An appeal to the global health community for a tripartite innovation: an “Essential Diagnostics List,” “Health in All Policies,” and “See-Through 21st Century Science and Ethics”

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Abstract

Diagnostics spanning a wide range of new biotechnologies, including proteomics, metabolomics, and nano-technology, are emerging as companion tests to innovative medicines. In this Opinion, we present the rationale for promulgating an “Essential Diagnostics List.” Additionally, we explain the ways in which adopting a vision for “Health in All Policies” could link essential diagnostics with robust and timely societal outcomes such as sustainable development, human rights, gender parity, and alleviation of poverty. We do so in three ways. First, we propose the need for a new, “see through” taxonomy for knowledge-based innovation as we transition from the material industries (e.g., textiles, plastic, cement, glass) dominant in the 20th century to the anticipated knowledge industry of the 21st century. If knowledge is the currency of the present century, then it is sensible to adopt an approach that thoroughly examines scientific knowledge, starting with the production aims, methods, quality, distribution, access, and the ends it purports to serve. Second, we explain that this knowledge trajectory focus on innovation is crucial and applicable across all sectors, including public, private, or public–private partnerships, as it underscores the fact that scientific knowledge is a co-product of technology, human values, and social systems. By making the value systems embedded in scientific design and knowledge co-production transparent, we all stand to benefit from sustainable and transparent science. Third, we appeal to the global health community to consider the necessary qualities of good governance for 21st century organizations that will embark on developing essential diagnostics. These have importance not only for science and knowledge-based innovation, but also for the ways in which we can build open, healthy, and peaceful civil societies today and for future generations.

“(R)evolutionary situations arise also in science when the legitimacy of the previously accepted order and ways of ‘doing things’ are questioned and eventually overthrown.”

Helga Nowotny (2007)

The Concept of Essential Medicines

The global health community recognizes the value and importance of ensuring populations have adequate and reliable access to certain medicines. Health authorities in countries need to know what to prioritize to ensure they have a basic health care system that can adequately serve the needs of the population. In this regard, the history of essential medicines is relatively recent. Consider that aspirin was only introduced in 1897 as the first synthetic pharmaceutical, and is arguably the first truly essential medicine that aimed to satisfy the health care needs of the majority of the population. Although the history is recent, already the concept of essential medicines is well recognized. In 1977, the World Health Organization (WHO) launched the forward-looking and dynamic “Model List of Essential Medicines”, and identified 208 individual medicines which together could provide safe, effective treatment for the majority of communicable and non-communicable diseases. The List is updated every 2 years by an international expert committee.

Essential medicines are “those that satisfy the priority health care needs of the population,” selected based on disease burden, efficacy, safety, and cost-effectiveness evidence (World Health Organization, 2013). The medicines listed are “intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford” (World Health Organization, 2013). The List is not intended as a global standard. Each country, or states within countries, may adopt the list of essential medicines based on local context and priorities.

Pharmaceuticals represent up to 66% of health-related expenditures in developing countries (World Health Organization, 2013). Since many international and nongovernmental organizations (NGOs) consider it as a guidepost, the List also assists in procurement, reimbursement, access, quality, and rational use of medicines. Essential medicines are often associated with principles of equity, pro-poor policies, and good governance. The latest 19th WHO Model List of Essential Medicines was published in May 2015 (World Health Organization, 2015). As important as an essential medicines list is for all countries, science and medicine have moved into new areas, accelerated in no small measure by Big Data (Jardog et al. 2014). This shift in science and medicine, and health care delivery, calls for innovative thinking to develop new governance tools that address the pressing health care needs of populations.

What about Essential Diagnostics?

Social studies of science scholar Helga Nowotny has noted that radically new ways of “doing things” emerge in the course of scientific practices (Nowotny, 2007). A crosscutting change, precision medicine develops and makes use of diagnostic tests that, through stratification, explain the basis of large person-to-person (or subgroup) variations in drug safety and efficacy. Beyond targeting medicines to the right person at the right dose, precision medicine also signals a shift from treatment to prevention in healthcare, ranging from identification of those at highest risk of developing a disease, adverse drug reactions (ADRs), treatment failures, to those who would benefit most from preventive interventions.

