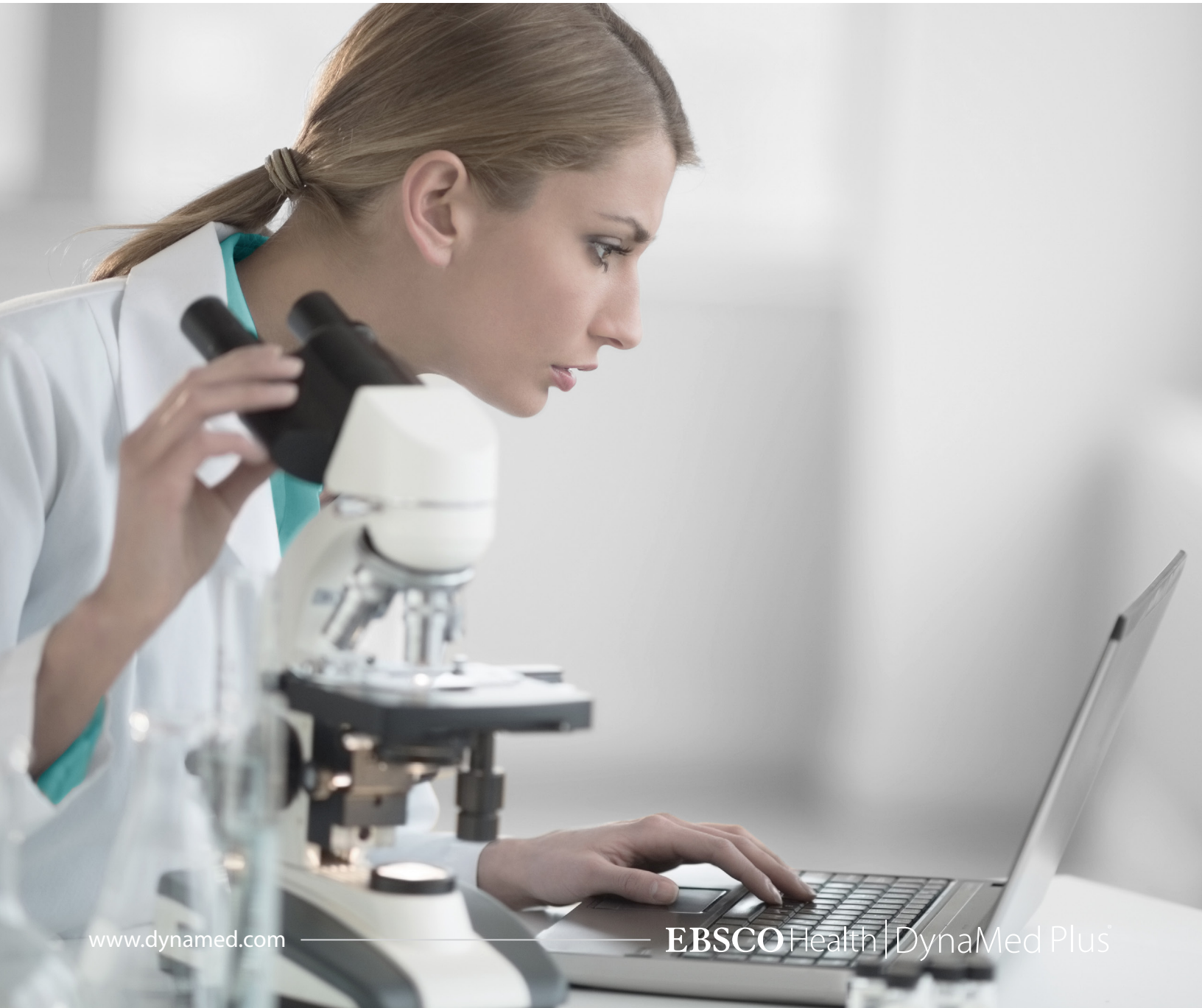
BRIDGING THE GAP

Accelerating Adoption of Clinical Research into Practice



RAPID PACE OF MEDICAL ADVANCEMENTS

Advancements in science and medicine have led to better understanding of the mechanism of diseases resulting in development of novel diagnostic tests and better targeted therapies. The unprecedented pace of emerging scientific discoveries and its transformative nature makes it imperative that these new advancements are quickly adapted into patient care. However, a significant delay exists in the translation of research evidence into clinical practice. A recent study on Zika virus highlights this point well [1]. Prior to the Zika virus outbreak in Brazil in 2015, a PubMed search about the infection yielded fewer than 110 research articles. The outbreak precipitated rapid research in the field, resulting in more than 3,000 articles being indexed in PubMed by 2017. Based on these research findings, the Centers for Disease Control and Prevention (CDC) recommended a comprehensive physical exam, head ultrasound and laboratory testing for infants born to Zika-exposed mothers in January 2016 [2]. Yet, by April 2017, only 25% of infants had received head ultrasound and 65% had laboratory testing for Zika virus infection [3]. The rapid translation, dissemination and implementation of research findings is especially critical for combating emerging infectious diseases like Zika due to the potential for widespread transmission. These trends underscore that any delay in translation of knowledge and research findings undermines initiatives aimed at providing optimal patient care.

Significant delay exists in the translation of research evidence into clinical practice

WHAT IS CAUSING THE DELAY IN IMPLEMENTATION OF KNOWLEDGE INTO PRACTICE?

To make the best use of medical advancements, clinicians must first identify the most useful and relevant information and distinguish it from background noise [4]. This involves asking appropriate questions and being able to find the answers quickly. An approach to finding evidence-based answers is to perform targeted literature searches for efficient retrieval of the best available evidence [5]. Both unfiltered resources (e.g., PubMed) and filtered resources (e.g., EvidenceAlerts) exist to help with locating individual articles. However, even with the availability of these resources, busy practitioners lack the time to find the best available evidence in the primary literature. Likewise, they often lack the skills to critically appraise the new information (i.e., to comprehend the strengths and weaknesses of the study to fully understand its usefulness). Finally, to make clinical decisions, clinicians must synthesize information from several sources, understand the new results in the light of previously published studies, and integrate the newly gained knowledge in the context of the clinical needs of patients. The entire process, from performing literature searches to critically appraising and synthesizing the information, takes several hours to days. The high workload of clinicians coupled with the explosion of scientific knowledge makes the process of identification, understanding and implementation of the most useful information into patient care impossible without help from synthesized sources of information.

