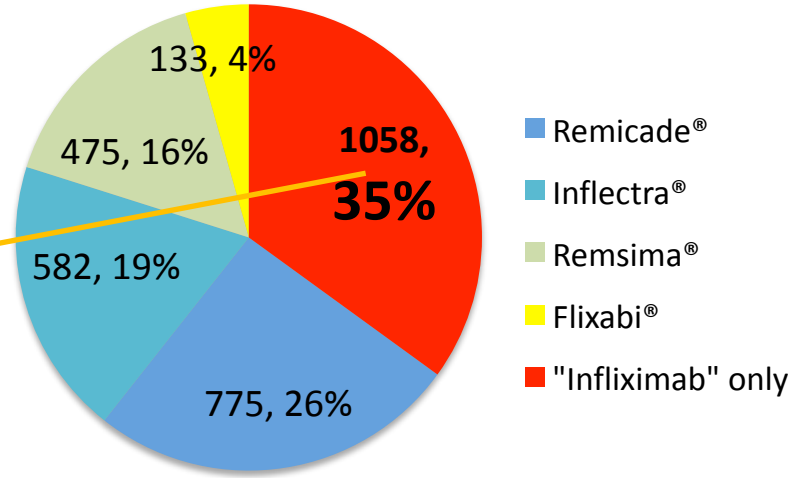
Data Quality Concerns

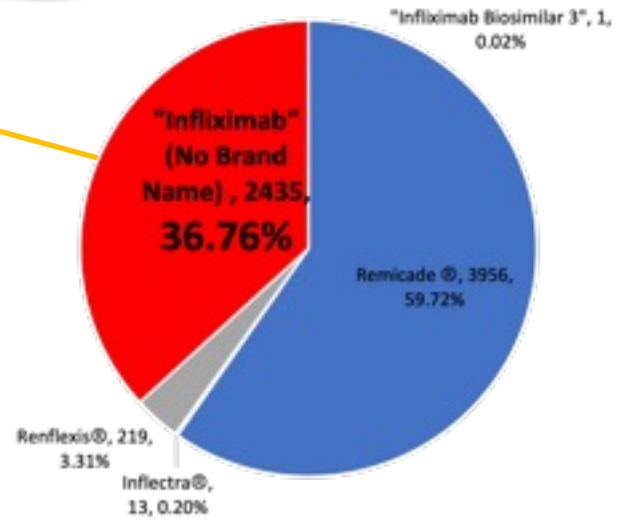
As we rely on analytics and "big data", the QUALITY of medical information used is critical.