The benefit of precision medicine to countries can be profound, not just in terms of promoting healthy aging, but also in realization of socioeconomic benefits. Using a health simulation model, a recent analysis published in The Lancet suggests that the years of healthy life that can be cultivated by a precision medicine approach in six diseases (cancer,
Diabetes, heart disease, high blood pressure, lung disease, and stroke) in the US population could generate, in the case of heart diseases, an impressive $607 billion in improved health over the next 50 years (Dzau et al., 2015).

Diagnostics spanning a wide range of biotechnologies, including genomics, proteomics, metabolomics, and nanotechnology, are emerging as companion tests to innovative medicines (Conde and Artzi, 2015; Higdon et al., 2015). The 19th WHO Model List of Essential Medicines brings to the fore innovative medicines for hepatitis C, breast cancer, leukemia, and multi-drug resistant tuberculosis (World Health Organization, 2015). Innovative medicines designated as “essential” can have enormous positive impacts on global health. Furthermore, innovative medicines might have even broader reception in future Essential Medicines Lists if we consider therapeutics with companion “essential diagnostics” aimed at prevention of ADRs and ineffective treatments.

Too often, however, diagnostics are overlooked as a critical component of modern health care (ElRakaiby et al., 2014; Özdemir and Cho, 2012). From a discovery science standpoint, not all innovative medicines may attain the status of an “essential medicine.” But they are more likely to emerge out of the laboratory and “into the street” if we move away from the traditional one-size-fits-all model of drug development by recognizing the omics basis of person-to-person heterogeneity in drug safety and efficacy by diagnostic tests (Higdon et al. 2015; Özdemir and Lerner, 2005). When an innovative medicine attached to a companion diagnostic is granted an essential medicine status, there is a need for parallel policy and regulatory mechanisms to govern and evaluate the diagnostic counterpart of such innovative essential medicines.

Thus, we propose and call for the development of an Essential Diagnostics List, which is comprised of the necessary diagnostics for robust and crosscutting impacts on global health, as well as societal endpoints such as sustainable development, gender parity, global health diplomacy/security, and inclusive and peaceful societies, among others. These essential diagnostics should be made available in an evidence-based, cost effective, and ethical manner at all times in health systems, together with essential medicines. An Essential Diagnostics List in an era of precision (stratified) medicine offers a real opportunity to improve rational therapy and health outcomes in subpopulations defined by diagnostic tests (Fig. 1) (Özdemir and Lerner, 2005; Tutton, 2012). Essential diagnostics and essential medicines are two sides of the same coin for rational therapeutics, and complement each other as concepts and practices (Fig. 2).

An Essential Diagnostics List places global health firmly on the life sciences innovation agenda. At the same time, we neither neglect nor underestimate potential trepidation that might exist within the global health community towards developing a list of essential diagnostics. Public health had a longstanding and laudable focus on addressing the needs of the entire population, but this view also risks treating communities as homogeneous organisms, overlooking the diverse needs of distinct subpopulations defined both by variations in biology and environment.

In the future, by using an essential diagnostic test, an innovative essential medicine might target a subpopulation wherein it may display maximum efficacy and minimum toxicity. No doubt this will (and ought to) raise ethical concerns about what may come of other subpopulations with unmet therapeutic needs. But one should also consider that failure to prevent ADRs and ineffective treatments, while diagnostics are increasingly available to identify at risk populations, is an ethical concern in its own right.

