MIT Center for Biomedical Innovation | BIO ACCESS A Global Health Initiative

Access-by-Design: Making Biologics Available to All

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WCBP Conference 2019
Plenary Session 6: Global Access - Transformative Technology
Wednesday, January 30 2019
The Mayflower Hotel, Washington, D.C

Outline

Global burden of non-communicable disease

BioACCESS at MIT

Research to enable *Access-by-Design*

Non-communicable diseases cause >70% of deaths globally

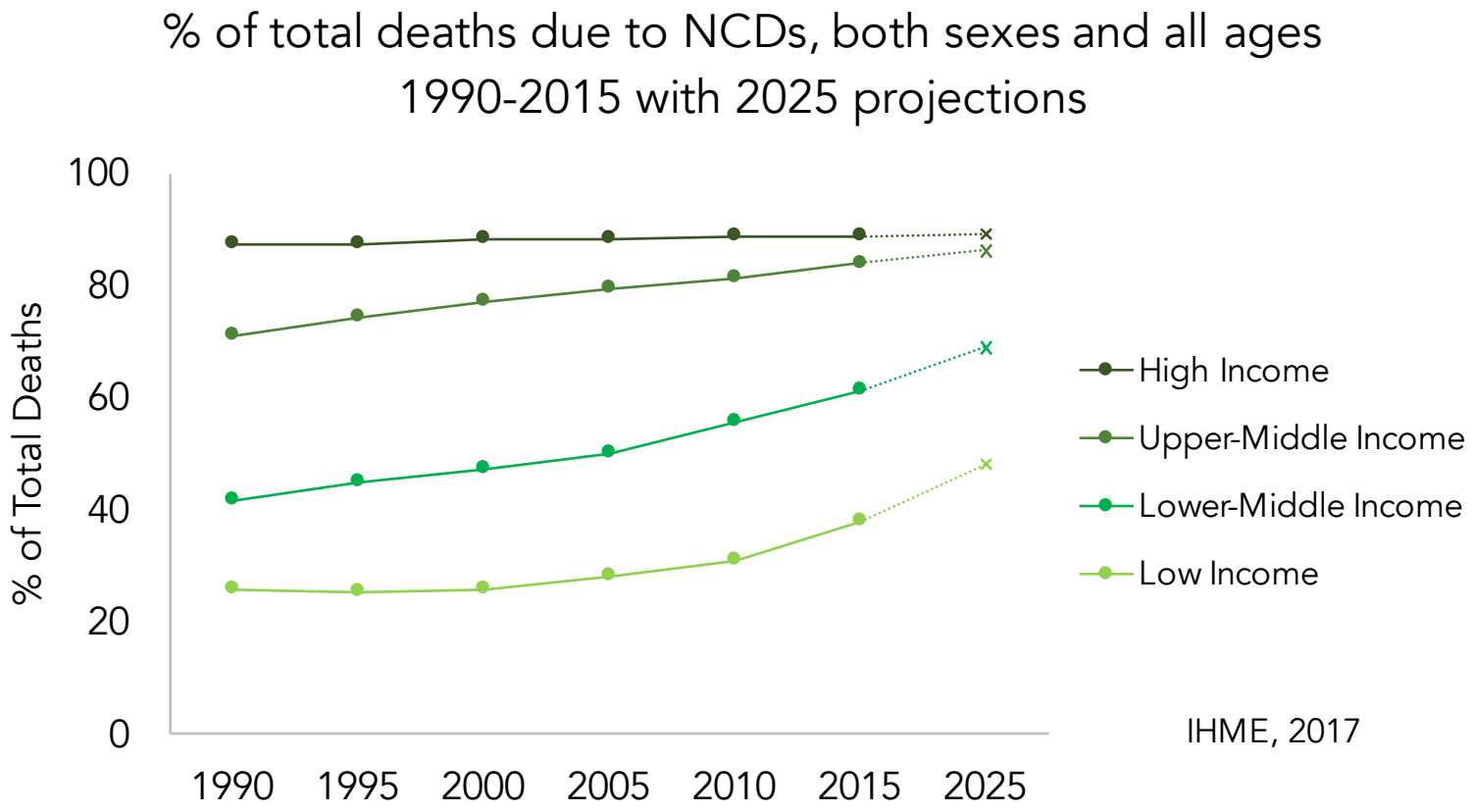
WHO, 2016

Non-communicable diseases

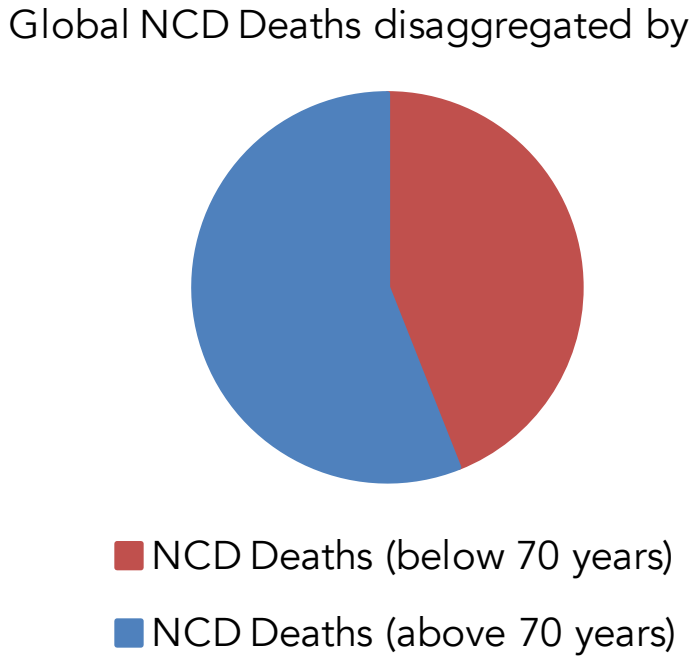
Infectious, maternal, perinatal and nutritional conditions