The intense workload of clinicians combined with the explosion of scientific knowledge makes it impossible for clinicians to identify, understand and implement new findings into patient care at a reasonable rate.

In this era of information overload and emergence of patients who gather medical information from the internet, there is an urgent need for physicians to continuously learn and improve their knowledge of medical advances in ways that will allow them use it towards the maximum benefit of patients. Not only should clinicians know the information thoroughly but they also have to be well equipped to explain the different diagnostic or therapeutic options available and why each option may or may not be suitable to the patient.

To keep pace with rapid advances in medicine and overcome the challenges of information retrieval and critical appraisal, clinicians increasingly rely on evidence-based point-of-care tools that provide instant access to pre-appraised summaries of recent medical advances [6]. However, when relying on such summaries, it is important to remember that the interpretation of evidence is highly subjective and can be influenced by the opinions of the author. In fact, a study points out that "the common biases encountered during interpretation of research evidence include confirmation bias, rescue bias, auxiliary hypothesis bias, mechanism bias, time will tell bias, and orientation bias" [7]. Additionally, several cognitive biases in clinical decision making have been identified that may be applicable to the interpretation of clinical evidence as well [8]. Therefore, clinicians require a resource that can provide them with objective and transparent summaries of the latest medical evidence.

Clinicians require a resource that can provide them with objective and transparent summaries of the latest medical evidence. Researchers are key players when it comes to providing that objective analysis.

REACHING OUT TO PARTNERS IN SCIENCE AND MEDICINE

What is the best resource that can provide clinicians with such pre-appraised summaries of the evidence? Taking cues from how other industries operate—management companies hire consultants with special skill sets to provide unbiased perspectives on the challenges faced by the company [9], builders rely on architects with expertise in construction methods to create blueprints, lawyers depend on paralegals well-versed in the legal system to gather details about a case [10]—it would seem obvious for developers of point-of care tools to rely on a resource with a solid foundation and understanding of scientific research.

