strategies and unsuitable technology such as Pap smears, we believe that LMICs can change the current pattern, leapfrog old technologies, ensure equitable access for rural and poor women, and reduce related mortality by half.⁵ Countries that can afford to do more than implement this basic approach, such as screening more than once or screening older women, can expect even greater disease reduction.

It's also important to build service delivery systems that can incorporate even better technologies as they become available. Argentina, El Salvador, Guatemala, Honduras, and Nicaragua have

An audio interview with Dr. Jerónimo is available at NEJM.org already taken steps in this direction, using self-collected specimens for HPV

testing. Some countries are now testing community tracking mechanisms that can ensure that women who have screened positive return for treatment, as well as incorporating relevant indicators in national health information systems.

The next steps for taking full advantage of this convergence of technological innovation and political commitment seem clear. First and foremost, the approach now being introduced in several Latin American countries, as described above, can be scaled up, applied in a few countries in Africa and Asia, and evaluated rigorously. The results would indicate what adaptations are needed in different environments to serve current generations of women, and the evaluation could provide essential data on costs and outcomes. Second, a virtual learning network could be developed for rapid sharing of lessons, enabling other countries and funders to apply them. Third, concerted and coordinated advocacy can spur greater investment at both national and global levels. Finally, continued technological innovation may well drive down the costs of rapid molecular tests.

Every year that we delay, we squander the scientific advances we have made, lose ground on building the evidence for effective strategies, and tragically, lose women who could have been saved.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From PATH (formerly the Program for Appropriate Technology in Health), Seattle.

1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012: estimated cancer incidence, mortality, and prevalence worldwide in 2012. Lyon, France: International Agency for Research on Cancer, 2013 (http://globocan .iarc.fr).

2. Markowitz LE, Liu G, Hariri S, Steinau M, Dunne EF, Unger ER. Prevalence of HPV after introduction of the vaccination program in the United States. Pediatrics 2016; 137:1-9.

3. Schiffman M, Wentzensen N. A suggested approach to simplify and improve cervical screening in the United States. J Low Genit Tract Dis 2016;20:1-7.

4. Bloom DE, Cafiero ET, Jané-Llopis E, et al. The global economic burden of non-communicable diseases. Geneva: World Economic Forum, 2011.

5. Campos NG, Tsu V, Jeronimo J, et al. When and how often to screen for cervical cancer in three low-and middle-income countries: a cost-effectiveness analysis. Papillomavirus Res 2015;1:38-58.

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Time for a Model List of Essential Diagnostics

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The Model List of Essential Medicines (EML) maintained by the World Health Organization (WHO) plays a central role in global health policy. We believe that it's time to establish a similarly influential Model List of Essential Diagnostics (EDL). According to the WHO, the items included in the EML are "drugs that satisfy the health care needs of the population [and] . . . are intended to be available at all times . . . at a price the individual and community can afford." Inclusion in the EML is often necessary before large funders (ministries of health, nongovernmental organizations, and insurers) will invest in and orchestrate negotiated, large-scale procurement of a given medication.

Diagnostic tests are also required for fulfilling the health care needs of populations. They are critical to the management of communicable and noncommunicable diseases, surveillance of emerging infectious threats such as the Ebola and Zika viruses, and the safe and rational use of EML medicines, including stewardship of antiinfective agents to reduce the likelihood of the development of microbial resistance. Improved access to diagnostics

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has been shown to quadruple the number of cases of human immunodeficiency virus (HIV) infection detected,¹ double the rate of adequate glycemic control,² and reduce overtreatment of malaria by 73%.³ Thus, an EDL could, like the EML, help drive improved health care delivery. The question is how to define essential diagnostics.

Our first step toward defining an EDL was to consider tests that enable safe and rational use of EML medicines. Although this approach may not be the most comprehensive one, an advantage is that it harnesses the EML efforts that have already been invested and it can also indicate leukemia; potassium levels might be monitored in patients receiving diuretic treatment for hypertension as well as in those with diarrheal fluid loss due to gastrointestinal infection. We incorporated this complexity into our choice of tests by considering the number of medicines whose use would depend on results in each test category. The table shows the 19 test categories that we found to be essential for the effective and safe use of at least 10 medicines or medicine combinations that appear in the EML.

How does this list compare with the diagnostic tests current-

Listed tests should be reasonably available for people who need them, whether in the form of point-of-care tests in physicians' offices and pharmacies or as high-complexity tests in reference laboratories.

in identifying disease priorities. There are 409 medicines in the EML and more than 300 medicines or medicine combinations in the core list. For each core medicine, we consulted a number of well-established sources to identify diagnostic tests considered essential for at least one of the following: diagnosing the condition for which the medicine is indicated, monitoring for medication efficacy, or monitoring for medication toxicity. In this way, we identified 147 essential laboratory tests, which we sorted into 57 categories.

