IMPACT OF TESTS ON DIAGNOSTIC AND CLINICAL DECISIONS

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Phased evaluation of medical tests: Diagnostic thinking efficacy

Levels/Phases
Technical efficacy
Intended use
Diagnostic accuracy
Usual range
Subgroups
Clinical population
Diagnostic thinking efficacy
Therapeutic efficacy
Patient outcome efficacy
Societal efficacy

Proposals for a Phased Evaluation of Medical Tests

Jeroen G. Lijmer, MD, PhD, Mariska Leeflang, PhD, Patrick M. M. Bossuyt, PhD

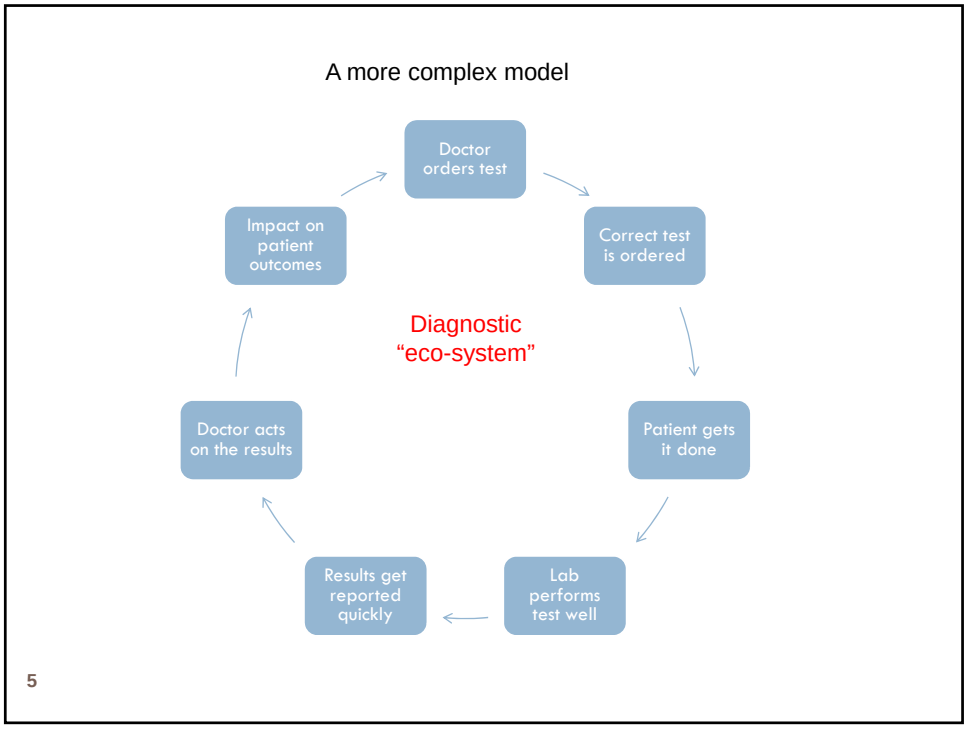
Med Desic Making 2009

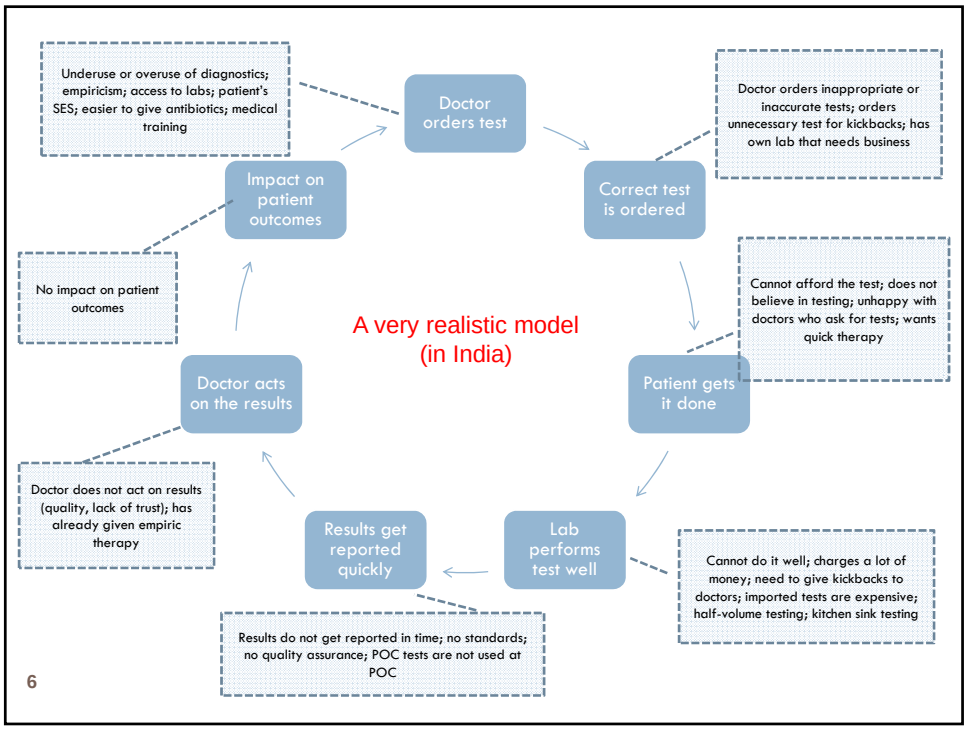
Why does it matter?