Currently there are MAJOR GAPS…

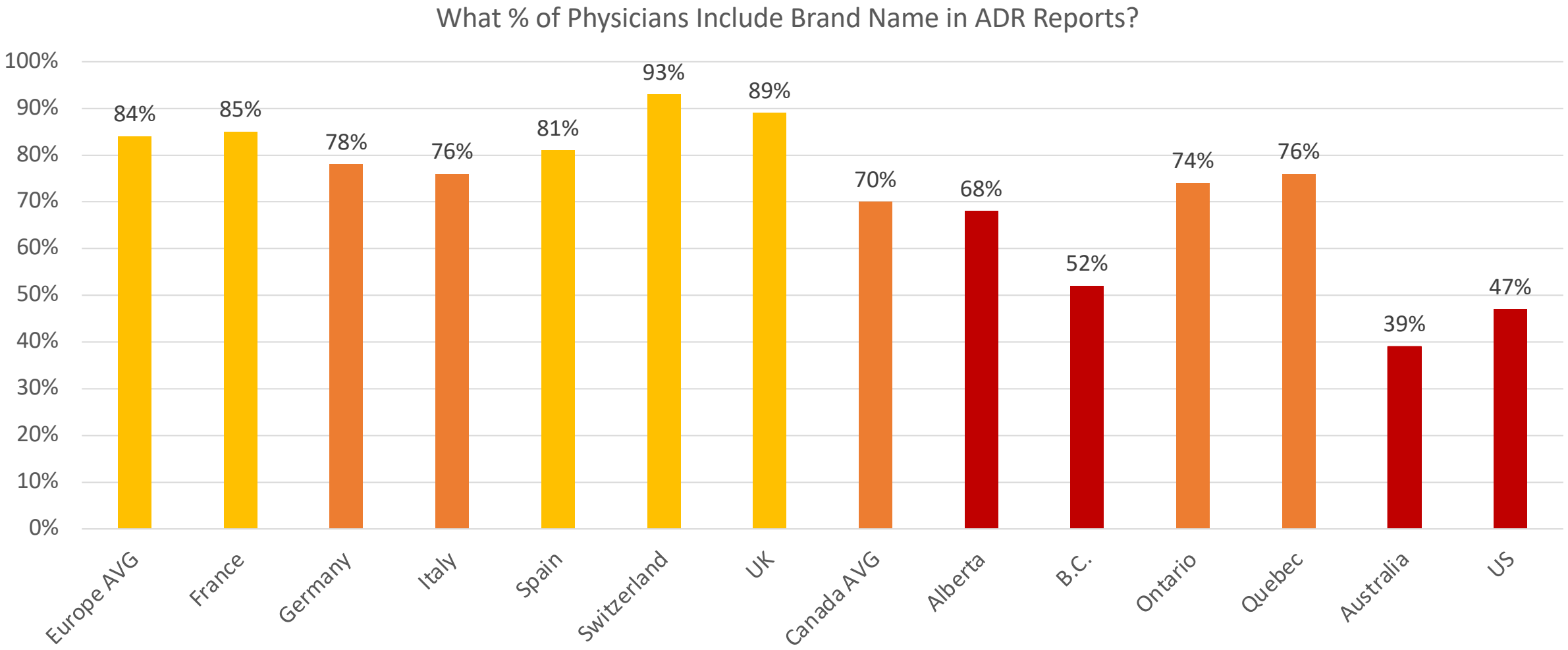
Adverse Event Reports Show Physicians Do Not Consistently Report Brand Name of Biologic. Example: 16 Infliximab products in EU