Injuries

Disproportional number of new NCD cases are in LMICs



44% of NCD-related deaths are premature (<70 years old) and considered to be preventable

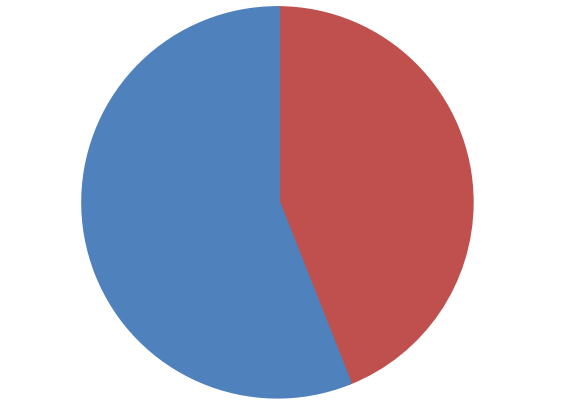


Credit: NCD Child

WHO, 2016

87% of premature NCD-related deaths are in LMICs

Global NCD Deaths disaggregated by age

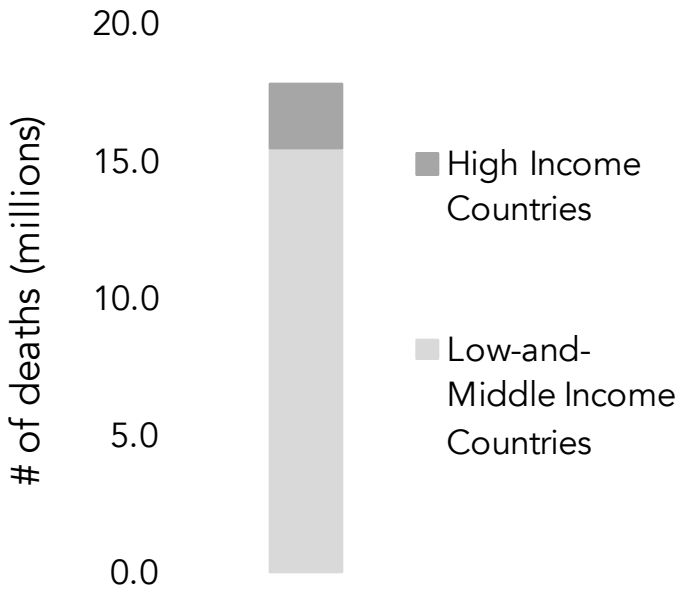


NCD Deaths (below 70 years)

NCD Deaths (above 70 years)

Disproportionate burden in **Low & Middle Income Countries**

Distribution of NCD-related premature deaths (2015)



WHO, 2016

WHO Global Action for preventing/controlling NCDs

Action to realize the commitments made is **inadequate** and the current level of progress is **insufficient** to meet targets….

"The world is reaching an inflection point…a **paradigm shift** is needed to do things differently to address obstacles in a new development era."

Report of the UN Secretary-General on NCDs, 2018

25% relative **reduction** in overall mortality due to NCDs (especially premature deaths) **by 2025**

80% availability of the **affordable basic technologies and essential medicines**, including generics, for NCDs in both public and private facilities **by 2025**

Examples of Initiatives aimed at increasing access:

ACCESS ACCELERATED
Moving NCD Care Forward

uicc
global cancer control

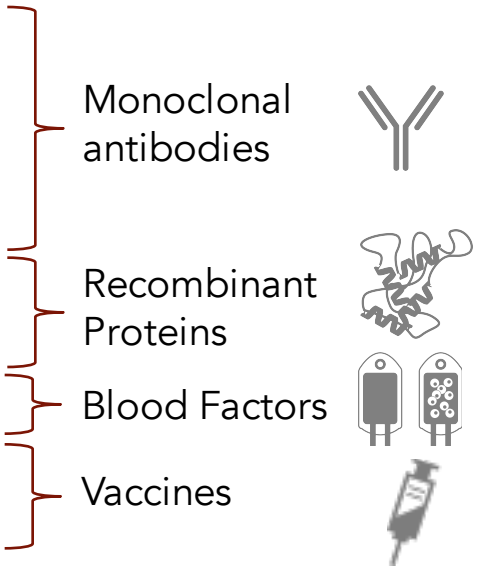
IFPMA

The NCD Alliance
Putting non-communicable diseases on the global agenda

COALITION FOR ACCESS TO NCD MEDICINES & PRODUCTS

Biologics are effective therapies for many NCDs

Disease	Standard of Care
B-cell lymphoma	Rituximab (Rituxan) *
HER2 positive breast cancer	Trastuzumab (Herceptin) *
Various tumors (anti-VEGF)	Bevacizumab (Avastin) *
Macular Degeneration	Ranibizumab (Lucentis)
Diabetes (all type I, some type II)	Insulin *
Hemophilia	Factor VIII *
Cervical Cancer (prophylactic)	HPV Vaccine *