- Why order tests if the results do not make any difference to clinical decisions?
- Test results will have an impact on patient outcomes, provided they correctly guide clinical decisions made by physicians

Change in physician's decisions or behavior is an intermediate step for improvement in patient outcomes

A simplistic model


A more complex model
Doctor orders test
Correct test is ordered
Patient gets it done
Lab performs test well
Results get reported quickly
Doctor acts on the results
Impact on patient outcomes
Diagnostic "eco-system"
5


Underuse or overuse of diagnostics; empiricism; access to labs; patient's SES; easier to give antibiotics; medical training
Doctor orders test
Doctor orders inappropriate or inaccurate tests; orders unnecessary test for kickbacks; has own lab that needs business
Impact on patient outcomes
Correct test is ordered
No impact on patient outcomes
Cannot afford the test; does not believe in testing; unhappy with doctors who ask for tests; wants quick therapy
A very realistic model (in India)
Doctor acts on the results
Patient gets it done
Doctor does not act on results (quality, lack of trust); has already given empiric therapy
Results get reported quickly
Lab performs test well
Cannot do it well; charges a lot of money; need to give kickbacks to doctors; imported tests are expensive; half-volume testing; kitchen sink testing
Results do not get reported in time; no standards; no quality assurance; POC tests are not used at POC
6

Example: influenza RIDTs

Impact of Rapid Diagnosis on Management of Adults Hospitalized With Influenza

ARCHIVES EXPRESS

Ann R. Falsey, MD; Yoshihiko Murata, MD, PhD; Edward E. Walsh, MD

Background: Rapid influenza testing decreases antibiotic and ancillary test use in febrile children, yet its effect on the care of hospitalized adults is unexplored. We compared the clinical management of patients with influenza whose rapid antigen test result was positive (Ag+) with the management of those whose rapid antigen test result was negative or the test was not performed (Ag0).

Methods: Medical record review was performed on patients with influenza hospitalized during 4 winters (1999-2003). Hospital policy mandated influenza testing (antigen or culture) for all patients with acute cardiopulmonary diseases admitted from November 15 through April 15. A subset of patients participated in an epidemiological study and had reverse-transcriptase polymerase chain reaction or serologic testing performed. Clinical data from Ag+ and Ag0 patients were compared.

Results: Of 166 patients with available records, 86 were Ag+ and 80 were Ag0. Antibiotic use (74 [86%] of 86 patients vs 79 [99%] of 80 patients; $P = .002$) was less and antibiotic discontinuance (12 [14%] of 86 patients vs 2 [2%] of 80 patients; $P = .01$) was greater in Ag+ compared with Ag0 patients. No significant differences in antibiotic days, length of hospital stay, or antibiotic complications were noted. Antiviral use (63 [73%] of 86 patients vs 6 [8%] of 80 patients; $P < .001$) was greater in Ag+ than Ag0 patients. Antigen status was independently associated with withholding or discontinuing antibiotics in multivariate analysis. Of 44 Ag+ patients deemed low risk for bacterial infection, 27 continued to receive antibiotics despite positive influenza test results. These patients more commonly had pulmonary disease and had significantly more abnormal lung examination results ($P = .005$) compared with those in whom antibiotics were withheld or discontinued.

Conclusions: Rapid influenza testing leads to reductions in antibiotic use in hospitalized adults. Better tools to rule out concomitant bacterial infection are needed to optimize the impact of viral testing.

