Infectious diseases POCT: How to translate into public health benefits?

Marc Struelens, Eeva Broberg, Katrin Leitmeyer
Microbiology Coordination Section, ECDC

8th Eurosurveillance Scientific Seminar, ESCAIDE, Stockholm, 27 November 2019

POCT: some official definitions

- Health Canada, 2016: **POCT** is performed near to, or at the site of, the patient, such as in a health care professional's office, a clinic, a pharmacy or at the bedside.

- EU Regulation (2017/746, Art 2)
  - **self-testing** device: intended to be used by lay persons;
  - **near-patient testing** device: intended to perform testing outside a laboratory environment, generally near to, or at the side of, the patient **by a health professional.**

- International Standard Organisation (ISO 15189:2012; ISO 22870:2016) : **POCT:** testing, performed near or at the site of a patient, with the **result leading to possible change in the care of the patient.**

Sources: https://www.cadth.ca/sites/default/files/pdf/es0308_point_of_care_testing.pdf
ISO 22870:2016(en) Point-of-care testing (POCT)- Requirements for quality and competence
Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices

POCT: a working definition

Person

- Test prescribed and used by a healthcare professional (not specialist in laboratory medicine).

Place

- near the patient, outpatient clinic or bedside (outside the "central laboratory").

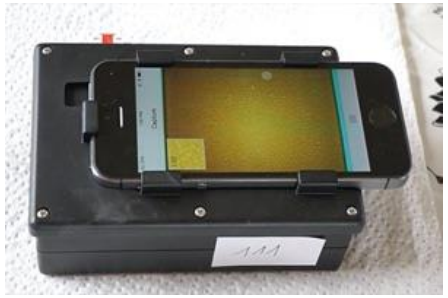
Time

- Sample collected and tested immediately at the time of patient presenting
- Results rapidly used for initial patient care and/or infection control management.

What does "outside the lab" mean in 2019?

From the central lab to "near-to-patient" satellite sites:

- "Statim lab": Emergency Room, ICU and primary care clinics
- Mobile Lab-in-a-container/suitcase: field treatment centres
- Desktop Lab-in-a-box: automated real-time PCR
- Smartphone-accessory: immunoassay cartridge, microscope
- Lab-on-a-chip: lap-top-connected real-time DNA sequencer