As with medicines, some diagnostic tests have utility in more than one condition. For example, an elevated white-cell count can be a consequence of infection, ly available in resource-poor settings? A recent comprehensive survey of laboratories and clinician offices in Kampala, Uganda, found 100 tests being offered in the city.4 Although this number is substantial, it does not ensure high-quality testing, nor does the mere availability of a test in the city ensure its accessibility. Although 822 laboratories offered malaria testing, for instance, only 5 offered glycated hemoglobin testing. The good news is that most tests we list in the table were among the ones more readily available in Kampala.4 However, along with glycated hemoglobin tests, other tests we've listed that have relatively low availability in Kampala include nucleic acid testing, bacterial culture and biochemical typing, and blood gas testing.

Some of the tests deemed essential will probably be too expensive for low-resource countries to sustain. This limitation raises the question of whether investments in strengthening laboratory diagnostics will prove cost-effective, but we believe they probably will. The best data we have to support this assertion come from highresource settings. For instance, in the United States, only 3% of Medicare Part B payments in 2010 were for laboratory expenditures, according to the Department of Health and Human Services. In addition, because 2% of laboratory tests account for 80% or more of total testing volume,5 most of the clinical data needed for care can be provided using a limited number of tests. Of course, health expenditure profiles may be different in low-resource settings, and diagnostics could require a larger share of overall expenditures than they do in high-resource settings. (According to the WHO, that is true of medicines.) Still, provision of essential diagnostics would probably entail a relatively small investment that could result in large synergies throughout the health care system.

Basing the EDL on the EML is advantageous, but it's a preliminary step. An eventual "official" EDL would have to incorporate diagnostic-specific criteria. For example, the selection process for adding a medicine to the EML includes evaluation of disease prevalence and public health relevance as well as review of the medication's comparative effectiveness and safety. In addition, consideration is given to affordability, regulatory status, and clin-

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Selected Laboratory Tests That Are Required for Use of Medicines on the WHO Model List of Essential Medicines (EML).		
Test	No. of Medicines on EML	EML Categories
Complete blood count	136	Affecting blood; anesthetics; antidotes; antiepileptics; antihepatitis; anti- infectives; antimigraine; antiparkinsonism; blood products; cardiovascu- lar; dermatologic; diuretics; gastrointestinal; hormones; immunologics; ophthalmic; oxytocics; palliative; psychiatric; rheumatologic
Liver enzymes	104	Anesthetics; antidotes; antiepileptics; antihepatitis; antiinfectives; anti- migraine; antiparkinsonism; cardiovascular; diuretics; gastrointestinal; hormones; oxytocics; palliative; psychiatric; rheumatologic; vitamins
Renal function	92	Anesthetics; antiallergics; antidotes; antiepileptics; antihepatitis; anti- infectives; antimigraine; antiparkinsonism; blood products; cardio- vascular; diagnostic agents; diuretics; ear, nose, and throat; gastro- intestinal; hormones; immunologics; palliative; psychiatric; respiratory; rheumatologic
Microscopy	85	Antiinfectives; blood products; dermatologic; hormones
Urinalysis	64	Anesthetics; antidotes; antiepileptics; antihepatitis; antiinfectives; blood products; cardiovascular; electrolyte solutions; gastrointestinal; hormones; immunologics; oxytocics; psychiatric
Nucleic acid testing, microbiology	62	Antihepatitis; antiinfectives; hormones; immunologics; ophthalmic
Electrolytes	56	Anesthetics; antiallergics; antidotes; antiinfectives; cardiovascular; diuretics; electrolyte solutions; ear, nose, and throat; gastrointestinal; hormones; ophthalmic; palliative; psychiatric; respiratory
Microbiologic culture (includes drug sensitivities)	51	Antiinfectives; dermatologic; immunologics; ophthalmic
Glucose	42	Affecting blood; antiallergics; antidotes; antiinfectives; cardiovascular; elec- trolyte solutions; gastrointestinal; hormones; immunologics; neonatal; palliative; psychiatric
Antigen testing (microbiology)	42	Antihepatitis; antiinfectives; gastrointestinal; immunologics
Serology (microbiology)	41	Antihepatitis; antiinfectives; hormones; muscle relaxants; ophthalmic
Human chorionic gonadotropin	30	Affecting blood; antidotes; antihepatitis; antiinfectives; hormones; immuno- logics; psychiatric
Biochemical bacterial typing	27	Antiinfectives; immunologics; ophthalmic
Lipid panel	24	Antiinfectives; cardiovascular; hormones; psychiatric
Lymphocyte CD4	21	Antiinfectives; immunologics
Blood-gas testing	18	Affecting blood; anesthetics; antidotes; antiinfectives; electrolyte solutions; hormones; muscle relaxants; neonatal
Coagulation function	14	Affecting blood; antiepileptics; antiinfectives; blood products; hormones; immunologics; psychiatric
Glycated hemoglobin	11	Antiinfectives; cardiovascular; hormones; immunologics; neonatal; psychiatric
Calcium	10	Antiallergics; antidotes; cardiovascular; diuretics; ear, nose, and throat; gastro- intestinal; palliative; respiratory; vitamins