Scientists fit this role well. They possess a repertoire of skills that are valuable not only for performing research, but also for communicating science to a wide variety of audiences. Over the course of their scientific training, they learn to identify the gaps in existing knowledge and frame appropriate questions to find answers. They quickly learn to assess reams of literature to develop targeted hypotheses, perform experiments and use statistical analysis to validate these hypotheses. Additionally, the constantly changing scientific landscape requires scientists to continuously learn new concepts and consider alternative viewpoints while critically appraising the existing evidence to 'sift through the dross to reveal the silver within [11].'

Medicine has always been a team sport. Indeed, most medical advancements have been made possible by the complementary contributions of scientists and clinicians. While scientists contribute to the understanding of basic biology and underlying disease mechanism, clinicians provide insights on disease symptoms and apply scientific findings in patient care. A good example is the discovery of the cholesterol biosynthesis and its metabolism, its association to atherosclerosis and the development of statins—a widely used and highly effective class of cholesterol-lowering medicines to treat [12].

Given the years of specialized training and different mentalities required to perform basic research and practice clinical medicine, it is natural for scientists and clinicians to work in silos. But in this era of rapid knowledge generation, it is crucial for scientists and clinicians to communicate effectively for translating information at the same pace at which it is generated.

One example of where researchers and clinicians have broken down silos is *DynaMed Plus®*. *DynaMed Plus* is a clinical information resource that provides summaries of the most current clinical evidence. Scientists and clinicians collaborate to develop pre-appraised summaries of the evidence that are transparent, unbiased and updated promptly. Clinicians frame clinical questions regarding disease epidemiology, diagnosis, treatment and prevention. Scientists work within this framework to identify and highlight the existing and emerging clinical evidence. They perform comprehensive searches of the literature and critically appraise studies to answer clinical questions. Since scientists are not directly involved in patient care and are not influenced by the clinical opinions of their peers, they can provide the much-needed precision and clarity in reporting findings from clinical studies. Clinicians then review the information synthesized by scientists for relevance and applicability at the point-of-care. The evidence is continuously updated by scientists and clinicians using systematic literature surveillance – a process that allows prompt translation of new medical discoveries from clinical research to practice [13].

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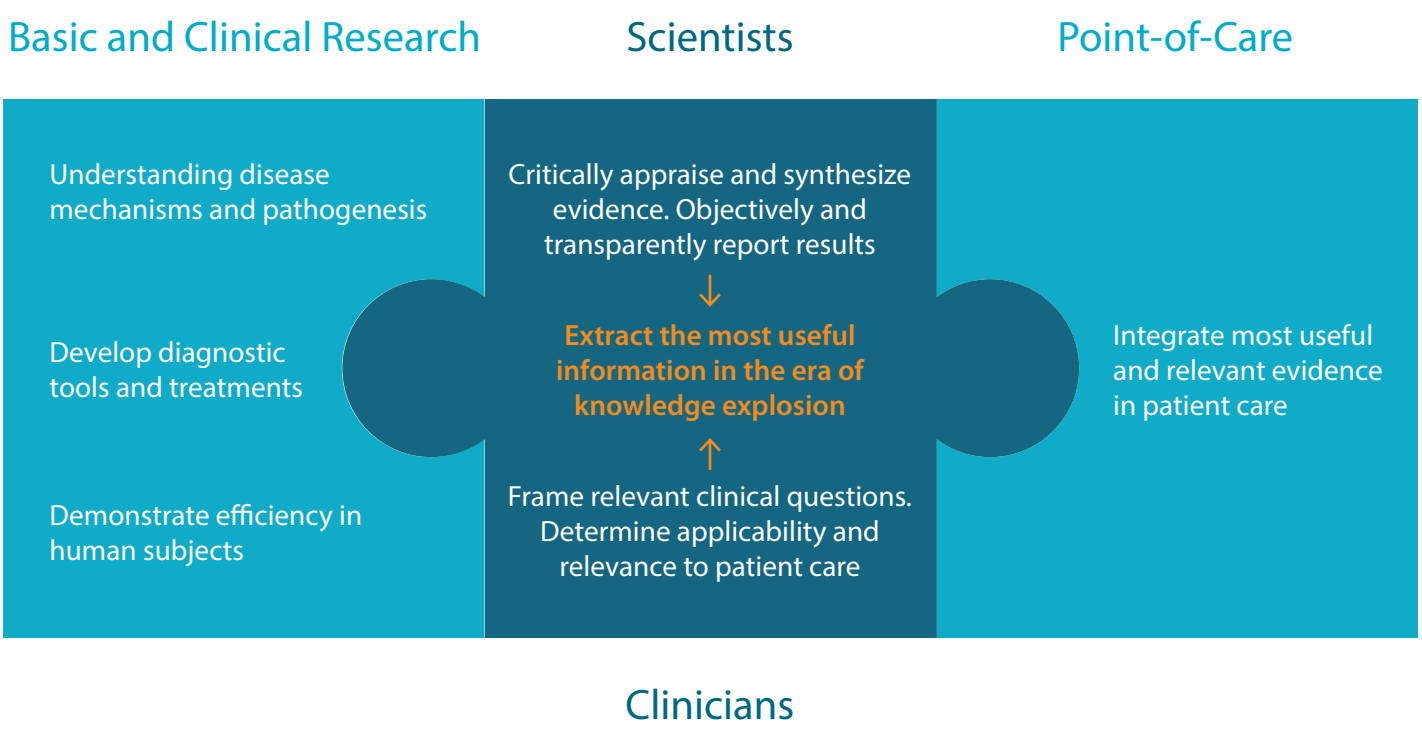

