

Medical Knowledge Synthesis: A Brief Overview

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Abstract

The value of medical research derives from its ability to impact further research and medical practice. Medical knowledge synthesis, bridging the gap between current research, future research and medical practice, is a rapidly changing industry. The expanding mass of medical information makes knowledge synthesis evermore essential to enable and inform evidence-based decision-making. Systematic reviews (SRs), clinical practice guidelines (CPGs), textbooks and electronic information tools are the dominant modes of medical knowledge synthesis.

Over the last fifty years, the number of systematic reviews and guidelines has increased more rapidly than the publication of new original research. High standards have been developed for SRs and CPGs, but they are not widely adopted. Some medical research questions are over-covered by multiple and sometimes contradictory systematic reviews and guidelines, while others questions are not covered at all by high-quality knowledge synthesis. Until recently, textbooks were, with colleagues, the main source of information for clinicians. They have been supplanted by the Internet and point-of-care resources. The integration of high quality and up-to-date evidence varies across textbooks and electronic information tools.

This white paper summarizes important and practical information on Systematic Reviews (SRs), Clinical Practice Guidelines (CPGs), medical textbooks and point-of-care resources, discusses their interrelationship and evolution, and the evidence on their quality, use and impact on medical practice.

Keywords: Systematic review, Clinical practice guideline, Textbook, Point-of-care resource

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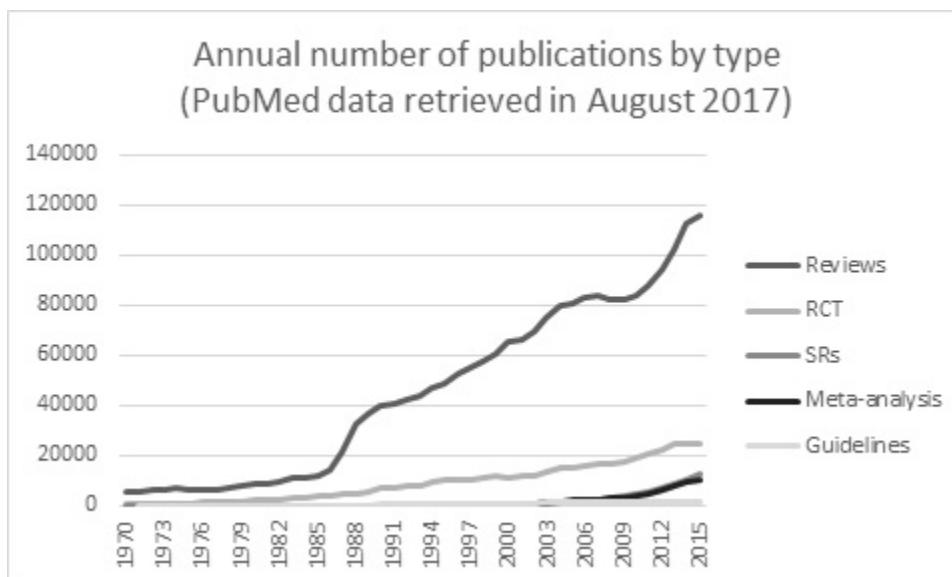
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1 Introduction

IBM Watson's website reports that "only 20 percent of the knowledge physicians use to make diagnosis and treatment decisions today is evidence based (...). The amount of medical information available is doubling every five years and much of this data is unstructured - often in natural language. And physicians simply don't have time to read every journal that can help them keep up to date with the latest advances - eighty one percent report that they spend five hours per month or less reading journals". New technologies based on natural language processing and artificial intelligence aim to help clinicians incorporate medical research, treatment guidelines and patient information into medical decision making. This new frontier of medical knowledge synthesis makes it even more important to understand the strengths and weaknesses of traditional forms of medical knowledge synthesis, to inform the improvement let alone automation of the process.

The value of medical research derives from its ability to impact further research and medical practice. Medical knowledge synthesis, bridging the gap between current research, future research and medical practice, is a rapidly changing industry. The number of systematic reviews and guidelines has increased more rapidly than the publication of new original research. High standards have been developed for SRs and CPGs, but they are not widely adopted. Some medical research questions are over-covered by multiple and sometimes contradictory systematic reviews and guidelines, while others questions are not covered at all by high-quality knowledge synthesis. Until recently, textbooks were, with colleagues, the main source of information for clinicians. They have been supplanted by the Internet and point-of-care resources. The integration of high quality and up-to-date evidence - including systematic reviews and guidelines - varies across textbooks and point-of-care resources.

In August 2017, PubMed included about 27 million citations, 500,000 clinical trials, 2 million reviews, 70,000 systematic reviews and/or meta-analyses, and 20,000 practice guidelines. The rate of information growth is exploding: from 10 new clinical trials per day in 1975, to 55 in 1995, and 95 in 2015.



In response to multiple academic, technological, and regulatory changes, the production of clinical research and knowledge synthesis has changed quantitatively and qualitatively over the last fifty years. Systematic reviews (SRs), clinical practice guidelines (CPGs), textbooks and electronic information tools are the dominant modes of medical knowledge synthesis.

A few definitions are needed to begin. A systematic review (SR) is a scientific investigation that focuses on a specific question and uses explicit, planned, scientific methods to identify, select, assess and summarize the findings of similar but separate studies. It may or may not include a quantitative melding and reanalysis (meta-analysis) of the results from separate studies. A meta-analysis is a systematic review that uses statistical methods to combine quantitatively the results of similar studies in an attempt to find valid new inferences to be derived and existing contradictions to be resolved from the larger combined samples of studies applied to the population of interest (Morton et al., 2011).

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options (Steinberg et al., 2011). Earlier definitions did not require that guidelines be based on systematic reviews.

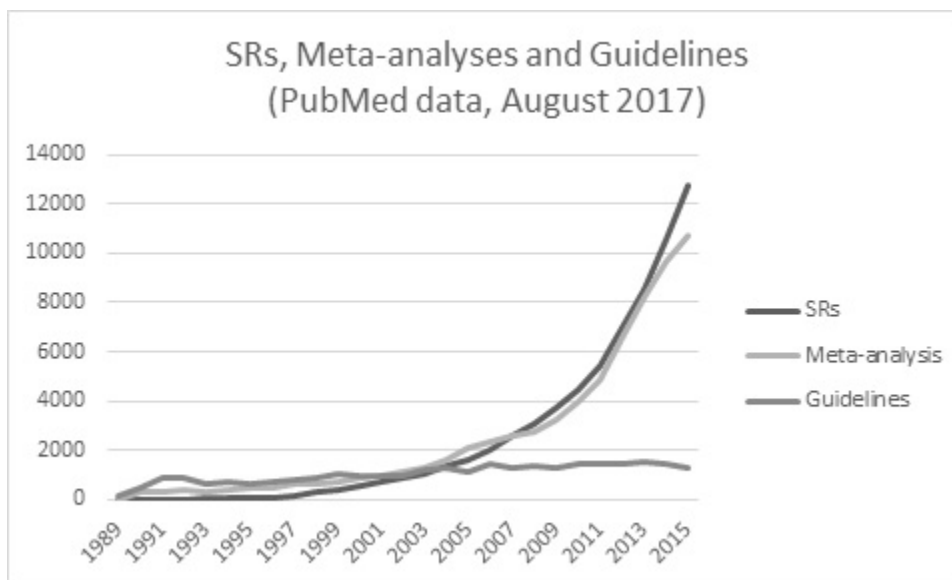
Medical textbooks constitute one of the most common resources used by doctors to an-

swer questions but they constitute a broad, ill-defined and evolving category. As opposed to systematic reviews and clinical practice guidelines, for which stable standards and consensus definitions have evolved, textbooks include a wide variety of products, formats and contents. With the development of electronic resources, the concept of textbooks has expanded from traditional printed textbooks to e-books and electronic information tools that enable practitioners to access information at the point-of-care on their desktop, phone or tablet, or through the electronic health record (EHR) (e.g., UpToDate, DynaMed).