Smartphone micro-video-diagnostics of *Loa loa* microfilaria

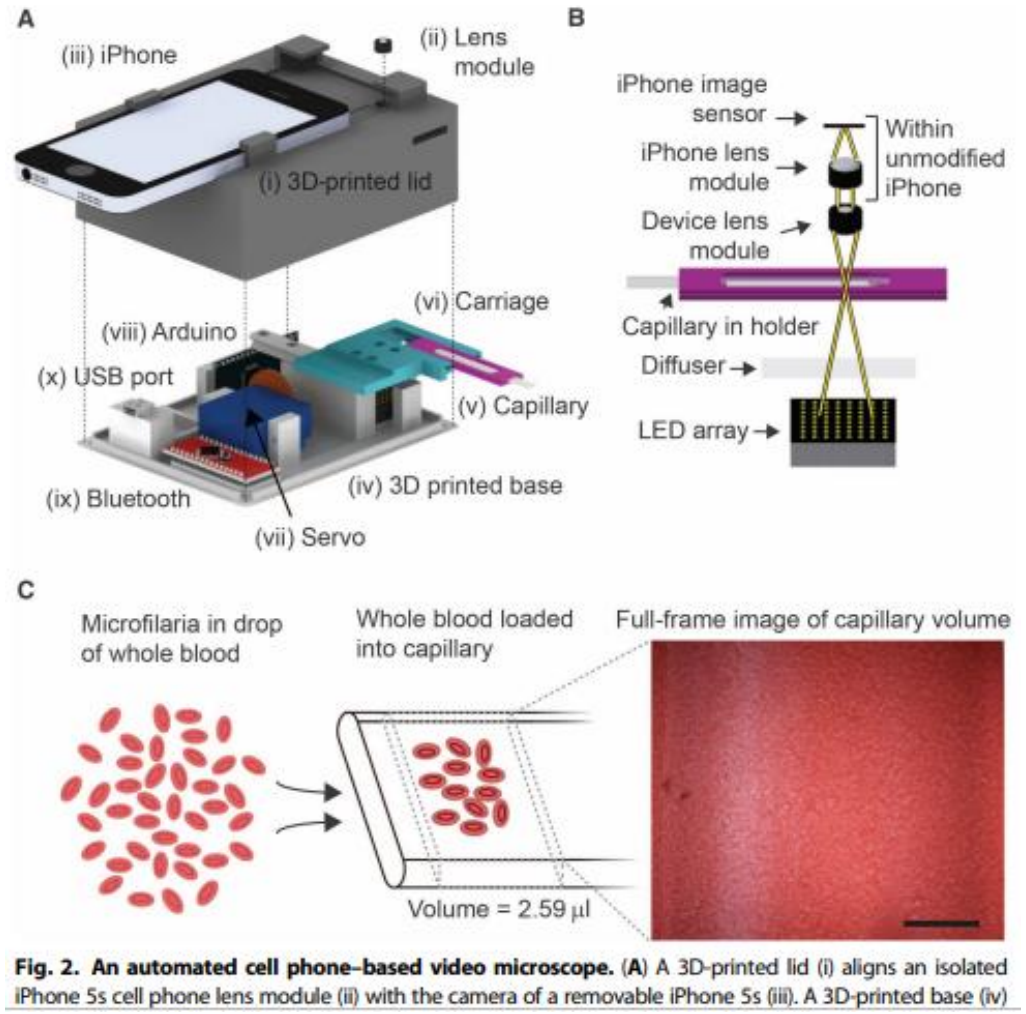


Fig. 2. An automated cell phone–based video microscope. (**A**) A 3D-printed lid (i) aligns an isolated iPhone 5s cell phone lens module (ii) with the camera of a removable iPhone 5s (iii). A 3D-printed base (iv)

Turnaround-time (TAT): 2 minutes

Negative predictive value: 99.7%

"test and (not) treat" strategy

- Use at the point of care in Central Africa
- To exclude patients at risk of adverse event from ivermectin treatment
- Allows safe expansion of mass drug administration programs for onchocerciasis and lymphatic filariasis

Source: D'Ambrosio et al. www.*ScienceTranslationalMedicine* 2015:7:286; Kamgno J et al *N Engl J Med* 2017; 377:2044-2052

The clinical microbiology service: information provider across the health care continuum

National & international epidemiologic networks

Public health agencies

Reference laboratories

Clinical microbiology

Infection control committee

Infectious diseases Service

Drugs and therapeutics committee

Infection control team

Clinical teams

Pharmacy Antimicrobial stewardship team

The microbiology laboratory service outputs

Patient care

- Timely and quality-assured diagnosis
- Organism identification and drug susceptibility with guidance for treatment
- Hospital AMR surveillance for up-to-date empiric therapy guidelines

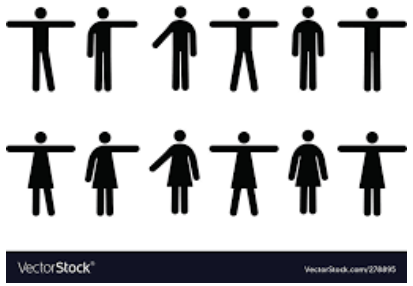
Infection control

- Early identification of local or regional outbreaks/incidents
- Molecular typing of organisms to solve outbreaks
- Screening MDROs for additional precautions (isolation, decolonisation)

Public health surveillance

- Consistent collection, coding and reporting of results (LIMS)
- Timely data reporting for event early warning

POCT: clinical, monetary and public health benefits



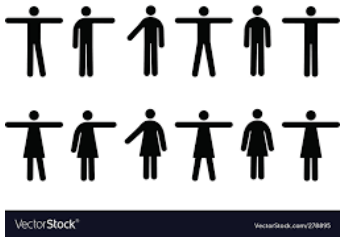
- Less invasive, patient-friendly sample collection
- Increased diagnostic access and outreach
- Decreased turnaround time leading to timely treatment
- Less hospital admissions and reduced length of hospital stays
- Reduction in inappropriate use of antimicrobial drugs
- Reduction in gut "dysbiosis" and antimicrobial resistance
- Early treatment reduces onward transmission
- Triage and isolation reduce onward transmission

POCT: potential pitfalls and safety issues

More expensive unit price than a test conducted in a central laboratory.