Arch Intern Med. 2007;167:354-360

Example: malaria RDTs

Kyabayinze *et al. Malaria Journal* 2010, **9**:200
http://www.malariajournal.com/content/9/1/200

MALARIA JOURNAL

RESEARCH Open Access

Use of RDTs to improve malaria diagnosis and fever case management at primary health care facilities in Uganda

Daniel J Kyabayinze*[1], Caroline Asiimwe[1], Damalie Nakanjako[2], Jane Nabakooza[3], Helen Counihan[4] and James K Tibenderana[1,5]

Abstract

Background: Early and accurate diagnosis of malaria followed by prompt treatment reduces the risk of severe disease in malaria endemic regions. Presumptive treatment of malaria is widely practised where microscopy or rapid diagnostic tests (RDTs) are not readily available. With the introduction of artemisinin-based combination therapy (ACT) for treatment of malaria in many low-resource settings, there is need to target treatment to patients with parasitologically confirmed malaria in order to improve quality of care, reduce over consumption of anti-malarials, reduce drug pressure and in turn delay development and spread of drug resistance. This study evaluated the effect of malaria RDTs on health workers' anti-malarial drug (AMD) prescriptions among outpatients at low level health care facilities (LLHCF) within different malaria epidemiological settings in Uganda.

Methods: All health workers (HWs) in 21 selected intervention (where RDTs were deployed) LLHF were invited for training on the use RDTs. All HWs were trained to use RDTs for parasitological diagnosis of all suspected malaria cases irrespective of age. Five LLHCFs with clinical diagnosis (CD only) were included for comparison. Subsequently AMD prescriptions were compared using both a 'pre - post' and 'intervention - control' analysis designs. In-depth interviews of the HWs were conducted to explore any factors that influence AMD prescription practices.

Results: A total of 166,131 out-patient attendances (OPD) were evaluated at 21 intervention LLHCFs. Overall use of RDTs resulted in a 38% point reduction in AMD prescriptions. There was a two-fold reduction (RR 0.62, 95% CI 0.55-0.70) in AMD prescription with the greatest reduction in the hypo-endemic setting (RR 0.46 95% CI 0.51-0.53) but no significant change in the urban setting (RR1.01, p-value = 0.820). Over 90% of all eligible OPD patients were offered a test. An average of 30% (range 25%-35%) of the RDT-negative fever patients received AMD prescriptions. When the test result was negative, children under five years of age were two to three times more likely (OR 2.6 p-value <0.001) to receive anti-malarial prescriptions relative to older age group. Of the 63 HWs interviewed 92% believed that a positive RDT result confirmed malaria, while only 49% believed that a negative RDT result excluded malaria infection.

Conclusion: Use of RDTs resulted in a 2-fold reduction in anti-malarial drug prescription at LLHCFs. The study demonstrated that RDT use is feasible at LLHCFs, and can lead to better targetting of malaria treatment. Nationwide deployment of RDTs in a systematic manner should be prioritised in order to improve fever case management. The process should include plans to educate HWs about the utility of RDTs in order to maximize acceptance and uptake of the diagnostic tools and thereby leading to the benefits of parasitological diagnosis of malaria.

TB EXAMPLE: DOES QUANTIFERON-TB GOLD HELP WITH LTBI TREATMENT DECISIONS IN CHILDREN?

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Rationale

Children are at high risk for TB disease, if latently infected

LTBI therapy (INH preventive therapy) is a key intervention to prevent disease

IGRAs are now available for clinical use, but do they influence clinical decisions?

Introduction of QFT at the Montreal Children's Hospital

L'Hôpital de Montréal pour enfants
The Montreal Children's Hospital
Centre universitaire de santé McGill
McGill University Health Centre

MEMORANDUM

In summary, the indications for pediatrics are as follow:

1. In support for the diagnosis of active tuberculosis in children (<18 years), in combination with other microbiological tests
2. Children in contact with a case of active infectious tuberculosis with a positive PPD
3. Immunocompromised children defined as:
   a. Receiving Prednisone (2 mg/kg/day) for 14 days or more
   b. Current chemotherapy or received in the past 3 months
   c. Pre or post- bone marrow transplant
   d. HIV positive children

   In whom a clinician is still concerned about the possibility of LTBI even after a negative PPD
4. Patients with inflammatory diseases prior to starting anti-TNF medication

Objective

To prospectively determine the impact of QuantiFERON (QFT) test results on diagnostic and treatment decisions made by pediatric respirologists in routine clinical practice

Methods

- Several subgroups of children were prospectively recruited
- Concordance was calculated for pre-defined subgroups
- A clinical impact questionnaire was used to assess clinical changes based on the QFT (e.g. LTBI ➔ no LTBI)

Subgroups

- Active TB suspects
- TB contacts
- Targeted screenings: TST+, foreign-born children from school-based or immigration screenings
- Immunocompromised children
- TB clinic consults: referrals from other MCH clinics to rule out LTBI (pre-treatment, NTM, etc.)