In the history of medical knowledge synthesis, expert-based texts appeared first. The oldest pre-modern texts are Egyptian papyrus (c. 1800-1200 BC), and Greek texts such as the Hippocratic Corpus (c. 400 BC to 200 AD). The most influential texts in the modern era include Osler's Principles and Practice of Medicine, first published in 1892, Cecil's Textbook of Medicine, first published in 1927, in its 25th edition in 2017, and Harrison's Principles in Internal Medicine, first published in 1950, in its 19th edition in 2017. Online textbooks, electronic information resources and point-of-care tools appeared in the Internet era. They developed and spread in the 2000s to become one of the most commonly used information resources by clinicians.

Guidelines have appeared in medical practice since the early 20th century. The Red-book of Infectious Diseases (1938) was one of the first US guidelines. Most early guidelines were developed by experts who had gained authority and influence within specific medical specialties. They were not originally based on a systematic review of the existing evidence. The first guideline indexed in PubMed dates from the late 1960s. The number of guidelines indexed annually increased fast in the late 1980s early 1990s, and plateaued around 1,500 in the 2000s. Guidelines gained influence after descriptions of unexplained variation in practice patterns in the 1970s, and the documentation of high rates of inappropriate care and unnecessary procedures in the 1980s (Wennberg, 1973; Chassin 1987). Guidelines became standardization tools to improve outcomes of care while controlling increasing costs.

Over the past half-century, the number of non-systematic reviews has increased faster



than the number of original research papers. The number of randomized controlled trials indexed annually in PubMed reached 25,000 in 2015. The number of non-systematic reviews published annually was close to 120,000 in 2015. Systematic reviews and meta-analyses of clinical research appeared in the 1970s and 1980s, and became popular in the late 1980s after seminal articles showed nonsystematic synthesis could be misleading (Goldschmidt, 1986; Mulrow, 1987). Regularly updated publications of systematic reviews and meta-analyses of trials started with the Oxford Database of Perinatal Trials in 1988, and extended, in theory, to all clinical research domains with the start of the international Cochrane Collaboration in 1993. Non-systematic reviews are still the dominant source of knowledge synthesis but the number of systematic reviews and meta-analysis is growing exponentially since the 1990s. In 2015, around 10,000 publications tagged systematic reviews and 10,000 publications tagged meta-analysis were indexed in PubMed.

Whether, how and how much medical research impacts medical practice depends on information seeking behavior of doctors and available information tools. Information seeking behavior of doctors has been studied extensively since the 1980s, when Covell found that only 30% of physicians' information needs were met during the patient visit, usually by another physician or health professional (Covell, 1985). In a 2007 review of the literature,

two-thirds of studies ranked traditional textbooks as the first information source used by doctors, humans / colleagues was second and electronic resources ranked third (Davies, 2007). In 2013, Clarke et al. found that colleagues remained a preferred information source among clinicians, but they increasingly relied on the Internet and electronic decision support tools. Promising areas for future research include the relationship between the use of different information tools by clinicians, medical practice and health care outcomes, and the effects of competition in medical information markets.

This white paper summarizes important and practical information on Systematic Reviews (SRs), Clinical Practice Guidelines (CPGs), medical textbooks and electronic information tools, discusses their interrelationship and evolution, and the evidence on their quality, use and impact on medical practice.

2 Systematic Reviews and Meta-analyses

2.1 Definitions

A systematic review (SR) is a scientific investigation that focuses on a specific question and uses explicit, planned, scientific methods to identify, select, assess and summarize the findings of similar but separate studies. It may or may not include a quantitative melding and reanalysis (meta-analysis) of the results from separate studies.

A meta-analysis is a systematic review that uses statistical methods to combine quantitatively the results of similar studies in an attempt to find valid new inferences to be derived and existing contradictions to be resolved from the larger combined samples of studies applied to the population of interest (Morton et al., 2011).

2.2 Process

The objective of an SR is to answer a specific question by using an explicit, pre-planned protocol to identify, select, assess, and summarize the findings of similar but separate studies.

SRs often include, but do not require, a quantitative synthesis (meta-analysis). SRs can be narrow in scope and consist of simple comparisons such as drug X versus drug Y. They can also address broader topics including comparisons of the effectiveness of drugs versus surgery for a condition, or watchful waiting when it is a reasonable clinical strategy.

The SR process has six steps (Morton et al., 2011): 1: Initiate the process, organize the review team, develop a process for gathering user and stakeholder input, formulate the research question, and implement procedures for minimizing the impact of bias and conflict of interest. 2: Develop the review protocol, including the context and rationale for the review and the specific procedures for the search strategy, data collection and extraction, qualitative synthesis and quantitative data synthesis (if a meta-analysis is done), reporting and peer-review. 3: Systematically locate, screen and select the studies for review. 4: Appraise the risk of bias in the individual studies and extract the data for analysis. 5: Synthesize the findings and assess the overall quality of the body of evidence. 6: Prepare a final report and have the report undergo peer review.

2.3 Repositories

PubMed Health provides information for consumers and clinicians on prevention and treatment of diseases and conditions, and specializes in reviews of clinical effectiveness research. PubMed Health includes: Plain language summaries and abstracts of Cochrane reviews; abstracts (short technical summaries) of systematic reviews in DARE, the Database of Abstracts of Reviews of Effects many of them with a critical summary of the review; Full texts of reviews from a growing group of public agencies; information developed by public agencies for consumers and clinicians that is based on systematic reviews; methods resources about the best research and statistical techniques for systematic reviews and clinical effectiveness research. PubMed Health includes systematic reviews on healthcare effects or clinical effectiveness research methods published since 2002. In May 2016, there were over 40,000 systematic reviews at PubMed Health. While Cochrane reviews are added when published,

reviews by public health agencies usually have a processing time lag.

2.4 Key producers

Many public and private organizations produce and/or fund systematic reviews. The three most expert sources for the production of systematic reviews are the Cochrane Database of Systematic Reviews (CDSR, UK), the Center for Reviews and Dissemination (CRD, UK) and the Agency Healthcare Research and Quality (AHRQ) Effective Health Care Program (Morton et al., 2011).

The Cochrane Collaboration (CDSR, UK)

Founded in 1993, the Cochrane Collaboration is an independent nonprofit multinational organization that produces systematic reviews of healthcare interventions. In August 2017, the Cochrane Database of SRs includes 7,384 systematic reviews and 2,927 review protocols. Cochrane systematic researchers work with one of 53 Cochrane Review Groups. Cochrane centers are funded by government agencies and private sources. Its infrastructure is supported by Cochrane Library subscriptions. Commercial funding of review groups is not allowed. Cochrane review abstracts and plain language summaries are free; complete SRs are available via subscription.

The Center for Reviews and Dissemination (CRD, UK)

The CRD is part of the UK National Institute for Health Research (NIHR) and a department of the University of York in the UK. Founded in 1994, CRD produces SRs of health interventions, SR method research, and guidance for conducting SRs. CRD also produced the Database of Abstracts of Reviews Effects (DARE) (which is still accessible, but includes records only through 2015), the National Health Service Evaluation Database and the Health Technology Assessment Database (HTA). The DARE database includes 21,931 CRD assessed reviews (bibliographic record), 13,324 CRD assessed reviews (full abstract), 8,801 Cochrane

reviews, and 1,254 Cochrane related review records (Cochrane reviews published in another source).

The Agency for Healthcare Research and Quality (AHRQ) Effective Health Care Program

AHRQ established Evidence-Based Practice Centers (EPCs) to promote evidence-based practice in everyday care in 1997. In 2017, there are 13 EPCs in university and private settings. In August 2017, there are 267 AHRQ produced systematic reviews. The US Department for Veterans Affairs, the US Preventive Services Task Force and the Center for Medicaid and Medicare Services use EPC reviews.