- 2018 Irish ADR reports for infliximab: **18% missing brand name**
- A 2018 review of EudraVigilance ADR reports for infliximab revealed that **35% contained no brand name.**
- A review of 2020 Canadian ADR reports for infliximab **are missing brand name 37% of the time.**
- 2019 UK BIOTRAC study: **only 38% of ADR Reports had an identifiable brand name.**





ASBM Survey Data Also Shows A Large Percentage of Physicians Worldwide Do Not Report Brand Name in Adverse Event Reports

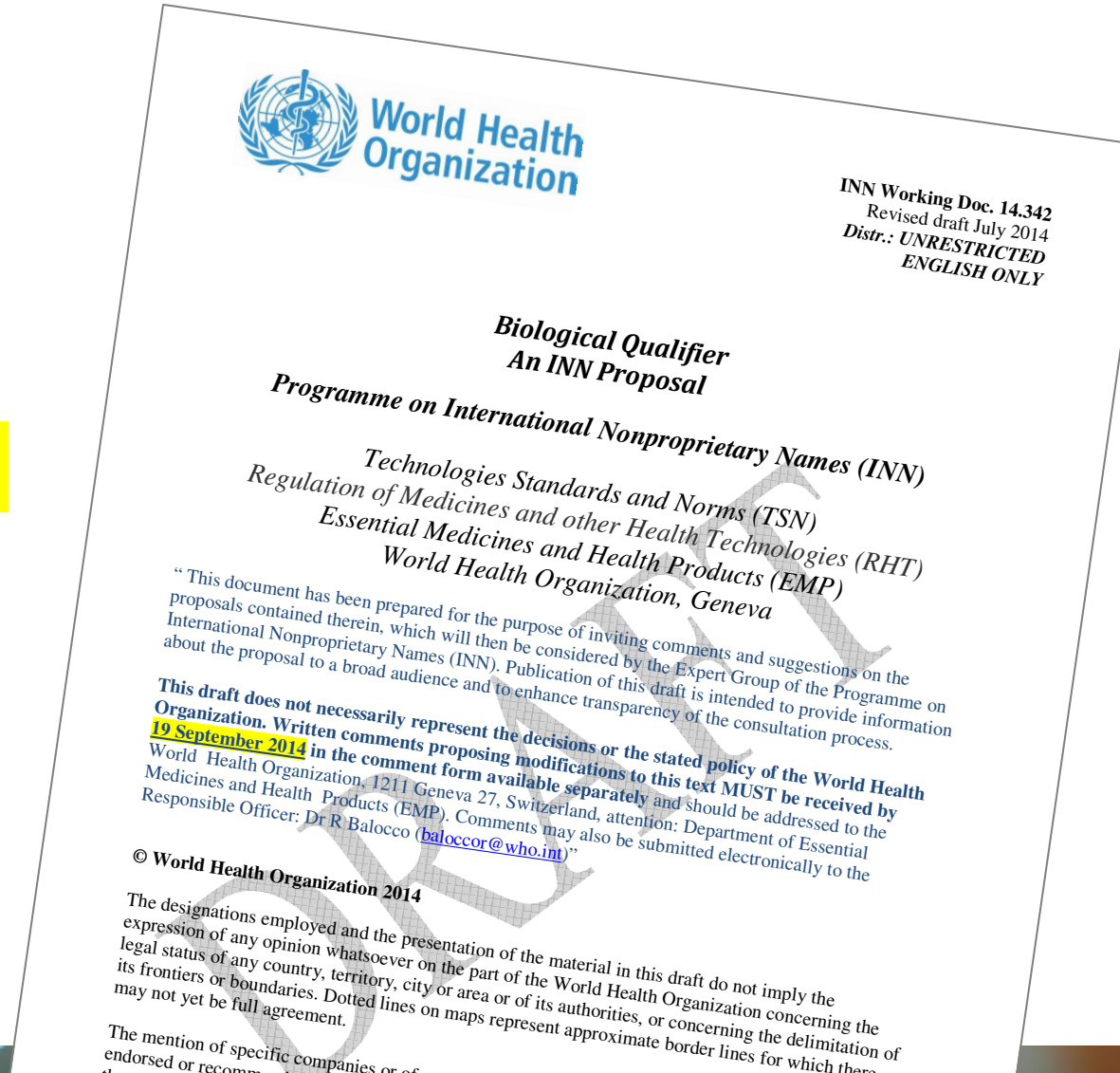


Source: Australia, Europe, and US physician surveys (2016-2019) www.safebiologics.org/surveys

WHO INN Expert Group Proposed a Solution

In 2014, the WHO's International Nonproprietary Names (INN) Expert Group recommended a four-letter distinguishing suffix be appended to each biologic that shares an INN, traceable to its manufacturer.

The "Biologic Qualifier" or (BQ).



World Health Organization

INN Working Doc. 14.342
Revised draft July 2014
Distr.: UNRESTRICTED
ENGLISH ONLY

Biological Qualifier
An INN Proposal

Programme on International Nonproprietary Names (INN)

Technologies Standards and Norms (TSN)
Regulation of Medicines and other Health Technologies (RHT)
Essential Medicines and Health Products (EMP)
World Health Organization, Geneva

" This document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein, which will then be considered by the Expert Group of the Programme on International Nonproprietary Names (INN). Publication of this draft is intended to provide information about the proposal to a broad audience and to enhance transparency of the consultation process.

This draft does not necessarily represent the decisions or the stated policy of the World Health Organization. Written comments proposing modifications to this text MUST be received by 19 September 2014 in the comment form available separately and should be addressed to the World Health Organization, 1211 Geneva 27, Switzerland, attention: Department of Essential Medicines and Health Products (EMP). Comments may also be submitted electronically to the Responsible Officer: Dr R Balocco (baloccor@who.int)"