ical guidelines. On the other hand, diagnostic-specific criteria for a formal EDL might include diagnostic accuracy and the likelihood that a test would alter patient care and improve outcomes. Further considerations might be the test's inclusion in medical management guidelines and the amount of infrastructural and human resources required to perform it.

In addition, a formal EDL would have to address conditions that public health surveillance

reveals to be important but for which the EML does not currently include medicines (e.g., Ebola and Zika virus outbreaks). Finally, designers of the EDL would have to strive to avoid some of the perceived shortcomings of

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the EML. Although the EML review process was formalized in 2001, some observers still express concern about the thoroughness of evidence-based evaluation, transparency of the decisionmaking process, lack of conflictof-interest statements by applicants, the inclusion of high-cost medicines, and country-specific regulatory hurdles for medicine registration.

The goal of an EDL would not be wholesale adoption by countries for use in all laboratories or for all patients. Rather, the list would represent tests that should be reasonably available for people who need them, whether in the form of point-of-care tests in physicians' offices and pharmacies or as high-complexity tests in reference laboratories. Furthermore, as with the EML, there could be individualized, countryspecific lists tailored to local burdens of disease. Expert groups could be responsible for reviewing applications and periodically updating the diagnostics list to account for improvements in technology and shifting disease epidemiology.

The question of whether such a model list would be best maintained by the WHO merits further discussion. Since the WHO maintains the EML and is instrumental in developing medical guidelines as well as laboratoryaccreditation schemes suitable for low-resource settings, it is an obvious choice. Alternatively, a nongovernmental organization devoted specifically to this problem might prove to be a more nimble option, provided that an EDL produced by such a group would convince ministries of health and large funders of its legitimacy.

Wherever the list is housed, its existence would facilitate group purchasing to reduce costs and inspire development of logistical solutions for laboratory testing in resource-poor settings. We believe the world can no longer wait to have laboratory testing available to all clinicians. An EDL would clarify priorities for policymakers and encourage setting common goals regarding laboratory testing, paving the way toward improved health care delivery and ultimately better patient outcomes.

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1. Sweat M, Morin S, Celentano D, et al. Community-based intervention to increase HIV testing and case detection in people aged 16-32 years in Tanzania, Zimbabwe, and Thailand (NIMH Project Accept, HPTN 043): a randomised study. Lancet Infect Dis 2011;11:525-32.

2. Windus DW, Ladenson JH, Merrins CK, et al. Impact of a multidisciplinary intervention for diabetes in Eritrea. Clin Chem 2007; 53:1954-9.

3. Mbonye AK, Magnussen P, Lal S, et al. A cluster randomised trial introducing rapid diagnostic tests into registered drug shops in Uganda: impact on appropriate treatment of malaria. PLoS One 2015;10(7):e0129545.

4. Schroeder LF, Elbireer A, Jackson JB, Amukele TK. Laboratory diagnostics market in East Africa: a survey of test types, test availability, and test prices in Kampala, Uganda. PLoS One 2015;10(7):e0134578.

5. Vreeman DJ, Finnell JT, Overhage JM. A rationale for parsimonious laboratory term mapping by frequency. AMIA Annu Symp Proc 2007;Oct 11:771-5.

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Passing the Baton — Harnessing the Full Value of Older Scientists

Eric Orwoll, M.D.

Deciding when and how to retire from a career as a scientist and principal investigator can be daunting. A mandatory retirement age — after which researchers are precluded from being principal investigators or the administrators of research funds — remains common in Europe

and Japan¹ but was abandoned in the United States in 1994, when the exemption for postsecondary institutions from the Age Discrimination in Employment Act was allowed to expire. Many investigators still choose to leave academia to pursue other opportunities later in life, but the absence of retirement mandates allows for other options as well. For example, some researchers give up being principal investigators but continue their involvement as teachers, mentors, coinvestigators, or entrepreneurs.¹

Nevertheless, an increasingly common career path for scien-

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