In this era of Big Data analytics and precision medicine, we must face proactively the reality that many biomarker
claims and diagnostics candidates are in transition from lab to applications as precision medicine diagnostics worldwide (Şardaş et al., 2014). This has already created unmet policy gaps on diagnostics in regards to what needs to be considered as “essential” for global health versus clinical practice versus personal utility versus recreational diagnostic tests with dubious value. Moreover, the impacts of new diagnostics on global health and societal endpoints regrettably are not often considered as a major criterion for adoption. We think such a criterion would be essential beyond clinical and personal utility for a diagnostic to be deemed “essential” (Fig. 2). An Essential Diagnostics List would help preserve scientific rigor and standards in resource-limited settings laden with economic, social, geographical and political instability or pseudo-scientific actors (Dandara et al., 2014; Özdemir, 2014; Özdemir et al., 2013; 2015a).

Having an Essential Diagnostics List in place could also serve as a guidepost to prevent “parachute science” in resource-limited regions that exploit local communities, their populations, and biodiversity, as de Vries and Pepper note:

The trend has been to use data derived from African populations to build research programmes and enhance individual careers in more affluent communities with little or no consideration for the populations from which this material was derived. (de Vries and Pepper, 2012).

At the same time, we must not leap into assumptions about where precision medicine is most achievable or suitable. In the 21st century, old binaries such as developed and developing country are increasingly blurred (Dove, 2013; Haffeld and Siem, 2013; Özdemir, 2015a). Peter Hotez has aptly noted that resource-constrained regions exist not only in developing world but also in major geographical parts of the G20 nations and the developed countries (Hotez, 2013). An Essential Diagnostics List would serve the global health community well as a new technology and innovation governance instrument.

Linking Diagnostics to Broad Societal Impacts

Health in All Policies (HiAP)

A key criterion for an essential diagnostic is veritable linkages with and impacts on broad societal outcomes beyond clinical utility (Fig. 2). A corollary of this is that the value of essential diagnostics cannot be deciphered solely through looking from inside the health ecosystem and related organizational structures. We need to look at health from the outside as well. Understanding health innovations such as essential diagnostics across sectors demands shared governance and knowledge of the “languages” and “ways of knowing” by other disciplines—in particular, anthropology, sociology, philosophy, and political science.

In the same way that molecular biology has made visible the pathways underlying diseases normally invisible to the naked eye—social science and humanities scholarship equips us with the knowledge of invisible societal and micro-level contexts and dynamics that shape, and are shaped by, scientific practices. In short, such interdisciplinary scholarship is instrumental to understanding the inner workings of human societies and the socio-material environments in which they are entrenched. For example, without a social sciences and humanities lens, we run the risk of turning a blind eye, willfully or unintentionally, to important justice issues such as human rights, ethics, and power dynamics in scientific practice, gender gaps, rural versus urban communities’
access to health in global society, and the structural and psychosocial constraints of laboratory and professional life.

If we are to link the selection of essential diagnostics not only to clinical utility but also to societal impacts, we need additional governance instruments grounded in social science and humanities, as well as (natural) science and technology. Health in All Policies (HiAP) is one such governance instrument that we suggest should be considered in tandem with decisions concerning the proposed Essential Diagnostics Lists. HiAP values the systems approaches often discussed in *OMICS: A Journal of Integrative Biology*; it highlights the need to heed both “trees” and “forests” to address complex life sciences and related societal challenges and opportunities.

HiAP examines, analyzes, and engages with health and non-health sectors to understand the root causes of illness and good health. In the context of HiAP, Ilona Kickbusch has noted the value of bi-directional linkages between health and sectors that are traditionally considered as being outside the scope of health and life sciences. These can include sectors such as global health diplomacy, security, and development:

This is critical for twenty-first century health policy because good or bad health outcomes depend on the action of other sectors but also affect the outcomes of a wide range of other sectors. (Kickbusch, 2010).

**Gender parity and maternal health diagnostics**

Essential diagnostics, if evaluated under the overarching frame of HiAP, could offer firm linkages with societal and global health endpoints neglected previously, such as gender parity. The World Economic Forum, amongst others, has asserted that gender parity is an indispensable dimension of 21st century organizations and society (World Economic Forum, 2015). Novel diagnostics impacting maternal health and by extension, gender parity, are important on principled ethics and human rights grounds as well (Tasioulas and Vayena, 2015).