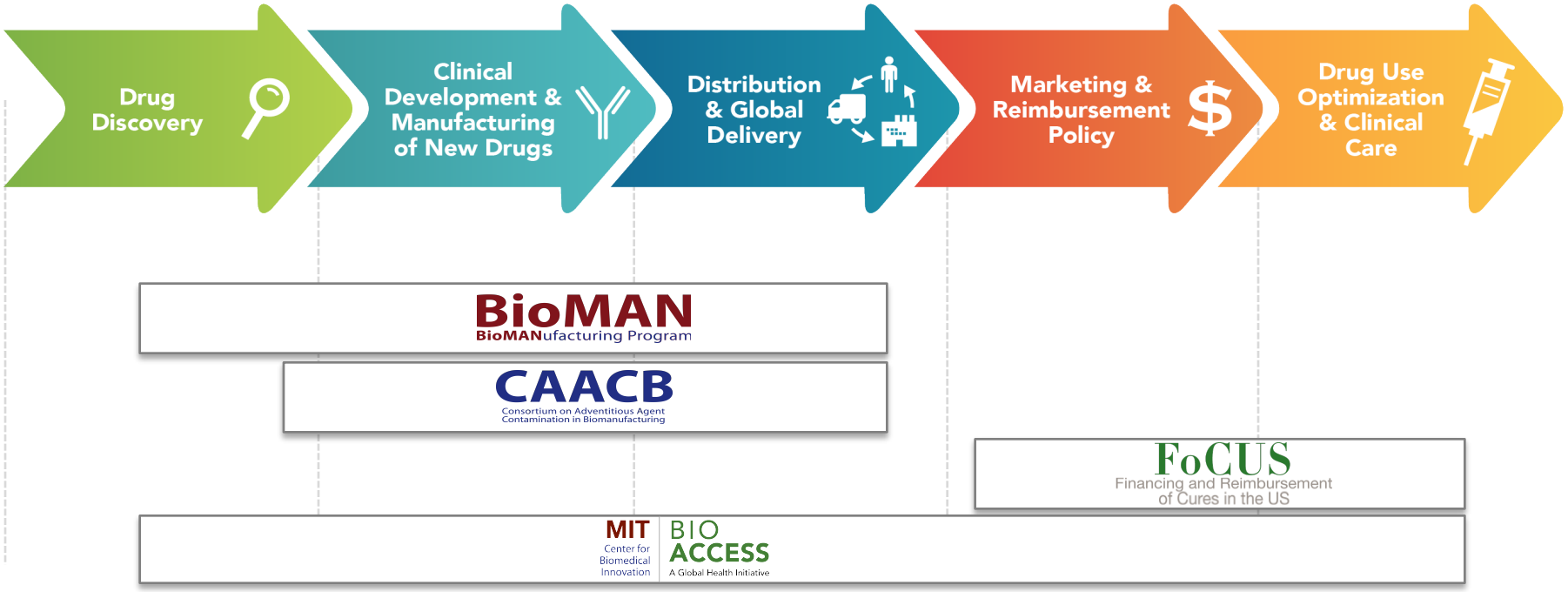


* On **WHO Model List of Essential Medicines** (March 2017)

MIT Center for Biomedical Innovation

MISSION: to improve global health by overcoming obstacles to the development and implementation of biomedical innovation

GLOBAL HEALTH DELIVERY SYSTEM



Mission of BioACCESS

MIT Center for Biomedical Innovation | BIO ACCESS
A Global Health Initiative

To enable global access to biotherapeutics through:

- Collecting data and building tools to identify systematic barriers
- Developing innovations and testing their potential impact
- Empowering a new generation of leaders to meet the challenges ahead

Administering meningitis vaccine in Burkina Faso
Credit: Compassion International

Building a BioACCESS community

- **Multidisciplinary** approach to achieving access-by-design
- **Convening** faculty from around the MIT campus and surrounding institutions

Jónas Jónasson
Operations Management, MIT

Sara Fisher Ellison
Economics, MIT

Veronika Wirtz
Global Health, BU

Reuben Domike
Manufacturing Technology, BYU

Amy Moran-Thomas
Anthropology, MIT

Rajeev Ram
Electrical Engineering, MIT

Key components of *Access-by-Design*

- Evidence-based learning
  - Identifying systematic barriers impeding access
  - Learning from successes and failures in small molecule / vaccines access
  - Modeling future scenarios
- Systems evaluation & optimization
  - Re-envisioning product development for access in LMICs
  - Optimize benefit/risk for all stakeholders in the system
  - Patient-centered product profiles for resource-limited settings
- *Mens et Manus* (technology development projects)
  - Leverage the best of MIT's Schools of Science, Engineering and Management to develop disruptive solutions in technology, manufacturing, supply chain management and policy

Impact of manufacturing models on global supply security

Centralized	De-centralized	Distributed	Point-of-Care
1 site in 1 region	n sites in 1 region	n sites in n regions	DIY – district/clinic level

Business drivers

- First-to-enter emerging markets
- Compulsory in-country manufacturing
- Flexibility to respond to changing demand
- Invest in local biotech industry to boost economy
- Reduce supply dependence