Figure: *Collaboration of scientists and clinicians to bridge the gap between knowledge generation and translation.*

Consider the following example that highlights the collaborative efforts of scientists and clinicians at *DynaMed Plus*® to critically appraise and objectively report a clinical study along with its clinical relevance:

In a recent study, the effect of cranberry capsules on bacteriuria plus pyuria and symptomatic urinary tract infections (UTIs) was evaluated [14]. In this trial, 185 elderly women with or without bacteriuria plus pyuria were randomized to cranberry capsules versus placebo for 1 year. Overall, no significant difference in the presence of bacteriuria plus pyuria was observed between those taking cranberry capsules or placebo. Additionally, no difference in the rates of symptomatic UTI was observed between the groups. Following thorough critical appraisal for study quality, the editorial team at DynaMed Plus concluded that cranberry capsules do not appear to reduce bacteriuria plus pyuria in elderly women residing in nursing homes [15].

The key shortcoming of this study was that it was not designed to detect a difference in the rates of symptomatic UTI - a clinical outcome that matters most to the patient. Therefore, the effect of cranberry capsules on the rates of UTIs is still unclear. However, the commentaries on the study concluded that "cranberry capsules do not reduce UTIs in older women [16]." Several articles in the media followed suite and represented the study as providing evidence that cranberry capsules have no effect on UTIs [17, 18, 19].

Do the results of this trial inform or change clinical practice? Given that bacteriuria plus pyuria is common among elderly women residing in nursing homes and usually does not require treatment, the results of the trial do not change clinical practice. If anything, the results suggest that more research is needed to better address the efficacy of cranberry products.

EXAMPLE: Do cranberry products have an effect on bacteriuria plus pyuria and/or symptomatic urinary tract infections in elderly women residing in nursing homes?		
Study analysis	Critical appraisal & objective reporting at *DynaMed Plus*	No critical appraisal & biased reporting by media
Study outcomes	Cranberry capsules do not appear to reduce bacteriuria plus pyuria.	Cranberry capsules have no effect on urinary tract infections (UTIs)
Outcomes	Insufficient evidence for determining effect on UTIs (relevant clinical outcome), more research required to evaluate clinical utility of cranberry products	Do not recommend cranberry products for UTIs

Conclusion

While the rapid pace of scientific advancements has significantly improved our understanding of science and medicine, it has also made the process of keeping abreast with new advancements more challenging. Adapting to and taking advantage of scientific advances in patient care requires the involvement of experts in research and clinical care working together. Teams of clinical experts and scientists need to work in concert to evaluate clinical evidence of new advancements focusing not just on the quality, validity, and utility, but also on clinical applicability and context. This will aid in the understanding of inconsistencies among clinical evidence and better address knowledge gaps. The scientists and clinicians at *DynaMed Plus* are well-placed to provide this sophisticated evaluation of the evidence, allowing clinicians to quickly find the objective information they need to provide the best care for their patients.

Authors

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