**A pharmacogenomics peace and conflict resolution clinic**

Yet another novel example of potential broader societal impacts of essential diagnostics could be drawn from the field of pharmacogenomics. Cytochrome P450 2D6 (*CYP2D6*) is one of the most intensively studied drug metabolizing enzymes, with extensive polymorphic pharmacogenomics variation across world populations. Aklililu and colleagues have shown that in Ethiopia, 29% of the study sample carried alleles with duplicated or multiduplicated *CYP2D6* genes, indicative of ultra-rapid metabolism, and which often leads to treatment failure (Aklililu et al., 1996). Owing in part to historical human migration patterns, there is a gradient (from high to low) of *CYP2D6* ultra-rapid metabolizers from Ethiopia to the Middle East to Spain and Northern Europe (Özdemir et al., 2006). Because conflict and war are not uncommon in certain points on this historical migration route (e.g., consider the ongoing conflict in Syria and the Middle East), conflicted populations that share similar genetic makeup, and thus need shared solutions for diagnostic tests for rational therapy, might be able to reconcile their perceived differences or at least “agree to disagree” in a peaceful manner when global health services are provided for shared health needs.

Moreover, a global health diplomacy and security initiative of *CYP2D6* testing and other diagnostics could offer a health-based conflict resolution forum. This would resonate very well with the ethos of HiAP. While we do not have HiAP in place in most parts of the world, these examples might help commence a multi-sector discourse on the subject matter of essential diagnostics in regions and for global health applications where HiAP is most needed.

Finally, as a complement to traditional academic publishing with a generally modest global circulation, engaging with mass media, both traditional and social, and in multiple languages, might offer ways forward for broader engagements central to HiAP. We suggest a need for greater engagement between scientists, communication sciences and mass media in ways that are credible, trustworthy, held accountable to and driven by society (Zhao et al., 2014).

**Who Shall Take on the Task? Designing New 21st Century Organizations**

*Governing innovations by “see-through science and ethics”*

From the invention of steam power at the beginning of the Industrial Revolution, to the growth of material industries (e.g., textiles, glass, cement, plastics) over the last 2 centuries, there has been a longstanding tradition to classify organizations as public, private, and public–private partnerships, among others. As we transition to a new revolution based not on manufacturing so much as “*mensa*facturing” (intellectual outputs), centered on knowledge society and much-hoped for knowledge-based innovations such as global health diagnostics (Dove, 2013; Özdemir, 2014), we need a new taxonomy of workplace and organizations. If knowledge is the currency of the current century, then we must think anew about organizational taxonomy informed by an approach that examines knowledge from all points, from its production aims, means, quality, distribution, access, and to the ends it serves (Birko et al., 2015; Dove and Özdemir, 2013; European Commission, 2007; Yearley, 2004).

Hence, this Opinion does not aim to appeal to any one particular organization, public, private, nongovernmental, nor any conceivable international agency, to take on the task of developing and promoting an Essential Diagnostics List. Instead, it aims to appeal to the readers of this journal and global health community at large, to consider thinking about the necessary qualities of new 21st century organizations before a discussion is launched to determine which actors should take on this challenging task.

No doubt, we need innovation in institutional design as well. Twenty-first century universities are sorely in need of evolution towards an expanded and productive dialogue between science and society (Callon et al. 2011; Nowotny, 2007). It is uncertain whether the current university designs and research funding mechanisms as we know them can adequately meet the challenges and prospects of emerging technologies and novel diagnostics (Özdemir et al., 2015b). Rather than convergent thinking, this is a time for *divergent* thinkers and perhaps unorthodox or “indie” and off-road organizations to come up with innovative institutional redesigns of 21st century science.
A starting point is to re-think scientific organizations (beyond research universities and the binaries of public versus private) and unpack the ways in which knowledge is co-produced together with values introduced by a range of actors, be they publics, scientists, citizen scientists, funders, academics, industry, governments, or policymakers. This “trajectory” focus is crucial and applicable across all sectors because it underscores the fact that scientific knowledge is a co-product of technology, human values, and social systems. By making the value systems embedded in scientific knowledge production transparent, we all stand to benefit from sustainable and transparent science (Birch and Tyfield, 2013; Özdemir, 2015).