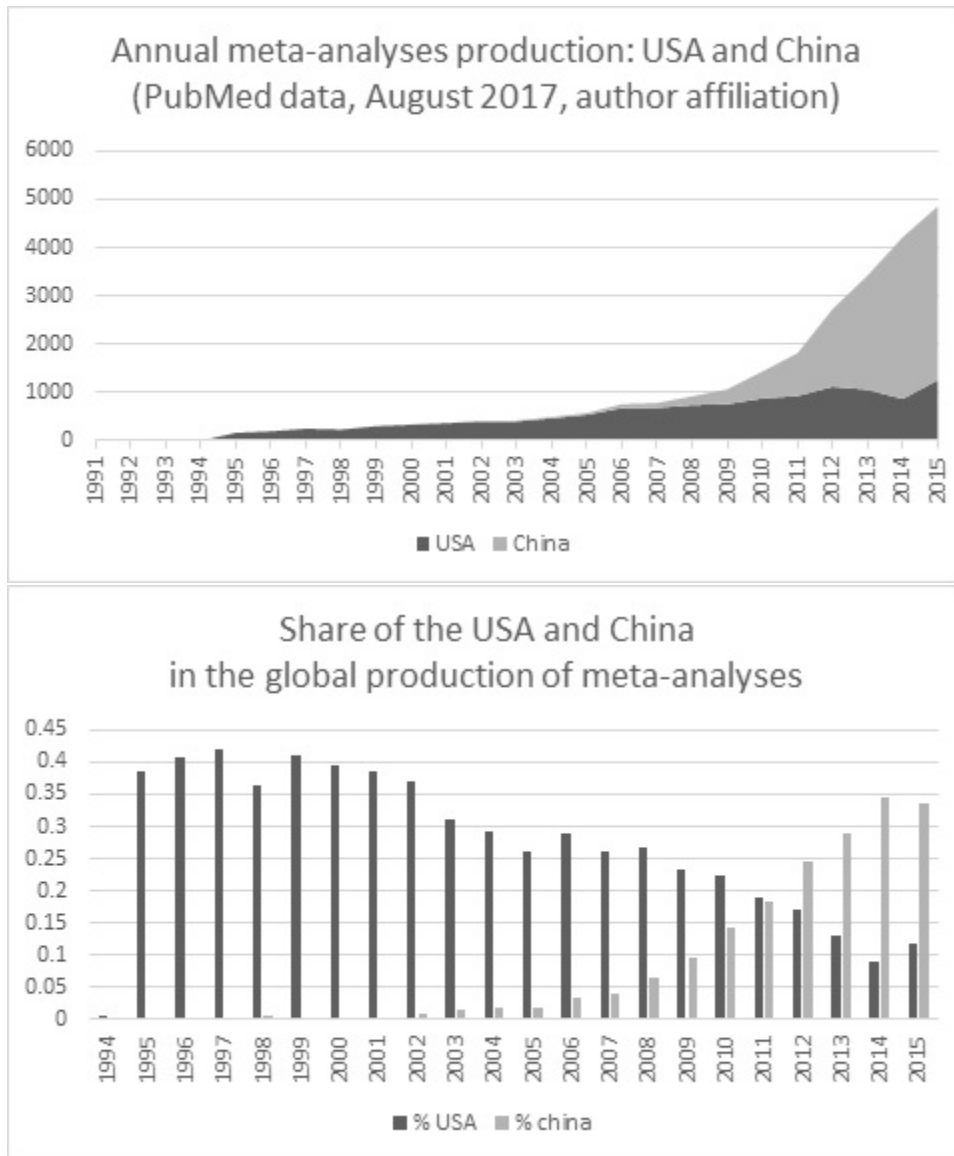
Other organizations

Beyond the three leading experts (AHRQ, the Cochrane Collaboration and CRD), many other organizations play a key role in sponsoring, conducting and disseminating SRs. These include US governmental agencies: such as the Centers for Medicaid and Medicare Coverage Advisory Committee (MEDCAC); the Drug Effectiveness Research Project (DERP); the National Institute of Health (NIH); the Centers for Disease Control and Prevention (CDC); and the U.S. Preventive Services Task Force. They also include US private organizations: such as ECRI Institute (Nonprofit organization, its products and methods are not available to the public.); Hayes, Inc (For-profit organization, collaborating center for the World Health Organization, but its products are generally not available to the public).

2.5 International trends

The recent explosion of systematic reviews and meta-analyses reflects a dramatic change in the geography of knowledge synthesis production.

While the production of meta-analyses in the US has increased slowly but steadily since 1995, China only started to produce meta-analyses in the mid-2000, but quickly became



the worlds largest producer. In 1995, the US represented 38% of the world production of meta-analyses and China represented 0.23%. By 2005, the share of the US decreased to 26% of the world production of meta-analyses, but China still represented only 1.6% of the world production. In 2015, China produces 33.6% of the global production, while the US share is down to 11.75%.

2.6 Quality and Impact

Systematic review quality is essential as reviews are at best useless and at worse misleading if their methods are flawed or their reporting incomplete. Awareness about the importance of high-quality SRs has increased over the past decade.

Important to SR quality is full access to original research studies and results. Progress came from the creation of clinical trial databases and prospective trial registration requirements to access negative trial results, which are seldom published. In the US, the trial registry, ClinicalTrials.gov, was created to register trials conducted under investigational new drug applications and became publicly available in 2000. In 2007, the Congress made detailed prospective trial registration legally mandatory. In 2016, HHS clarified and expanded the registration and results information submission requirements. Registering full protocols and reporting in these registries, together with quality monitoring of the registration process (now variably reliable), are the next frontiers. In 2004, the World Health Organization (WHO) established the International Clinical Trials Registry Platform (ICTRP).

Validity of knowledge synthesis comes from the methods used to develop SRs and meta-analyses. In 1999, to address suboptimal meta-analyses, an international group developed the Quality of Reporting of Meta-analyses (QUOROM Statement), a guide to reporting of meta-analyses of randomized controlled trials. In 2009, this guide was updated to address conceptual and practical scientific advances, and was renamed PRISMA (Preferred Reporting Items of Systematic reviews and Meta-Analyses). PRISMA is an evidence-based minimum set of items for reporting in SRs and meta-analyses. PRISMA focuses on the reporting of SRs evaluating randomized trials, but can also be used as a basis for reporting SRs of other types of research, particularly evaluations of interventions (Liberati et al., 2009).

Following publication of PRISMA, the UK Centre for Reviews and Dissemination (CRD) at the University of York developed an international prospective registry of systematic reviews with health-related outcomes, PROSPERO, to reduce unplanned duplication of reviews and provide transparency in the review process, with the aim of minimizing reporting

bias. PROSPERO is an international database of prospectively registered health-related systematic reviews in health and social care, welfare, public health, education, crime, justice, and international development. Key features from the review protocol are maintained as a permanent record. In August 2017, PROSPERO included 25,898 records.

The exact share of biomedical journal articles with empirical data included in a source of knowledge synthesis is not known. In a random sample of 259 biomedical journal articles with empirical data from PubMed published between 2000 and 2014, only 16 studies (6.1%) had their data included in a subsequent systematic review or meta-analysis (Iqbal et al., 2016). The small proportion of papers included in systematic knowledge synthesis could have several explanations such as preponderance of low impact articles, reviewer narrowness (i.e., within discipline or school of thought only) of outlook, reviewer bias.