Technology drivers

(Semi-) continuous systems

Process intensification / automation

Single-use technology

Emerging manufacturing platforms

Just biotherapeutics for all

UNIVERCELLS

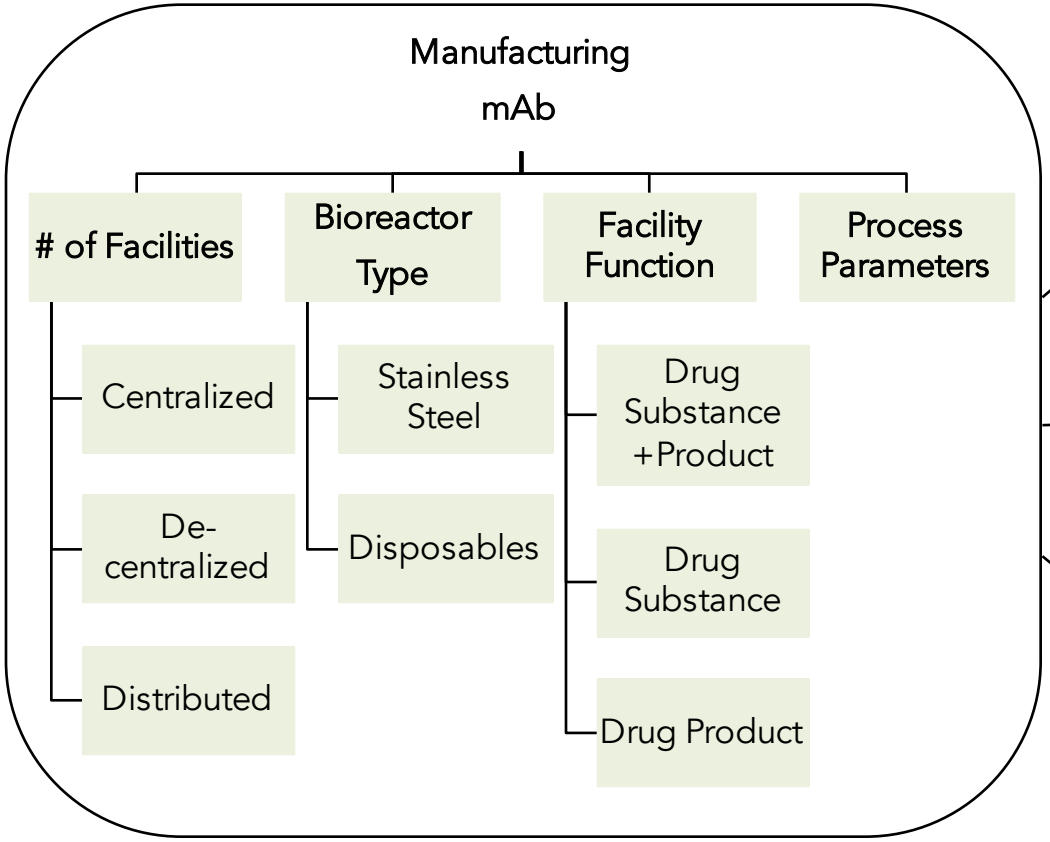
ultra

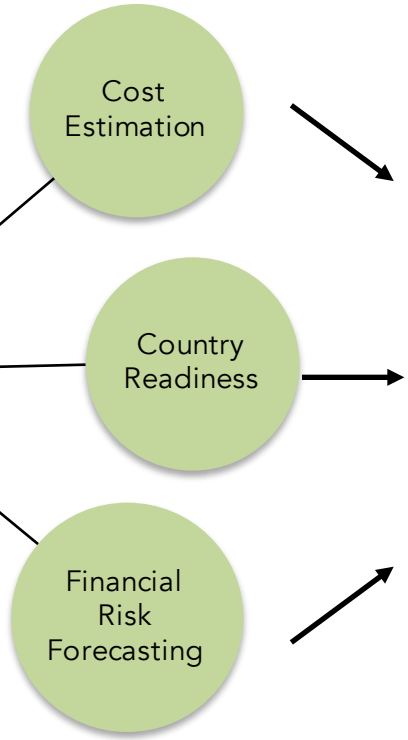
Economic evaluation of manufacturing innovations

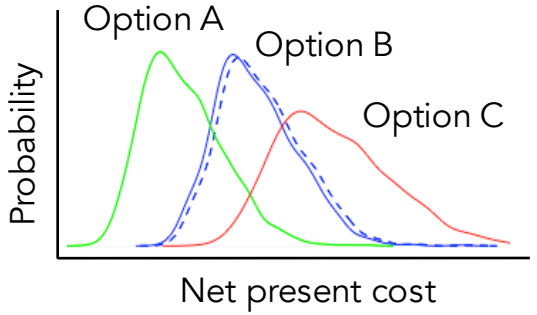
Design Options

Simulating Scenarios

Evaluating Tradeoffs





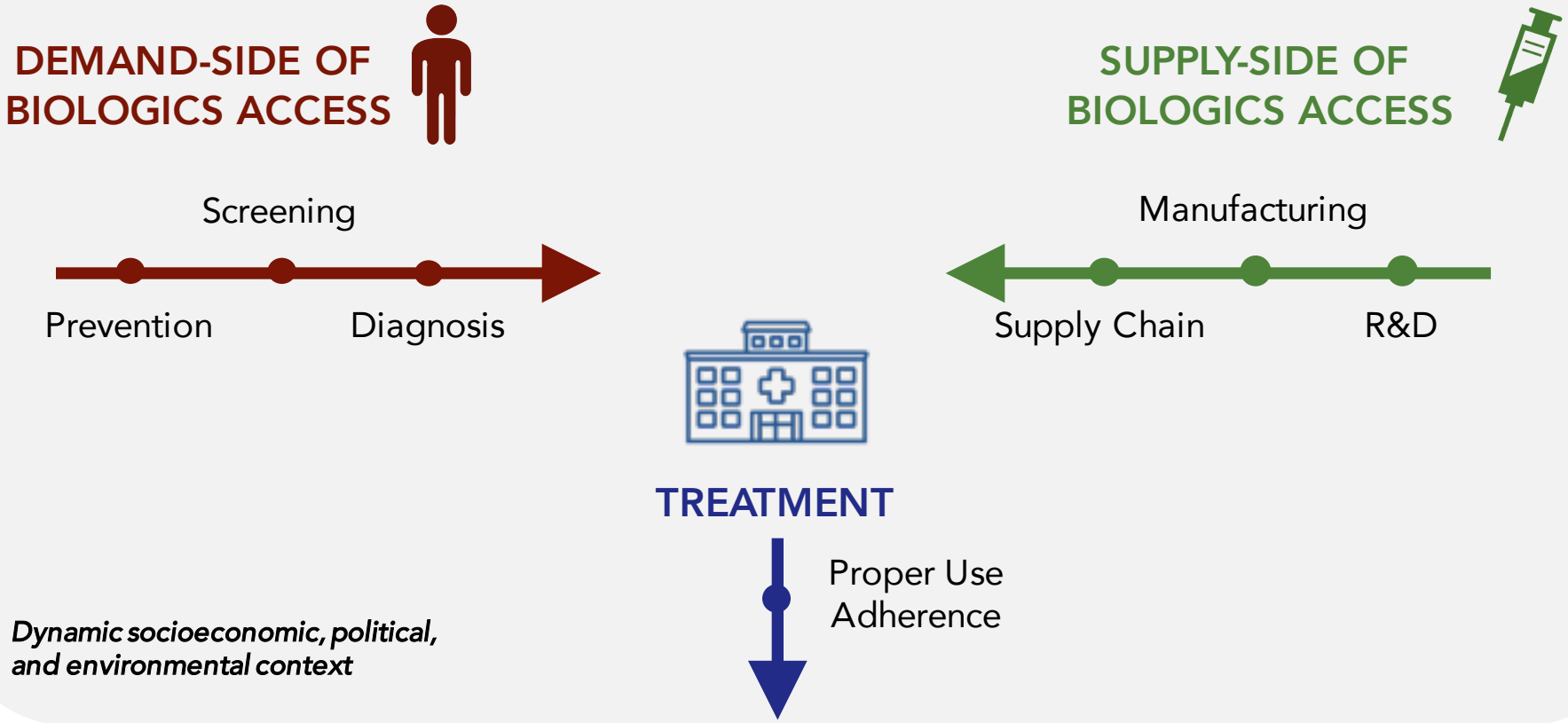


Criteria for evaluation:

- ❑ COGs & 10-yr NPC
- ❑ Time to market
- ❑ Supply security
- ❑ Technology transfer
- ❑ Other factors

(e.g. geographic proximity of facilities)

Integrated, whole-of-system approach to access



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Advances in Diagnostic Technology to Support Global Access

Dr. Rajeev Ram

Professor of Electrical Engineering and Computer Science, MIT

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Requirements for high impact diagnostics in the developing world

http://www.nature.com/diagnostics

World Health Organization

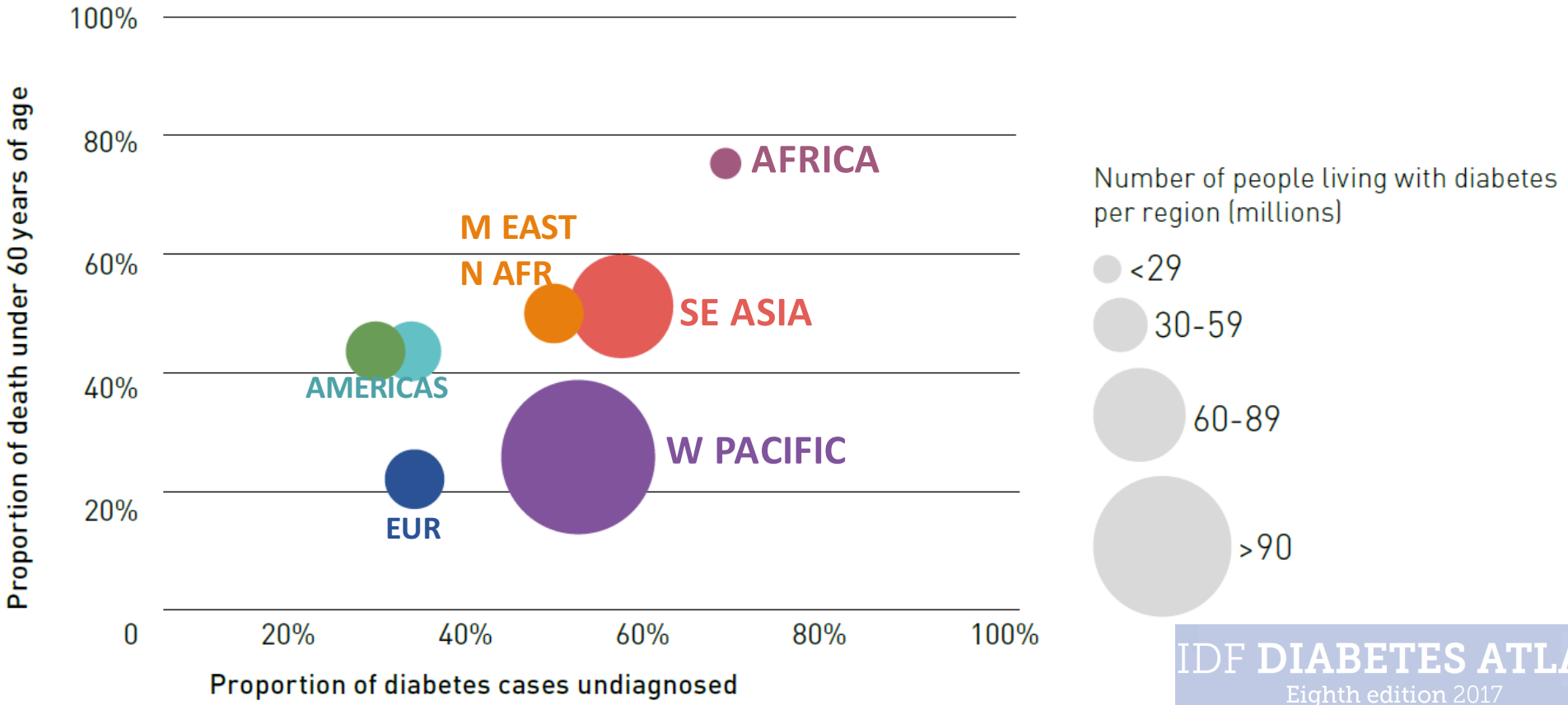
	Health-care setting (personnel)	Summary of resources and capabilities
No laboratory infrastructure	In the community or home (possibly health-care worker, pharmacist or family member)	No electricity or clean water available; no t room temperature not controlled; venipunc required to prescribe treatment before pati
Minimal laboratory infrastructure	Health clinics in Africa; rural health clinics in Latin America and Asia (nurse)	No reliable electricity and clean water; min occasionally available; room temperature r rapid answer required to prescribe treatme
Moderate to advanced laboratory infrastructure	Urban health clinics in Asia and Latin America; hospitals in Africa, Latin America and Asia (nurses, technicians and physicians)	Dependable electricity and clean water ava storage available; room temperature some children); time to answer usually less cruci physician oversight routine.