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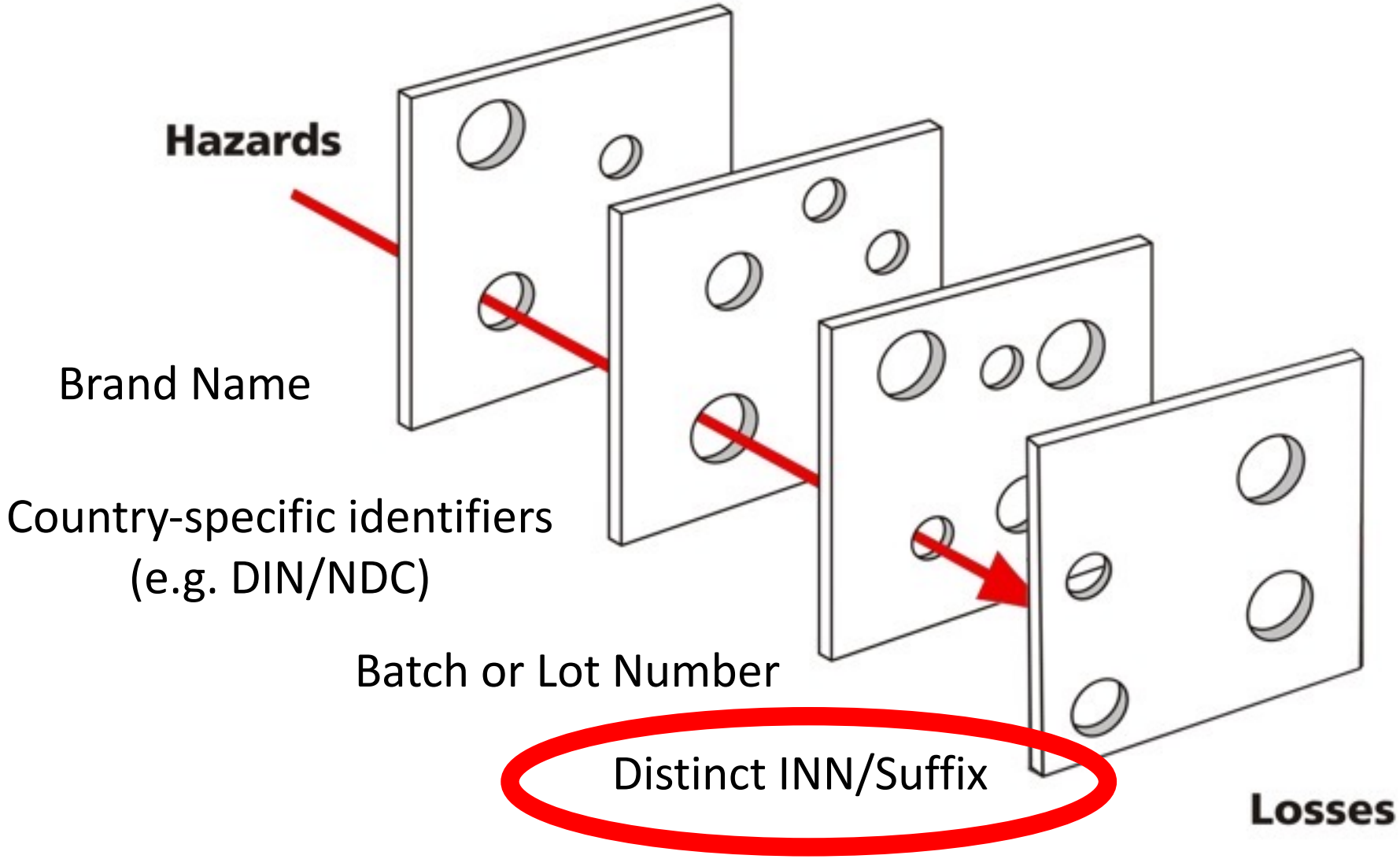
The mention of specific companies or of

DRAFT

Distinguishable INN/Suffix as a “Defense” in Identification of Biologic Medicines



Improved Data Quality Through Distinct/Distinguishable Biologic Nomenclature

- **CLEAR PRODUCT IDENTIFICATION** – Distinguish the biosimilar from its reference/originator product, and from all other approved biosimilars.
- **CLEAR PRESCRIBING & DISPENSING -** Helps prevent accidental or inappropriate substitution.
- **BETTER PHARMACOVIGILANCE** - proper attribution of adverse events to the right product.
- **INCREASED MANUFACTURER ACCOUNTABILITY** -

Broad Support for Distinct Naming Among Physicians

68% *of Canadian physicians support Health Canada issuing distinct names. (2017)*

94% *of Latin American Physicians consider WHO's BQ Proposal to be "useful" in helping patients receive the correct medicine. (2015)*

85% *of US physicians support FDA issuing distinct names. (2019)*

76% *of Australian physicians support TGA issuing distinct names (2016)*

Summary

- As pharmacovigilance strategies shifts to AI and big data, practitioners and patients remain an important source of information about ADEs
- Reporting practices and databases need to be improved to assure confidence in the data that is collected.
- Potential strategies to improve data quality include expanded use of distinct non-proprietary names/identifying suffixes, including international harmonization.
- RWE will complement (if not replace) RCTs because of timeliness and expense.
- Patients and practitioners will and should remain a source of providing this important drug safety information.


SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES
Thank You for Your Attention