A first challenge is to identify the research questions in need of knowledge synthesis, and the corresponding number of systematic reviews needed to cover the literature. In 2003, the Cochrane Collaboration estimated that at least 10,000 separate and up-to-date systematic reviews would be needed to cover most common health care problems (Mallett & Clarke, 2003). This estimate was based on a calculation using the number of randomized controlled trials referenced in the CENTRAL registry at that time (300,000 studies) and the average number of studies included in existing reviews. In August 2017, the CENTRAL registry included 1,077,831 trial reports, and the Cochrane Database of Systematic Reviews included 7,400 reviews. In the last 15 years, the number of trials has increased by 259% and the number of reviews by 362%. The estimation of the number of reviews needed to cover the existing literature remains difficult.

The number of reviews needed to cover the literature depends on whether or not trials cluster around topics. If many papers are one of a kind, studying questions that no other papers examine, then there is less necessity for knowledge synthesis. But many papers are artificially one of a kind: Only a tiny fraction of biomedical articles are truly disruptively innovative. The vast majority of articles are neither innovative nor identical to previous

work they are made deliberately different in one or more aspects (). Investigators generally do not admit that they examine the same questions as previous work, most likely because they do not want to be thought of as producing what is commonly derided as me too articles. The reality is these articles address questions largely previously investigated the masquerade is done so well that a systematic reviewer may be at a loss as to whether these studies can be put together in a systematic review that will not depend on multiple subjective, and thus questionable, selection choices. (Ioannidis, 2016)

While many topics are not yet covered by any systematic review or knowledge synthesis, and many trials are not included in any systematic reviews, some research questions concentrate a large number of similar, (sometimes contradictory) reviews of varied quality. This asymmetric distribution of knowledge synthesis across topics reflects misaligned incentives for the publication of unnecessary reviews: (1) Researchers face pressures to publish (or perish) in order to advance their careers. (2) Journal editors recognize that publishing SRs increase their impact factors since such articles tend to be cited more. (3) Knowledge synthesis sources are increasingly used as marketing tools by industry. (Page & Moher, 2016)

Ioannidis (2016) summarizes the problem of redundancy: Most topics addressed in meta-analyses of randomized trials have overlapping, redundant meta-analyses; same topic meta-analyses may exceed 20... Some fields produce massive numbers of meta-analyses, 185 meta-analyses of antidepressant for depression were published between 2007 and 2014. These meta-analyses are often produced either by industry employees or by authors with industry ties and results are aligned with sponsor interests.

A study investigated the reporting quality of a random sample of systematic reviews published in 2004: 66% reported the year of their search, 69% assessed study risk of bias, 23% formally assessed evidence for publication bias, and 60% reported the funding source of the SR. 20% were Cochrane reviews (Moher, 2007). From a random sample in 2014, 300 reviews, Page et al (2016) found reporting improved compared to 2004 but remained suboptimal. There were large and statistically significant differences in reporting characteristics between

Cochrane and non-Cochrane systematic reviews. Cochrane reviews (which accounted for 20% of the sample in 2004, 15% of the sample in 2014) had more complete reporting than all other types of SRs.

While the importance of systematic reviews is now widely recognized, their impact is difficult to measure. Previous research found that knowledge codification and knowledge synthesis is important for knowledge diffusion and use (Cowan, 2000; Phelps, 2012). Once knowledge is created, cognitive and other resources are needed to transform and translate it to facilitate its transfer, adoption and use in subsequent recombination efforts (Carlile, 2004).

A recent mixed methods study attempted to measure the impact of Cochrane reviews and found that Cochrane Reviews appeared to have led to a number of benefits to the UK health service including safer or more appropriate use of medication or other health technologies or the identification of new effective drugs or treatments. However, whether or not these changes were directly as a result of the Cochrane Review and not the result of subsequent clinical guidance, or commercial promotion, was difficult to judge. Potential benefits of Cochrane Reviews included economic benefits through budget savings or the release of funds, improvements in clinical quality, the reduction in the use of unproven or unnecessary procedures and improvements in patient and care provider experiences (Bunn et al., 2015). A first step in the measurement of the impact of systematic reviews, the authors noted that more work is required to develop suitable methods for defining and quantifying the impact of research.

The impact of Systematic Reviews may increase, as the new definition of CPGs includes a requirement that they should be based on systematic reviews: Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options (Steinberg et al., 2011).

In several countries, like in England, since 2013, the National Institute of Health Research

(NIHR) has required applicants for support of new primary research to reference an existing SR as well as relevant literature published subsequent to that SR or when no such systematic review exists, applicants must review the relevant evidence, which must also include reference to all relevant on-going studies from trial registries (Moher, 2016).

3 Clinical Practice Guidelines (CPGs)

3.1 Definition

Clinical practice guidelines are statements that include recommendations intended to optimize patient care as informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options (Steinberg et al., 2011). Previous definitions did not necessarily express the requirement that guidelines should be based on systematic reviews.

3.2 Process

The idea that clinical practice guidelines should be based on a high-quality systematic review of the evidence has achieved consensus (Steinberg et al., 2011). Early groups applying systematic reviews to CPGs include the US Preventive Services Task Force (USPSTF) (1984) and the American College of Physicians Clinical Efficacy Assessment Project (1980). The involvement of specialty societies in practice guidelines development increased dramatically in the 1980s. By 1989, more than 35 medical societies had developed at least one CPG (Steinberg et al., 2011). The American Medical Association (AMA) and the Council of Medical Specialty Societies became important coordinators and guideline development process "standardizers" (Woolf, 1990, Steinberg et al., 2011).

However, there exist several possible modes of interaction between systematic review and guideline developers. Table 1 describes the benefits and concerns relative to each model.

Table 1: The relationship between guidelines and systematic reviews

	Complete Isolation (synchronous)	Complete Isolation (asynchronous)	Limited Interaction	Complete Interaction
Membership	No overlap in membership between CPG team and SR team	No overlap in membership, but a member of the SR team may later participate in the CPG	Selected members of CPG team interact with SR team to refine the key questions, define review criteria, and interpret evidence; SR methodologists do not make CPG recommendations	The same individuals conduct the SR, grade the evidence and generate the guideline
Theoretical Benefits	Prevents biases in one group from influencing the other group	Efficiency of using pre-synthesized and rated evidence	Ensures that at least the key questions of the CPG team will be addressed by SR	Ensures that all issues known between the CPG and SR groups will be addressed in SR. CPG team will have a better understanding of the evidence. Efficiency of having the same group review evidence and formulate guidelines.
Concerns	CPG team limited to questions formulated by the initial question-setting panel; questions may not be complete or what the CPG team considers important. CPG team does not interact with SR team to appreciate nuances of evidence review. SR team working without input of CPG team that will use the evidence may not optimally structure the synthesis and reporting of evidence.	SR may not fully address all of the CPG panels clinical questions. SR may not include the latest studies. SR team working without input from CPG team that will use the evidence may not optimally structure the synthesis and reporting of evidence	Limited interaction may result in some areas being inadequately addressed in SR. The subgroup of CPG team that interacts with the SR team may be biased or lack expertise in specific topics, or it may not cover all the questions and concerns of the entire CPG group.	May introduce bias into evidence review. Unlikely that the same individuals have the time or skills to conduct both SRs and CPGs.

Source: Lau 2010, adapted from Steinberg et al., 2011, p.94-95.

3.3 Repositories

The National Guideline Clearinghouse

The National Guideline Clearinghouse (NGC) is a US publicly available database of evidence-based clinical practice guidelines and related documents. It included 1,782 guidelines in August 2017. AHRQ updates the NGC weekly, in partnership with the American Medical Association (AMA) and the American Association of Health Plans (AAHP) Foundation.

The NGC also includes guideline syntheses, important given frequent disagreements or contradictions between CPGs produced by different organizations. Syntheses are systematic comparisons of selected guidelines that address similar topic areas. Key elements of each synthesis include a discussion of areas of agreement and difference, the major recommendations, the corresponding strength of evidence and recommendation rating schemes, and a comparison of guideline methodologies. Also included are the benefits/harms of implementing the guideline recommendations and any associated contraindications.