Operator errors (lack of clinical staff training, supervision and quality assurance).

Lack of connectivity of results to the patient medical record.



Lack of transmission of results to public health authorities.

Lack of transmission of isolates to public health laboratories.

Failure to clean and disinfect POCT devices can lead to disease transmission.

The in vitro diagnostic medical devices regulation (EU) 2017/746: A watershed moment for IVDs

Currently ~90% of devices self-certified

~85% of devices will need notified body oversight for the 1st time

Source: European commission, DG GROW, EVD-LabNet meeting, November 2019

Regulation 2017/746/EU on In vitro diagnostic devices

- **Device scope expansion**: instruments, reagents, software and kits.
- **Near patient testing (=POCT) devices:** subject to a premarket approval.
- **Reclassification of devices according to risk:** from Class A for low risk devices to Class D for high risk devices. **ID devices** in **class C and D.**
- **More rigorous clinical evidence:** Manufacturers to provide stronger evidence of device safety and performance according to risk class.
- **More rigorous device verification and post market surveillance**.

The (accredited) medical laboratory testing process

Conventional

Preanalytic	Analytic	Postanalytic
Collection Transport	Processing Testing	Reporting Intervention

Turnaround time

ISO 15189— Requirements for medical laboratories quality and competence

- Laboratory Information Management System (LIMS)
- Director competent in laboratory medicine