Clinical impact questionnaire

1) My Final Diagnosis (after work-up):

____ Latent TB infection (LTBI) ____ Active TB disease ____ No TB infection or disease

2) Did QFT test play any role in making the above DIAGNOSIS?

____ Yes ____ No ____ Not applicable, QFT was not requested or results were not available to me

3) If Yes to the above question, how was it useful?

Latent TB

	TST	QFT	Decision
☐	+	--	I used the negative QFT to rule out LTBI
☐	--	+	I used the positive QFT to diagnose LTBI
☐	+	+	I used both the positive TST and QFT to diagnose LTBI
☐	?	+	I used the positive QFT to diagnose LTBI (regardless of TST result)
☐			Other explanation:

Active TB

	QFT	Decision
☐	+	I used the positive QFT and other signs/features to diagnose active TB
☐	--	I used the negative QFT to rule out active TB
☐		Other explanation:

Clinical impact questionnaire

4) If I had not ordered QFT, my diagnosis would have probably been:

____ Latent TB infection (LTBI) ____ Active TB disease ____ No TB infection or disease

5) My Final Treatment Decision (after work-up):

____ No prophylaxis for LTBI
____ LTBI prophylaxis: INH for 6 or 9 months or specify other regimen: _____
____ Active TB disease therapy

6) Did QFT test play any role in the above TREATMENT decision?

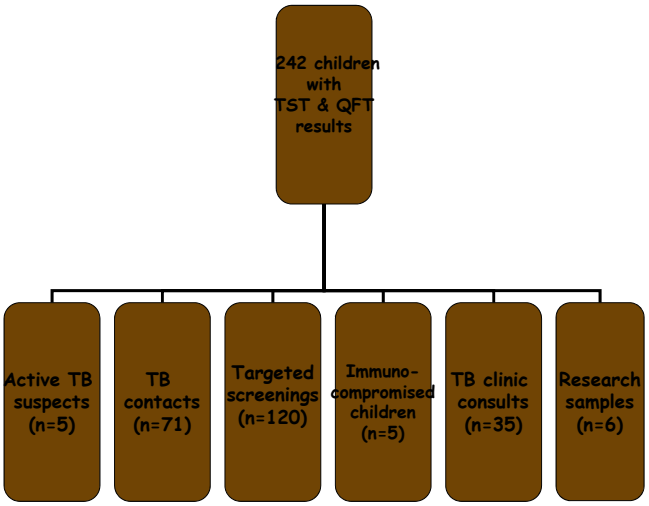
____ Yes ____ No ____ Not applicable, QFT was not requested or results were not available to me

7) If Yes to the above question, how was it useful?

	TST	QFT	Decision
☐	+	--	I used the negative QFT to withhold LTBI prophylaxis
☐	--	+	I used the positive QFT to initiate LTBI prophylaxis
☐	+	+	I used both the positive TST and QFT to initiate LTBI prophylaxis
☐	?	+	I used the positive QFT to initiate LTBI prophylaxis (regardless of TST result)
☐	Active TB	+	I used the positive QFT & other signs/features to initiate anti-TB therapy
☐			Other explanation:

Signature_____ Date_____ Chart #_____

Results



Results – Clinical Impact

Data on the clinical impact of QFT were available in 119/242 (49%) children who had already returned for their follow-up visit.

Clinical Impact

- TB contacts: In all QFT- contacts, the QFT was not used to change clinical decisions. INH was prescribed regardless of the QFT result.

TB contacts (n=71)		
	TST +	TST -
QFT +	23	0
QFT -	24	21
QFT indeterminate	2	1

Clinical Impact

- Targeted screening: The QFT changed the initial diagnosis from LTBI ➔ no LTBI in 70% of children. INH was withheld or stopped after a while.

Targeted screenings (n=120)		
	TST +	TST -
QFT +	22	X
QFT -	97	X
QFT indeterminate	1	X

Follow-up for patient outcomes

- For children not prescribed INH, follow-up with phone call to see if they have developed symptoms consistent with active TB
- Ongoing, but no TB cases thus far…
- This illustrates the importance of thinking beyond change in decisions to real patient outcomes
- There are many issues which may confound physician's behaviors – not easy to capture in research studies