The Guideline International Network Database

In August 2017, the Guidelines International Network (G-I-N) Database, founded in 2002, included 6,413 guidelines, produced by 96 organizations in 84 countries. The network includes 103 organizations and 156 individual members representing 47 countries from all continents. The G-I-N mission is to lead, strengthen and support collaboration and work within the guideline development, adaptation and implementation community.

PubMed and PubMed Health

PubMed and PubMed Health can be searched using Guidelines and Practice Guidelines in Publication Type. PubMed includes 29,667 guidelines (among which 23,137 practice guidelines). PubMed Health includes 8,836 guidelines (545 practice guidelines).

3.4 Key producers

Expert guideline developers include government agencies, academic institutions, clinical specialty societies, disease or population specific organizations, other private organizations and international organizations, and commercial corporations.

The Agency for Healthcare Research and Quality (AHRQ)

In the 1980s, CPGs they started to be perceived as a possible solution to control healthcare spending. In 1989, the US Congress increased funding for effectiveness research and created a federal agency, The Agency for Health Care Policy and Research (AHCPR), to develop and disseminate CPGs. Over the next years, AHCPR developed about 20 guidelines across several clinical areas. However, in 1995, back surgeons disagreed with the agency's guidelines for the treatment of lower back pain (which questioned the value of back surgery), and called for its elimination (Field & Lo, 2009). Following congressional threats to withdraw its funding, the agency, renamed the Agency for Healthcare Research and Quality (AHRQ) limited its responsibilities to financial support of Evidence-Based Practice Centers (EPCs) production of SRs (Steinberg et al., 2011). AHRQ remains involved in guideline dissemination via the National Guideline Clearinghouse, a web-based collection of CPGs.

The US Preventive Services Task Force (USPSTF)

The USPSTF is an independent panel of experts in primary care and prevention who systematically review the evidence of effectiveness and develop recommendations for clinical preventive services. The USPSTF uses transparent standards, relies on systematic reviews, includes multidisciplinary experts in the development process and updates its guidelines every 5 years or as needed. The USPSTF focuses on screening, counseling, immunizations, and preventive medications and services. In August 2017, it includes 129 recommendations.

The Center for Disease Control (CDC)

The CDC Infection Control Guideline Library includes guidelines on basic infection prevention and control, antibiotic resistance, device associated, procedure associated, disease / organism specific, healthcare worker guidelines and setting specific guidelines. There are 26 current infection guidelines.

The Morbidity and Mortality Weekly Report (MMWR) is the CDC's primary vehicle for scientific publication of timely, reliable, authoritative, accurate, objective, and useful public health information and recommendations. MMWR readership predominantly consists of physicians, nurses, public health practitioners, epidemiologists and other scientists, researchers, educators, and laboratorians. The Morbidity and Mortality Weekly Reports (MMWR) Recommendations and Reports contain in-depth articles that relay policy statements for prevention and treatment on all areas in CDC's scope of responsibility (e.g., recommendations from the Advisory Committee on Immunization Practices).

The CDC Prevention Guideline Database (up to 1998): the Prevention Guidelines Database, a comprehensive compendium of CDC guidelines and recommendations for the prevention of diseases, injuries, and disabilities was developed to give public health practitioners and others quick access to the full set of CDC's guidelines. Now it is maintained only for historical purposes, with no entries since October 1998.

The Veterans Health Administration, Department of Defense Guidelines

The Veterans Health Administration (VA), in collaboration with the Department of Defense (DoD) has been developing CPGs since the early 1990s and has been identified as a leader in CPG development by the Institute of Medicine in 2010. The VA uses guidelines to improve quality of care and reduce inappropriate variation in practice across geographic areas. Several guidelines are embedded in the VA's electronic health record, and used to develop performance measures. The guidelines cover the following topics: chronic disease in primary care, mental health, military related issues, pain, rehabilitation and women's health.

The Community Preventive Task Force (CPSTF)

CPSTF is an independent, nonfederal panel of public health and prevention experts providing evidence-based findings and recommendations about community preventive services, programs, and interventions aimed at improving population health. Its members represent research, practice, and policy expertise in community preventive services, public health, health promotion, and disease prevention. The 225 Task force findings cover topics such as: adolescent health, asthma, birth defects, cancer, cardiovascular disease, diabetes, emergency preparedness, alcohol excess, health communication, health equity, hiv/aids, pregnancy, mental health, motor vehicle injury, nutrition, obesity, oral health, physical activity, tobacco, vaccination, violence, and worksite health. The Task Force findings are sorted into three categories: insufficient evidence, recommended and recommended against.

The National Institute of Health Consensus Development Program

In 2013, the Office of Disease Prevention (ODP) formally retired the Consensus Development Program. The CDP served a role now served by other organizations. Formed in 1977, the CDP produced unbiased, evidence-based assessments of controversial medical issues important to researchers, healthcare providers, policymakers, patients, and the general public. The consensus statements were used by numerous professional organizations to develop guidelines for clinical practice; the over 160 CDP statements (not updated) can be found in the online archive.

Clinical Specialty Societies

Many medical societies and organizations produce guidelines. Some such as the American College of Physicians (ACP), the American College of Cardiology (ACC), the American Thoracic Society (ATS) devote significant resources to guideline development, seek high quality based on comprehensive SRs and use clear conflict of interest policies for panel members.

ACP's Guidelines: ACP develops several different types of clinical recommendations: Clinical Practice Guidelines, Clinical Guidance Statements, Best Practice Advice, and High Value Care Advice. ACP's Guidelines meet the standards for development as set by the National Academies of Medicine and the Guidelines International Network. ACP voluntarily completes standards reporting forms to increase the transparency and trustworthiness of its guidelines. Guidelines focus on screening, prevention and management (e.g., appropriate antibiotic use, cardiac screening, diabetes).

ACC's guidelines: The American College of Cardiology Foundation provides a framework of evidence-based clinical statements and guidelines developed by leaders in the field of cardiovascular medicine. Methodologies for the development of clinical statements and guidelines are available on the ACC website. In September 2017, the ACC website includes 205 guidelines.

ATS's guidelines: ATSS guidelines make recommendations for patient care. The recommendations are based upon a systematic review or pragmatic evidence synthesis, and then formulated and graded using the GRADE approach. Topics re classified in 16 categories, including, for instance, allergy and asthma, COPD, and critical care.

Other societies devote less resources to guidelines development and do not necessarily comply with the highest standards. Most societies work independently on guidelines although they may address the same conditions and develop related CPGs. Guidelines from different specialty societies may be redundant and/or even contradictory, often between evidence based societies and procedurally oriented ones.

Several tools help guideline users with disagreements and/or contradictions between guidelines. The National Guideline Clearinghouse (NGC) guidelines syntheses summarizes areas of agreement and difference between guidelines. Recent advances in Natural Language Processing (NLP) aim to automate the identification of disagreements and contradictions in medical guidelines (Zadrozny, 2017).

Disease or population specific organizations

37 disease specific societies have guidelines included in the National Guideline Clearinghouse. These disease specific societies include organizations such as the Alzheimers Association, the American Epilepsy Society, the Brain Trauma Foundation and the Cystic Fibrosis Foundation. These societies mostly produced one or two guidelines. Only 17 (46%) of these guidelines meet the 2013 NGC inclusion criteria.

Private organizations and commercial guidelines

Several private organizations, such as large healthcare organizations, for instance Kaiser Permanente, academic medical centers, quality improvement organizations and commercial companies also develop CPGs.

Kaiser Permanente's Clinical Guidelines To develop the guidelines, teams of Kaiser Permanente doctors, other health care providers, and scientists review the best published medical and scientific research on a clinical topic. They use that information to develop recommendations for screening, prevention, and treatment.