Characteristics of the ideal diagnostic test for the developing world: ASSURED

- **A**ffordable by those at risk of infection.
- **S**ensitive (few false-negative results).
- **S**pecific (few false-positive results).
- **U**ser-friendly (simple to perform by persons with little training).
- **R**apid treatment at the first visit and robust use without the need for special storage.
- **E**quipment-free (that is, no large electricity-dependent instruments needed to perform the test; note that portable handheld battery-operated devices are acceptable, which differs from the criterion of the original authors).
- **D**elivered to those who need it

Undiagnosed Diabetes

Proportion of early deaths, undiagnosed diabetes and number of diabetes per region.



IDF DIABETES ATLAS
Eighth edition 2017

Deeper Dive: Diagnosing Diabetes

INITIAL lab glucose

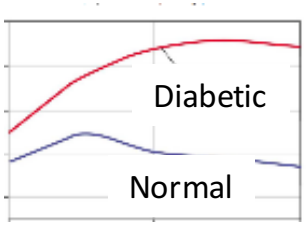
random glucose 7.8 – 11.0 mmol/L

suitable for HbA_{1C}?

NO

OGTT

	not diabetic	high risk	diabetes
fasting glucose	≤6.0	6.1 – 6.9	≥ 7.0
AND / OR	AND	OR	OR
2-hr glucose	≤7.7	7.8 – 11.0	≥ 11.1

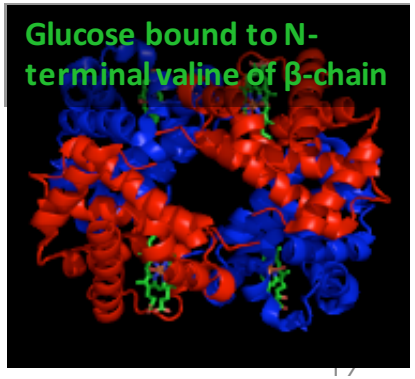


YES

HbA_{1C}

not diabetic	high risk	diabetes
≤41 mmol/mol	42 – 47 mmol/mol	≥48 mmol/mol

- Abnormal red cell turnover
- Abnormal haemoglobin
- Renal disease
- Liver disease
- Pregnancy



HbA1c in the Field

Selecting an A1C Point-of-Care Instrument

Heather P. Whitley,[1,2] Ee Vonn Yong,[1] and Casey Rasinen[1]

DOI: 10.2337/diaspect.28.3.201

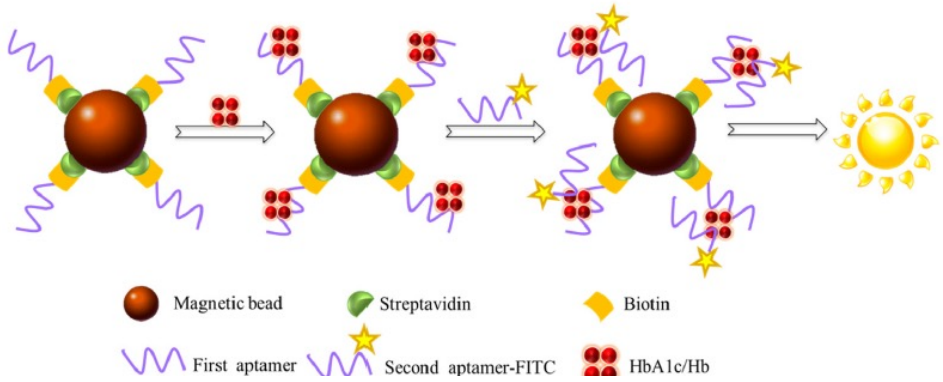
Characteristic	Bayer A1CNow (22)	Axis-Shield Afinion (21)	Siemens DCA Vantage (20)
Assay methodology	Immunoassay	Boronate affinity separation	Immunoassay (latex agglutination inhibition)
Blood sample size (µL)	5	1.5	1
Analysis time (min)	5	3	6
Reporting A1C range (%)	4.0–13.0	4.0–15.0	2.5–14.0
Storage	• Store the test kit refrigerated (2–8°C) until the expiration date or at room temperature (15–25°C) for up to 4 months.	• Store the test kit refrigerated (2–8°C) until the expiration date or at room temperature (15–25°C) for up to 3 months.	• Store the test kit refrigerated (2–8°C) until the expiration date or at room temperature (15–25°C) for up to 3 months.
Approximate cost per unit (prices vary by distributor)	$40 for unit with 2 cartridges (for the home-use version) $170 for unit with 20 cartridges	$3,500 for base station $120 for 15 single-use testing kits $60 for 2 control sets	$2,100–3,600 for base station $75 for 10 single-use testing kits $60 for 2 control sets

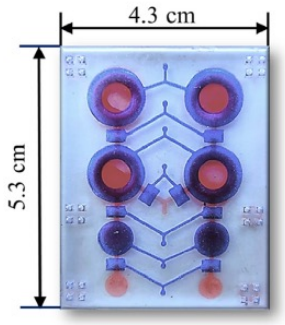
Costs ($7+/test) and supply chain for reagents becomes challenging

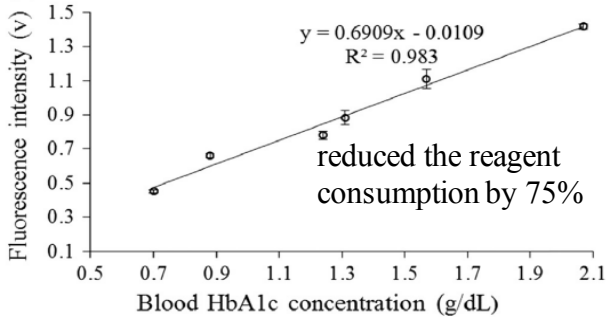
Next Generation Instrumentation: Microfluidics

On-chip, aptamer-based sandwich assay for detection of glycated hemoglobins via magnetic beads ☆

Jinglun Li[a], Ko-Wei Chang[a], Chih-Hung Wang[a], Ching-Hsuan Yang[d], Shu-Chu Shiesh, Gwo-Bin Lee[a,b,c,**]