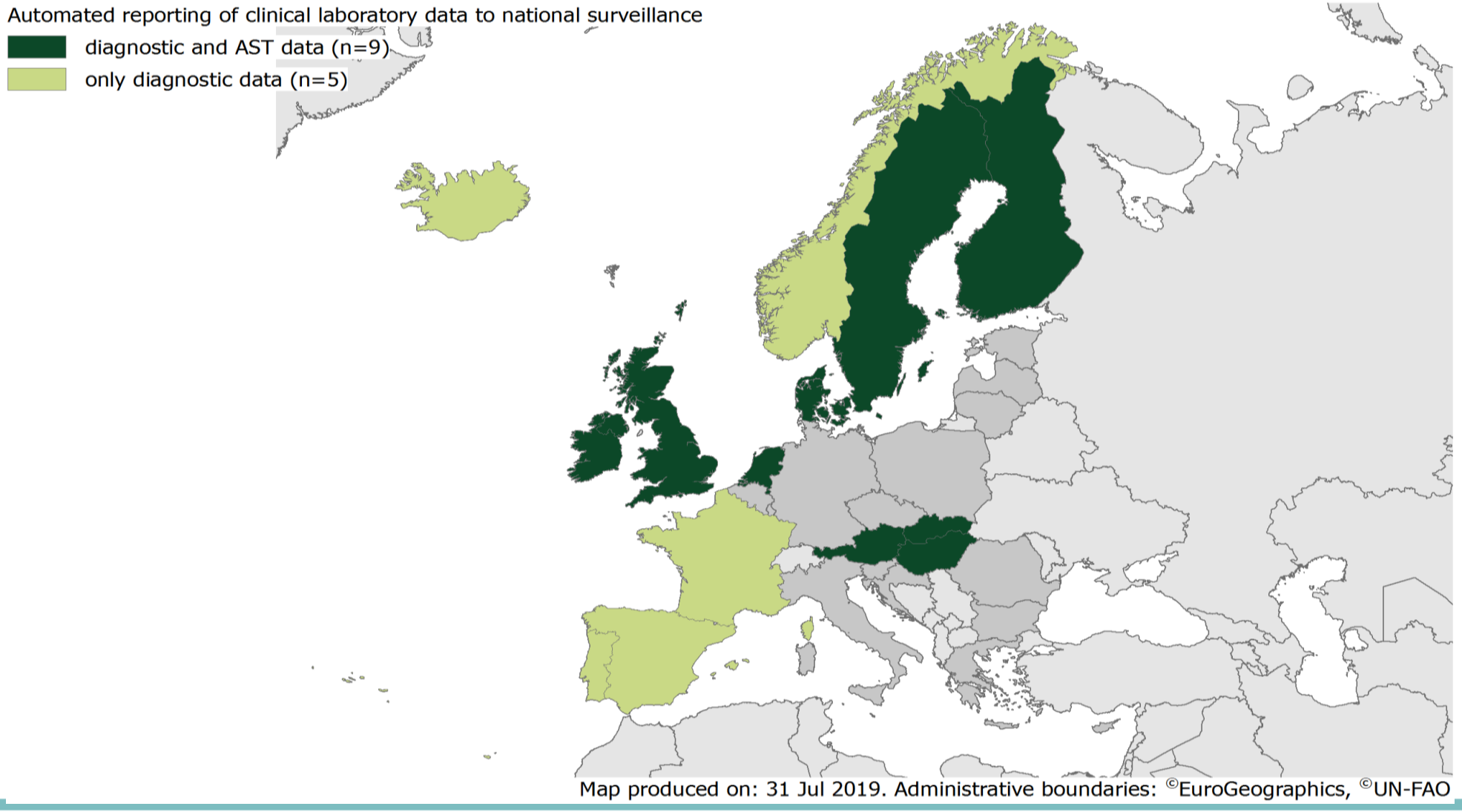
CT

ytic	Post analytic
Collection ~~Transport~~	~~Processing~~ Testing	~~Reporting~~ Intervention

Turnaround time

Source: Adapted from Diekema DJ. *Clin Infect Dis. 2013*; 56 (11): 1614-1620 and ISO Standard 15189:2012 (the International Organization for Standardization)

Clinical LIMS data reporting by machine-to-machine to national surveillance systems, by data type, EU/EEA 2018



Source: Leitmeyer K et al; NMFP EU/EEA survey 2018, submitted

Adapting surveillance of foodborne diseases to culture-independent POCT: the Canadian approach

Active engagement between primary diagnostic laboratories and provincial public health laboratories to determine:

- Workflow and protocols for culture of POCT-positive samples;
- Best practices to enhance recovery and referral of bacterial isolates;
- Modification of notifiable disease definitions.

Canadian Public Health Laboratory Network position statement. *Can Commun Dis Rep*. 2017;43(12);279-81.

POCT for STI screening and management

- Oral saliva POC tests for HIV, HCV and syphilis antibodies for self-testing.
- POC STI tests can be used to expand screening, improve syndromic management and reduce loss to follow up.
- Increasing equity and access to testing and accelerated treatment initiation.
- New social and financial models of community-based testing services.
- New challenges in linkage to care, quality assurance, partner services and monitoring of disease trends.

Source: Tucker J et al *Curr Opin Infect Dis*. 2013; 26(1): 73–79

Public health guidance on HIV, hepatitis B and C testing in the EU/EEA - An integrated approach