The Institute for Clinical Systems Improvement (ICSI) ICSI was established in 1993 to improve patient care in Minnesota through innovations and partnerships in evidence-based medicine with founders HealthPartners, Mayo Clinic and Park Nicollet Health Services. ICSI guidelines are free to ICSI members and sponsors and health care organizations in Minnesota but all others need to purchase them. The collaborative brings medical organizations, non-profit health plans, consumers and business representatives into the decision-making process. ICSI has a rigorous process for developing and maintaining evidence-based guidelines and protocols. ICSI utilizes the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system as a method of assessing the quality of evidence and writing recommendations for guidelines. ICSI requires the disclosure of all conflicts of interest. The ICSI website currently includes 26 guidelines on topics such as diagnosis and management of asthma, diagnosis of breast disease, and diagnosis and management of chronic obstructive

pulmonary disease (COPD).

Some guidelines are also produced commercially. Commercial guidelines producers include, for instance McKesson/Change Healthcare and MCG. These proprietary guideline reportedly concentrate on quality of care, efficient resource expenditure and reduction in inappropriate practice variation. What distinguishes these guidelines from most publicly available CPGs is their technological integration with electronic health records (EHR) and healthcare organizations data systems. Even federal agencies (including CMS) use these commercially produced guidelines to help support quality oversight, utilization review, and appeals decisions.

McKesson/Change Healthcare produces clinical practice guidelines used by over 4,600 hospitals and facilities, but also by the Centers for Medicare & Medicaid Services (CMS). Eight of the ten largest U.S. health plans and more than 1,600 hospitals use MCGs evidence-based guidelines and software, covering over 208 million people.

3.5 International trends

Foreign organizations have contributed 610 of the 1791 guidelines included in the National Guideline Clearinghouse (34%) in August 2017. Such guidelines may be developed by foreign medical societies, disease organizations or government entities. Important foreign guidelines developers include, for instance, the National Institute for Health and Clinical Excellence (NICE, UK), or the World Health Organization (WHO).

3.6 Quality and Impact

CPGs aim to reduce inappropriate practice variation, enhance translation of research into practice and improve healthcare quality and safety. Guideline derived measures have been used to measure physician and hospital performance or quality and to design economic incentives to improve the quality of care. However, there has been considerable concern about the quality of the processes supporting development of CPGs and the resulting questionable

validity of many CPGs and CPG-based clinical performance measure. Concerns included limitations in the scientific evidence base on which CPGs rely, a lack of transparency of development groups methodologies, conflict of interest among guideline development group members and funders, and regarding how to reconcile conflicting guidelines (Steinberg et al., 2011).

The 2011 IOM committee found that there was a pressing need for standards regarding many dimensions of guideline development, including: potential for conflict of interest; transparency of the guideline development process; appropriate type and level of patient and public input into the CPG development process; reasoning supporting each CPG recommendation; approaches used to rate the quality of evidence underlying and strength of each recommendation; need to ensure that CPGs take account of patients with coexisting conditions; relationship between individuals who develop a guideline and those who perform SRs on topics relevant to the CPG (Steinberg et al., 2011).

In 2012, 2 articles investigated policies in force around the time of the 2011 IOM report. In a study of 37 organizations that frequently issued guidelines, the authors found only 17 had a COI policy for practice guidelines. Of the 17 with a policy, 9 did not meet any of the 7 IOM conflict standards (Norris et al., 2012a).

Public disclosure is another problem. A study found that 86% (N=217) of a random sample of 250 guidelines were developed by sponsors that had a guideline specific COI policy. However, only 35% (N=87) of the 250 guidelines provided publicly accessible conflict disclosure statements for all authors (Norris et al., 2012b).

4 Textbooks and Point-Of-Care Resources

4.1 Definitions

As opposed to SRs and CPGs, there is no consensus definition of a medical textbook. The best resource to define the universe of medical textbooks comes from Doodys Review Services

Database, an exhaustive data source designed for large medical textbook consumers like medical and hospital libraries, which includes expert reviews of medical textbooks. Resources labelled Medical textbooks can also be identified from sellers (e.g., Amazon, Google Books...). These sellers include some information about users ratings and best-selling books. To my knowledge, there is no repository for point-of-care resources.

Point-of-care tools are those research and reference resources that a clinician can utilize immediately at the point-of-care with a patient. They are meant to be easy to use and contain filtered information. Most of the evidence-based point-of-care tools include levels of evidence, rating scales or grade recommendations as well as citations back to the original research studies, systematic reviews, or guidelines. An extensive but non exhaustive list for these resources is provided below.

4.2 Repositories

Textbooks: Doodys Review Service

When Doody's Book Review Service started in 1993, the Medical Library Association endorsed it as a "valuable collection development, cataloging and reference tool." The information needs of health sciences libraries are the primary focus of Doody Enterprises. The Doodys Review Service database, includes bibliographic information about more than 140,000 entries of books, eBooks, and software in health sciences including clinical medicine and other health related disciplines. It is accessible via subscription and links to over 20 eBook aggregators for digital versions of titles and apps.

The Doodys Review Service database includes 32,000 expert reviews and a star rating based on a score calculated from the following: (1) Are the product's objectives met?, (2) Does the website help achieve the purpose?(3) Rate the worthiness of those objectives. (4) Is this directed to an appropriate level? (5) Is there significant duplication? (1=significant, 5=insignificant), (6) Are there significant omissions? (1=significant, 5=insignificant), (7) Rate the authority of the authors, (8) Are there sufficient illustrations? (9) Rate the peda-

gogic value of the illustrations. (10) Are there sufficient references? (11) Rate the currency of the references. (12) Rate the helpfulness of the index. (13) Rate the added value from the online version. (14) Is the online version easy to access? (15) Rate the ease of navigation/search. (16) Rate the pedagogic quality of images on the online version. (17) Rate the value of added audiovisual features online. (18) Is there sufficient use of hypertext links? (19) Are there hyperlinks from references to journal articles? (20) Is there appropriate use of features like bookmarking, printing/exporting? (21) Is this a worthwhile contribution to the field? (22) If this is a 2nd or later edition, is this new edition needed? The Doody's Review Service also includes a list of core titles, described in the next section.

Textbooks: Amazon

In September 2017, Amazon included more than 200,000 medical textbooks in medicine, classified in seven categories: general, clinical medicine, medical education and training, basic sciences, special topics, medical diagnostics and labs, and biotechnology.

Textbooks: Google Books

In September 2017, Google Books retrieved more than 420,000 results for Medical textbook.

Point-of-care resources (POC): an extensive list

Products such as UpToDate and DynaMedPlus provide predigested syntheses of medical research intended to be used when the patient and physician interact, and are increasingly integrated into hospitals and practices electronic health records (EHR). They provide summary information on presentation, differential, diagnosis, treatment, prevention, and prognosis for a wide variety of clinical conditions. An extensive but non-exhaustive list of common point-of-care resources is provided below.

5 Minute Consult includes USPSTF guidelines, diagnostic and treatment algorithms, procedure skills videos, laboratory test information, medical calculators. Price: \$99/year.

AHRQ Electronic Preventive Services Selector (ePSS) Decision support regarding U.S. Preventive Services Task Force (USPSTF) guidelines. Free.

American College of Physician (ACP) Smart Medicine (Previously PIER, now included in Dynamed) Electronic, evidence-based, decision-support tool designed for point-of-care use by internists and other physicians, developed and supported by the American College of Physicians. The Physicians' Information and Education Resource (PIER) was launched in 2002. It was replaced with ACP Smart Medicine in 2013. In August 2015 the American College of Physicians in partnership with EBSCO Health incorporated ACP Smart Medicine's content into EBSCO Health's DynaMed Plus evidence-based clinical decision support tool.