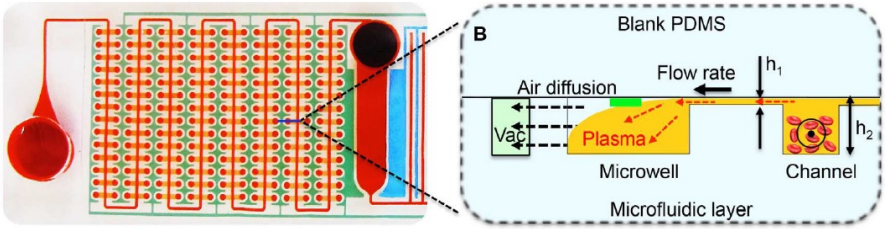


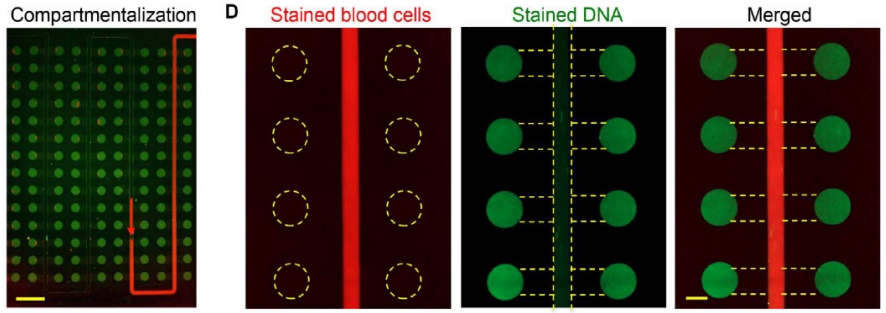


reduced the reagent consumption by 75%

Self-powered integrated microfluidic point-of-care low-cost enabling (SIMPLE) chip

Erh-Chia Yeh,[1,2] Chi-Cheng Fu,[1,2] Lucy Hu,[1] Rohan Thakur,[1] Jeffrey Feng,[1] Luke P. Lee[1,2]





Lessons from Glucose Test Strips

Cost to manufacture: ~ $0.15

Glucose oxidase electrode + ferricyanide mediator + electrode

Sale price in West: ~ $0.35-$1

Annual glucose testing/person: $80/yr

Medical Devices: Evidence and Research 2018:11 51–56

Glucose testing costs:

Senegal	$2-2.5
Gambia	$2-2.5
Mali	$2.38

L.A. Motta, et al., Point-of-care testing improves diabetes management in a primary care clinic in South Africa, Prim. Care Diab. (2017), http://dx.doi.org/10.1016/j.pcd.2016.09.008

Non-Invasive Glucose Detection

Open Access Full Text Article

REVIEW

Disruption in the diabetic device care market

"It should be noted that the performance of GlucoTrack is inferior to that of current SMBG and CGMs, mainly due to the indirect non-invasive nature of the measurement that subjects it to suffer from a relatively low signal-to-noise ratio. For this reason, GlucoTrack should not be used for diagnosis and medications intake or treatment decisions should not be based only on measurements obtained by it."

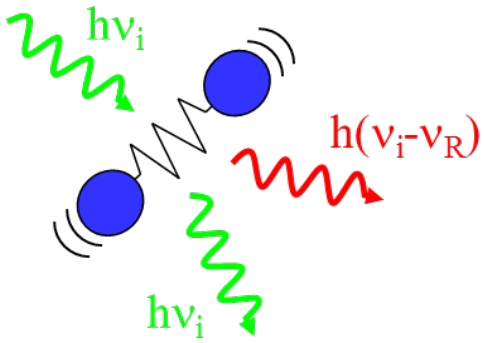
JOURNAL OF DRUG ASSESSMENT, 2018
VOL. 7, NO. 1, 1–7
https://doi.org/10.1080/21556660.2018.1423987