Thinking about the ways in which science is constructed is not an intellectual project that ended with the Enlightenment. We continue to make the case, conceptually and empirically, that knowledge experts bring their socially constructed values to the laboratory and influence, and are influenced by, the social and political systems that characterize their fields. Although the long-held, widely accepted version of scientific history since the early luminaries of the Enlightenment has promoted the view that scientific practice and knowledge are neutral, value free, and inherently objective, we know this is more myth than reality (Birko et al., 2015; Callon et al., 2011; Dove and Özdemir, 2013; Editorial, 2013; Yearley, 2004). For example, while scientific evidence is considered an important gatekeeper for adoption of diagnostics, it also begs the question of “which evidence” produced “by whom”, to benefit “which stakeholders,” and under “what societal context, values and priorities” (Birko et al., 2015; Nowotny, 2007).

To enable a broad and open discussion of essential diagnostics, therefore, we offer below a taxonomy, in part building on nested governance systems designed by the late Elinor Ostrom (Ostrom, 1990), and in part based on our past synthesis for omics systems sciences (Dove et al., 2012; Özdemir et al., 2015a). Here, knowledge experts are classified as actors (e.g., scientists producing knowledge), narrators (e.g., ethicists, social scientists and humanists observing and analyzing knowledge co-production practices), and independent blue skies scholars (IBSS) who generate and analyze “social metadata” on the sorts of questions noted above that impact not only scientists, but also ethicists’ and social scientists’ daily practices (Dove et al., 2012; Dove and Özdemir, 2014; Özdemir et al., 2015a) (Fig. 3).

Such a taxonomy of the innovation trajectory makes explicit that no knowledge expert is “above the fray”: all shall remain accountable and make their practices transparent. The taxonomy invites us to be self-critical and reflexive (e.g., how do our own values, motivations, and expectations influence our actions and the conclusions we reach?). Through the triadic taxonomy described in Figure 3, knowledge experts can create a trustworthy and “see-through science and ethics”

FIG. 3. A triadic taxonomy and design for “See-Through Science and Ethics” and new 21st century scientific institutions for knowledge-based innovations. These envisioned 21st century organizational re-designs of work and society could contribute to the proposed post-2015 United Nations Sustainable Development Goals (SDGs) such as peaceful and inclusive societies. At the heart of the proposed taxonomy rests “nested architectures” that help foster environments of transparency and trustworthiness, and balanced power in society and its science and technology institutions. The proposed taxonomy is comprised of Actors who produce knowledge (e.g., scientists), Narrators (e.g., social scientists, humanists, ethicists) who observe the actors and their practices in real-time, and Independent Blue Skies Scholars (IBSS) who are not entrenched in traditional professional network structures (e.g., independent scholars, scholars-in-residence, society-driven self-organized groups or citizen scientists), and thus can offer truly independent broad systems-oriented (blue skies) analyses of both actors’ and narrators’ practices. The term IBSS was coined in an earlier article (Özdemir et al., 2015a).
knowledge commons where power differences among the ecosystem’s actors and narrators are kept in check in real-time. This proposed model warrants field-testing and should be compared to existing science organizations in regards to impacts on sustainable science and responsible innovation.

Conclusions

With the arrival of Big Data and many biomarker claims—some valid and others less valid or even irrelevant—developing essential diagnostics will be critical if we are to link technology to responsible innovation in ways that concretely and positively impact global health. Developing an Essential Diagnostics List provides an opportunity to harness the latest science and diagnostic technology to establish linkages with health policies that are crosscutting across sectors inside and outside health (e.g., the application of whole genome sequencing in pharmaco-genomics) (Mizzi et al., 2014), and with science and ethics that are fully transparent and held accountable to global society. This we hold to be essential, too, not only for global health and knowledge-based innovation, but also for the ways in which we can build open, healthy, and peaceful civil societies today and for future generations.

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