BestBets BETs (Best Evidence Topics) were developed in the Emergency Department of Manchester Royal Infirmary, UK, to provide rapid evidence-based answers to real-life clinical questions, using a systematic approach to reviewing the literature. BETs take into account the shortcomings of much current evidence, allowing physicians to make the best of what there is. Although BETs initially had an emergency medicine focus, there are a significant number of BETs covering cardiothoracics, nursing, primary care and pediatrics. Free.

BMJ Best Practice **BMJ** Point of care tool from BMJ Evidence Centre designed to support clinicians in their decision making from diagnosis to treatment. Research evidence, guidelines and expert opinion presented in a step-by-step approach and covering prevention, diagnosis, treatment and prognosis. Price: 192 euros/year.

Clinical Access (McGraw-Hill) Decision support tool based on answers to over 120,000 questions, based on experience and actual approaches to the patient, using established texts to assist with decision-making throughout diagnosis and treatment. Price: \$995/year.

ClinicalKey Elsevier Information portal to medical books, journals and guidelines published by Elsevier, graphics, pictures, procedure videos, patient education. Price: \$449-\$1248/year depending on package.

Cochrane Clinical Answers Cochrane Clinical Answers (CCAs) provide a readable, digestible, clinically focused entry point to rigorous research from Cochrane systematic reviews. They are designed to be actionable and to inform decision making at the point of care. Each Cochrane Clinical Answer contains a clinical question, a short answer, and an opportunity to drill down to the evidence from relevant Cochrane reviews. The evidence is displayed in a user friendly format, mixing narrative, numbers and graphics. Price: \$327/year.

Decision Support in Medicine Decision Support in Medicine includes texts in multiple specialties, written by key leaders in their field. Every disease-specific text includes step-by-step sections providing concise direction on screening, diagnosis and treatments, supported by evidence-based data. Chapters vary in length and complexity depending on the condition and may include signs and symptoms; the imaging or testing needed and when; how and what to communicate to patients and their families; or pathophysiology. Price: Available after registration.

DynaMed /DynamedPlus (EBSCO) Targeted concise overviews and recommendations, graphics, pictures, charts, drug contents partnered with Micromedex. Price: \$200/year, student: \$100/year.

EBM guidelines (Wiley) Easy-to-use collection of clinical guidelines for primary and ambulatory care linked to evidence and continuously updated. Designed for use at the point of care, the guidelines are delivered in a format that makes it easy for a clinician to make a decision regarding treatment. Price: depends on institution.

Epocrates Essentials Targeted concise summaries of practice guidelines, ICD and CPT

codes, diseases, drug content and pill ID, alternative medications, drug interaction checks, drug cost information / formulary, diagnostic/lab tests. Price: \$175/year.

EssentialEvidenceTopics / EssentialEvidencePlus (Wiley) Targeted concise summary of practice guidelines, Cochrane Systematic Reviews, graphics, pictures, diagnostic/lab tests, medical calculators, ICD and CPT codes. Price: \$85/year

eTG Complete (Therapeutic Guidelines) Explicit instructions for therapy, and drug information on more than 2,500 guideline topics. The website of Therapeutic Guidelines mentions that: Independence is an essential feature of this organization it is completely self-supporting financially through revenue from sales. No grants. No advertising. No shareholders. No sponsors. To protect and maintain this independence a strict policy on conflict of interest is in place. Price:\$356/year

GP Notebook GPnotebook is an online encyclopaedia of medicine that provides immediate reference resource for clinicians in the UK and internationally. Updated continually, the database includes over 26,000 pages of information. Price: from 30 pounds/year.

LabGear (App Store) Medical Laboratory tests with peer reviewed content. Price: \$2.99.

Lexicomp Concise, point-of-care drug information, including dosing, administration, warnings and precautions, and clinical content, such as clinical practice guidelines, IV compatibility from Trissel's 2 Clinical Pharmaceutics Database, and other tools. Linked with UpToDate. Price: \$175-798/year depending on package.

Map of Medicine (UK) Locally customized pathways, centrally controlled referral forms and clinical information during a consultation. In the UK, access for local health-care organizations is typically arranged and funded through the local NHS Clinical Commissioning Group, Trust or Health Board. The company also provides access to MedicareLocals in Australia, and District Health Boards in New Zealand. Price: Not publicly available - Institutional funding (UK).

Micromedex (Truven IBM Watson) Evidence-based resources at the point of care for medication management, toxicology, and disease and condition management. Price: \$2.99/year.

NICE Pathways Everything NICE says on a topic in an interactive flowchart. This tool helps you find our guidance and advice for health and social care quickly and easily. Free.

Nursing Reference Center / Plus (EBSCO) Evidence-based information for point of care, continuing education, nursing research and more. Quick lessons that provide disease and condition overviews that map to the nursing workflow, evidence-based care sheets that provide summaries of what is known about a disease or condition and the best treatment options, nursing cultural competencies that provide information on how to treat patients from diverse cultures, patient education handouts, point-of-care drug information. Nursing Reference Center can be integrated into a hospital's EMR system or intranet to streamline workflow. Price: Available on request.

PEMSOft EBSCO unclear whether it will be maintained as a standalone product or integrated into another EBSCO product. EBSCO acquired PEMSOfT, premiere pediatric point-of-care clinical information resource, in 2013. PEMSOfT is a medical reference system, online clinical library and multimedia decision support system addressing acute and chronic illness and injury conditions in children from newborn to young adult. Content is designed for rapid clinical decision-making at the point of care. PEMSOfT includes more than 900 topics, 2,750 proprietary high-quality medical images and more than 120 short videos. Price: Free trial, price available after registration.

PEPID Primary Care Plus Ambulatory Care Specialized Clinical Content, ICD-10 Lookup, Pill Identification Tool, Differential Diagnosis Generator, Drug Interactions Checker, Drug-Allergy Checker, IV Compatibility, Laboratory Manual, Illustrations, Dosing Calculators, Medical Calculators, Evidence-based Medicine. Price: \$299.95/year.

Pocket Lab Values (App Store) Lab tests with differential diagnosis. Price: \$2.99.

Prodigy Originally developed by Newcastle University and supported by the UK Department of Health, discontinued and relaunched as part of a private company, Clarity Informatics, in 2017. PRODIGY is a guideline-based decision support system used by GPs in the UK. PRODIGY models guidelines for the management of chronic diseases, such as asthma, hypertension and angina, in primary care. Guidelines are organized as a network of patient scenarios, management decisions and action step which produce further scenarios. Scenarios are patient states defined by the patient's condition and current treatment. Price: from 100 pounds/year.

QxMD Calculate Point-of-care tools in the areas of cardiology, internal medicine, nephrology, general practice, hematology, gastroenterology, emergency medicine, oncology, orthopedics, respiratory, neurology, neurosurgery, general surgery and obstetrics. Risk calculator decision support, detailed references with PubMed integration. Free.

Rehabilitation Reference Center (EBSCO) Evidence-based, point-of-care resource is for physical therapists, occupational therapists, speech therapists and rehabilitation professionals.

Stanford Guide to Antimicrobial Therapy Exclusively Infectious disease related information, dosing calculators and algorithms, separate versions for HIV/AIDS and hepatitis. Price: \$30/year.

UpToDate (Wolters Kluwer) Targeted concise overviews and recommendations, patient education, medical calculators, drug contents partnered with Lexicomp, links to full-text articles, graphics, pictures and charts. Price: \$495/year, students: \$199/year.

Visual DX Diagnostic clinical decision support system, software guides to differential diagnosis (machine learning based tools), extensive database of images, therapeutic guidelines, ICD and CPT codes. Price: \$399.99/year.

4.3 Key products

For a very short list in medicine, the four textbooks included in the Access Medicine package (which claims to deliver the complete spectrum of medical knowledge for learning and practice) are: Harrison's Internal Medicine, Tintinallis Emergency Medicine, Current Medical Diagnosis and Treatment and Goodman & Gilman's The Pharmacological Basis of Therapeutics.