Ultrasonic + Conductivity + Heat Capacity

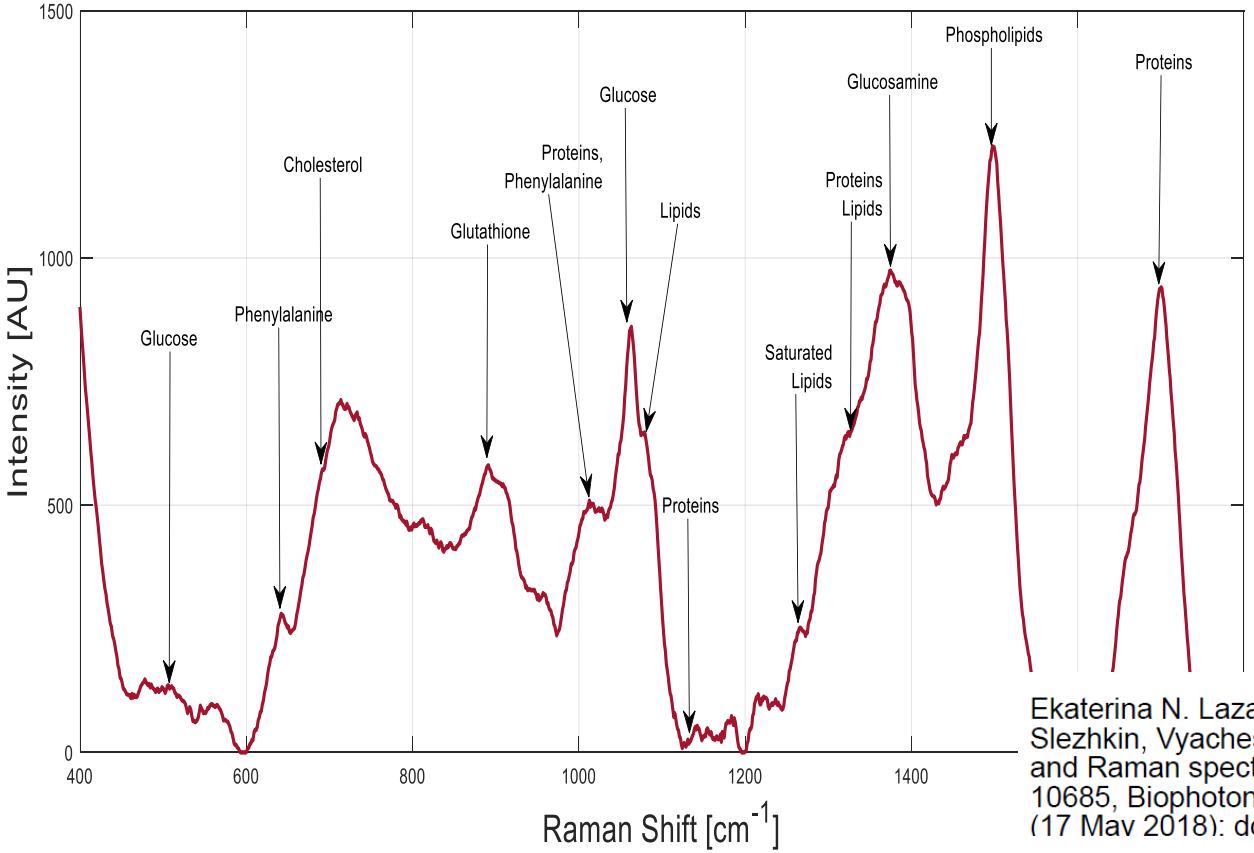
Emerging Markets: Clinical Spectroscopy

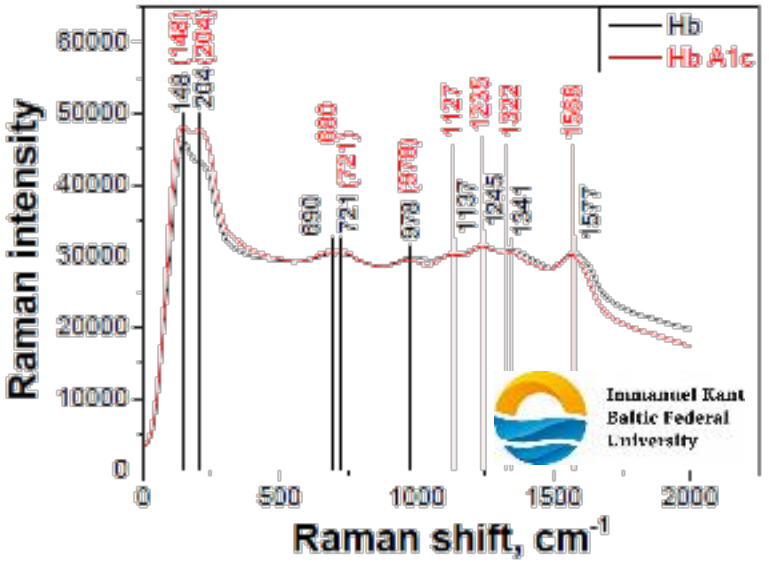
Chem Soc Rev. 2016 March 29; 45(7): 1958–1979. doi:10.1039/c5cs00581g

Disease	Group	Publication Year	Patient Number	Specificity (%)	Selectivity (%)
Barrett's esophagus	Huang et al	2014	373	87 (high grade	84.7
Cervical precancer	Mahadevan-Jansen et al.	2011	172	96.5 (dysplasia)	97.8
GI cancer	Huang et al.	2011	164	92.5 (bevelled probe)	93.1 (bevelled probe)
GI cancer	Huang et al.	2014	450	81.3 (prospective)	88.3
Oral cancer	Gupta et al.	2014	199	96 (malignant)	99 (normal)
Skin cancer	Zeng et al.	2012	453	90 (cancer vs. benign)	64



Reagentless Blood Diagnostics: Raman Spectroscopy





Ekaterina N. Lazareva, Andrey Y. Zyubin, Ilya G. Samusev, Vasiliy A. Slezhkin, Vyacheslav I. Kochubey, Valery V. Tuchin, "Refraction, fluorescence, and Raman spectroscopy of normal and glycated hemoglobin," Proc. SPIE 10685, Biophotonics: Photonic Solutions for Better Health Care VI, 1068540 (17 May 2018); doi: 10.1117/12.2307102

The Landscape is Changing Rapidly

Hardware

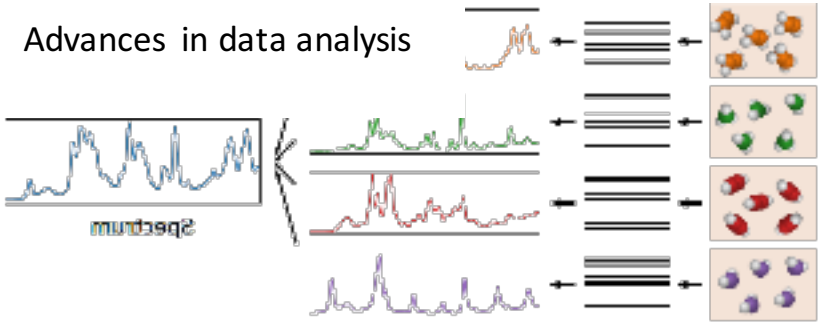
For low-value add, hardware needs to be cheap

cheap lasers

cheap sensors

Computation

Advances in data analysis



Requirements for high impact diagnostics in the developing world

http://www.nature.com/diagnostics

World Health Organization

Characteristics of the ideal diagnostic test for the developing world: ASSURED

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- **S**ensitive (few false-negative results).
- **S**pecific (few false-positive results).
- **U**ser-friendly (simple to perform by persons with little training).
- **R**apid treatment at the first visit and robust use without the need for special storage.
- **E**quipment-free (that is, no large electricity-dependent instruments needed to perform the test; note that portable handheld battery-operated devices are acceptable, which differs from the criterion of the original authors).
- **D**elivered to those who need it

Equipment-lite
Reagent-free
Supply-chain tolerant