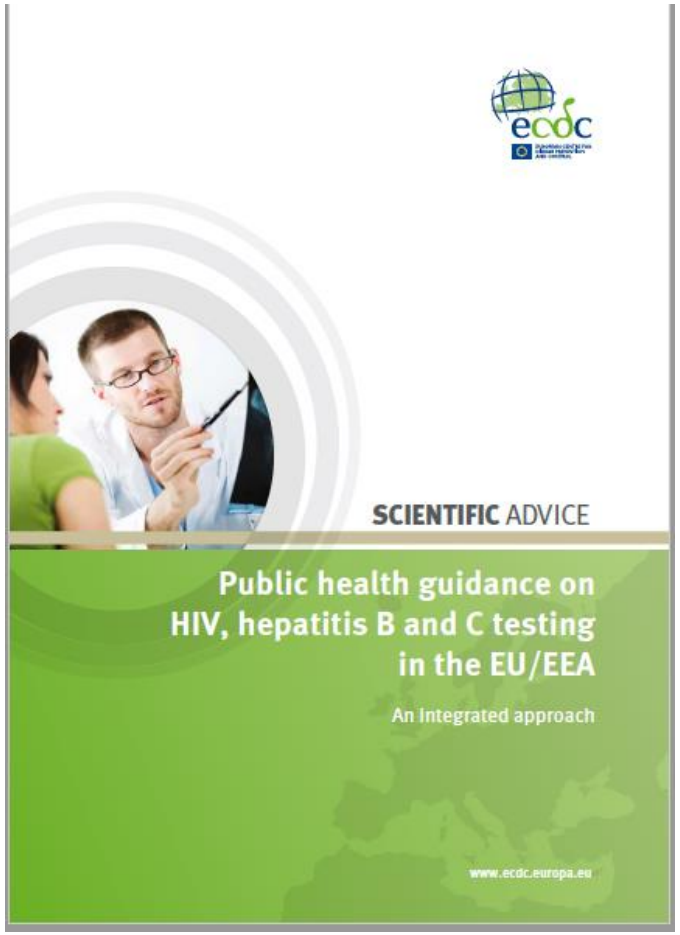
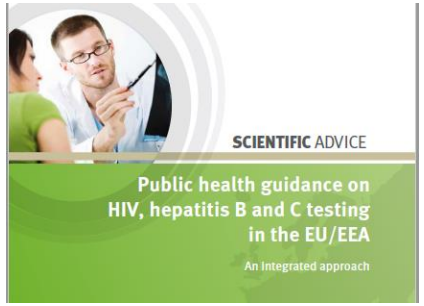


Figure 1. Core principles of integrated testing of HBV, HBC and HIV

Source: Public health guidance on HIV, hepatitis B and C testing in the EU/EEA – An integrated approach. Stockholm: ECDC; 2018.



ECDC guidance: HIV, hepatitis B and C testing in the EU/EEA

Where, how and when to test: evidence-based options of testing in:

- All healthcare settings
- Primary healthcare
- Hospital care
- Other settings (e.g. STI clinics, pharmacies, prisons, …)
- Community settings (including self-testing).

Source: Public health guidance on HIV, hepatitis B and C testing in the EU/EEA – An integrated approach. Stockholm: ECDC; 2018.

ECDC-RAND Europe POCT project, 2019-2020.

To obtain an overview of available POCT devices for EU notifiable communicable diseases and related health issues.

To map the use of POCT devices in clinical infectious disease management and public health practice in the EU/EEA.

To hold a technical expert consultation on their impact on and opportunities for disease surveillance, prevention and control.

Source: E. Broberg, ECDC; RAND Europe.

How to translate POCT into public health benefits?

1. Disease prevention and control

- ***Industry***
- develop adaptive, multiplex POCT devices, including for emerging diseases and drug resistance
- ***EU and National IVD regulators***
  - pre/post-market validation of POCT accuracy and medical added value
- ***National regulators of laboratory medicine***
  - POCT use supervised by accredited clinical diagnostic laboratory service providers to ensure QA and connect devices to LIMS
- ***Public health authorities***
  - National integrated testing strategies linked to care and prevention programme evaluation

How to translate POCT into public health benefits?

2. Surveillance and alert

- ***POCT results e-reporting***
  - from diagnostic LIMS to public health e-surveillance systems at national and EU levels
- **"Reflex culture"**
  - clinical laboratories incentive/obligation to culture POCT positive samples and refer isolates to NRL
- ***Metagenomics- POCT***
  - extraction of WGS and drug resistance data for surveillance

POCT beyond medicine: we can make it a tool for Precision Public Health!

Precision Medicine: "Delivering the right treatment at the right time, every time to the right person." (Obama, 2015).

Precision Public Health: "Improving the ability to prevent disease, promote health and reduce health disparities in populations through the application of technology and the development of targeted programs and health policy" (Khoury 2018)

Delivering the right intervention at the right time, every time to the right population.

Source: Weeramanthri TS. Editorial *Front. Public Health*, 30 April 2018 | https://doi.org/10.3389/fpubh.2018.00121