But since the 1940s, there have been three main generations of selected lists of core/essential medical textbooks: (1) the lists of the American Medical Association (1940-1959), (2) the Brandon/Hill Selected Lists (1965-2003) and (3) the Doodys Core Titles in the Health Sciences (2004-now).

Textbooks: current list of core titles

Since 2004, Doody Enterprises produces Doody's Core Titles in the Health Sciences. Access to DCT is limited to customers who have paid for the current edition. Customers can choose between DCT Basics (\$52.50 in 2017) and DCT Premium (\$157.50 in 2017). DCT Basic presents comprehensive bibliographic information on the full title list, with individual title scores and Essential Purchase recommendations in 121 specialties. DCT Premium includes all of the DCT Basic features plus the full reviews and star ratings of any titles reviewed in Doody's Book Review Service more than 32,000 reviews.

The selection process uses online publication systems, the collective judgment of approximately 200 content specialists and librarians to form a comprehensive list covering 121 specialties. Titles are selected by the content specialists and librarians. The librarians then score each title and make Essential Purchase recommendations.

Textbooks: previous lists of core titles

Between 1940 and 1959, the American Medical Association sporadically published a list of Recent books and periodicals selected for the small medical library (AMA, 1959). In 1959,

the AMA announced that this publication would no longer be revised. By the mid-1960s, the list was out-of-date.

In 1965, the first "Brandon-Hill Selected List of Books and Journals for the Small Medical Library" was published (based on an update of the AMA 1959 list) and it was updated biennially until 2003. Since 2003, the Brandon/Hill Selected Lists have not been updated. This list supported the concept of a core collection of essential medical texts. Its original purpose was to assist hospital librarians with acquiring quality medical literature. The list quickly became a standard collection development tool for medical libraries. It was used by librarians, health care practitioners and publishers. The selection process resulted from the subjective work of two experienced, respected collection development medical librarians. Books and journals are categorized by subject; the book list is followed by an author/editor index, and the subject list of journals by an alphabetical title listing.

The most recent Brandon-Hill selected list (2003) included 672 books and 141 journals. Due to requests from librarians, a minimal core list consisting of 104 titles was pulled out. In 2003, to purchase the entire collection of 672 books and to pay for 141 print journal subscriptions required \$144,486. The minimal core list book collection cost approximately \$18,236.

Leading point-of-care tools

From several medical library websites, UpToDate and DynaMedPlus appear to be the two leaders in the market of point-of-care tools. BestPractice, ClinicalEvidence, EBMGuidelines and ClinicalKey are often compared with UpToDate and DynaMed / DynaMedPlus in the literature on point-of-care tools evaluation (see next section), thus suggesting that they offer comparable products.

4.4 Quality and impact

There is little literature evaluating and comparing printed textbooks. However, since the 2000s, a literature on online textbooks and electronic information tools has developed. A stream of research identifies and evaluates point-of-care summaries for currency, type of evidence and references, breadth of disease coverage, evidence-based methodology, editorial quality/transparency, and ease of use.

Jeffery et al. determined the frequency with which topics in leading online evidence-based textbooks report treatment recommendations consistent with recently published research evidence, finding the proportion of topics with potentially outdated treatment recommendations varies substantially across textbooks (2012). Four online textbooks were included: UpToDate, Physicians Information Education Resource (PIER), DynaMed and BestPractice. The study compared treatment recommendations in 200 clinical topics with articles identified in an evidence rating service (McMaster Premium Literature Service PLUS) and calculated the proportion of topics which potentially required updating in each textbook. The proportion of topics for which up-to-date evidence-based treatment recommendations differed was 23% for DynaMed, 52% for UpToDate, 55% for PIER and 60% for BestPractice. The time since the last update for each textbook averaged from 170 days for DynaMed to 488 days for PIER (PIER was integrated into DynaMedPlus in 2017).

Banzi et al. (2011) used a prospective cohort study bibliometric analysis to evaluate the ability of five point-of-care information summaries ClinicalEvidence, EBMGuidelines, eMedicine, Dynamed and UpToDate to update evidence relevant to medical practice. As samples, they chose high-quality systematic reviews (such as Cochrane Reviews) and assessed every month for a year whether each sampled review was cited in at least one chapter of five point of care summaries. At nine months, DynaMed had cited 87% of the sampled reviews, while the other summaries had cited less than 50%. As pointed out by the authors, POC information summaries include evidence at different speed and a further analysis of updating mechanisms is needed to determine whether greater speed is associated with appropriate

incorporation of new information.

A study comparing the type of evidence behind five POC information products found surprisingly, that the rate of citation overlap was less than 1% for each topic across all five products (McKibbon et al., 2011). This study included ACP PIER, ClinicalEvidence, DynaMed, FirstCONSULT (which was integrated into ClinicalKey in 2017) and UpToDate. The number and types of references cited for each topic varied between products. DynaMed had the largest total number of references and the largest proportion of current references. FirstCONSULT had the greatest proportion of references with higher levels of evidence (systematic reviews, RCTs) although it contained the lowest number of total references.

In 2008, Goodyear-Smith et al., evaluated the acceptability and utilization of three electronic textbooks (DynaMed, MDConsult (now ClinicalKey) and UpToDate) in 122 general practitioners and found no significant difference in preference for or usage level of the three (2008). In 2011, another study compared four evidence-based textbooks by comparing efficacy of their use by clinical residents (Ahmadi et al., 2011). The rate of answer retrieval was 86% in UpToDate, 69% in FirstConsult, 49% in ACP PIER and 45% in ClinicalEvidence. UpToDate was also faster than the other evidence-based textbooks. However, user satisfaction was higher in ACP PIER and FirstConsult.

A 2016 study systematically identified and evaluated point-of-care information tools. It included 23 products, most of which were developed by major publishers in the US of the UK (Kwag et al., 2016). Two reviewers evaluated the products for breadth of disease coverage, editorial quality and evidence-based methodology. A third author was consulted for any unresolved discordances. Best practice, Dynamed and UpToDate scored the highest across all dimensions. In another study published in the same year, two reviewers independently evaluated six leading point-of-care tools (DynaMed, DynaMedPlus, Epocrates, EssentialEvidencePlus, Medscape and UpToDate) for breadth of coverage, ease of use and quality (Johnson et al., 2016). They found similar breadth of coverage among Medscape, UpToDate, DynaMedPlus and EvidencePlus, with Dynamed and Epocrates scoring signifi-

cantly lower. Ease of use DynaMedPlus highest and EvidencePlus lowest. All tools got the same quality score, except for Medscape, which was rated lower.

There is wide variation in currency, type of evidence and references, breadth of coverage, ease of use, evidence-based methodology and other quality criteria across point-of-care resources. A small number of products, including DynaMedPlus and UpToDate, rank higher on most dimensions studied and appear as leaders in the market of point-of-care tools.

5 Conclusion

The value of medical research derives from its ability to impact further research and medical practice. Medical knowledge synthesis, bridging the gap between current research, future research and medical practice, is a rapidly changing industry. The number of systematic reviews and guidelines has increased more rapidly than the publication of new original research. High standards have been developed for SRs and CPGs, but they are not widely adopted. Some medical research questions are over-covered by multiple and sometimes contradictory systematic reviews and guidelines, while others questions are not covered at all by high-quality knowledge synthesis. Until recently, textbooks were, with colleagues, the main source of information for clinicians. They have been supplanted by the Internet and point-of-care resources. The integration of high quality and up-to-date evidence including systematic reviews and guidelines varies across textbooks and point-of-care resources. Promising areas for future research include the relationship between the use of different information tools by clinicians, medical practice and health care outcomes, and the effects of competition in medical information markets.

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