Serveur Académique Lausannois SERVAL serval.unil.ch

Author Manuscript
Faculty of Biology and Medicine Publication

This paper has been peer-reviewed but dos not include the final publisher proof-corrections or journal pagination.

Published in final edited form as:

serval
serveur académique lausannois

UNIL | Université de Lausanne
Faculté de biologie
et de médecine

ORIGINAL ARTICLE

Feasibility and clinical outcomes when using practice guidelines for evaluation of fever in returning travelers and migrants : a validation study.

Yolanda Mueller*MD MIH[1], Valérie D'Acremont* MD MIH PhD[1,3], Anne-Emanuelle

Ambresin* MD[1], Isabelle Rossi*ᵞ MD MPH[1,2], Olivier Martin* Msc[1], Bernard Burnand MD

MPH[2], and Blaise Genton*# MD PhD[1,3,4]

[1]Travel Clinic, Department of Ambulatory Care and Community Medicine, University of

Lausanne, Lausanne, Switzerland

[2] University Institute of Social and Preventive Medicine (IUMSP), University of Lausanne,

Switzerland

[3] Swiss Tropical and Public Health Institute, University of Basel, Switzerland

[4]Infectious Disease Service, Department of Internal Medicine, Lausanne University Hospital,

Switzerland

Running title: Feasibility of guidelines for fever in travelers

Corresponding author:

Valérie D'Acremont, MD MIH PhD

Travel Clinic, Department of Ambulatory Care and Community Medicine

rue du Bugnon 44

CH-1011 Lausanne, Switzerland

Tel: +41 79 5562551, Fax +41 61 284 81 05

E-mail: Valerie.dacremont@unibas.ch

Abstract

Background: Practice guidelines for the evaluation of patients presenting with fever upon

return from the tropics have been developed to assist primary care physicians for decision-

making. The level of evidence available in this field is low. There was therefore a need to

validate these guidelines, and assess their feasibility in the context they have been designed

for.

Objectives: i) to evaluate physicians' adherence to recommendations, ii) to investigate

reasons for non-adherence, and iii) to ensure safety of the recommendations for the targeted

patients. The ultimate goal was to improve the quality of the guidelines, in particular to tailor

them for the needs and wishes of the target audience.

Methods: Physicians who consulted the freely available guidelines on the internet

(www.fevertravel.ch) were invited to participate to the study component. Navigation through

the decision chart was automatically recorded, including diagnostic tests performed, initial

and final diagnoses as well as final outcome. Reasons for non-adherence were investigated.

Qualitative feedback from users was also collected.

Results: 539 cases (physician/patient pairs) were included. Full adherence to guidelines was

observed in 30% of the cases. Figure-specific adherence rate was 54.8%. The main reasons

for non-adherence were: no repetition of malaria tests (111/352), no presumptive treatment in

case of febrile diarrhoea (64/153) or abdominal pain without leucocytosis (46/101). Overall,

20% of diversions from guidelines were considered reasonable. No death was recorded and all

3

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

complications could be attributed to the underlying illness rather than to adherence to

guidelines.

Conclusions: Almost one third of primary care physicians strictly adhered to the guidelines.

The others used the guidelines not to forget specific diagnoses, but finally diverge from the

proposed attitudes, partly because of the peculiarity of individual situations that cannot be

taken into account in a decision chart. Use of these guidelines proved to be feasible, useful

and safe.

Background

Validation of practice guidelines should involve, on the one hand, the demonstration of their

efficacy in improving patient outcomes and, on the other hand, the evaluation of their

implementation and their impact on physicians' practices (often expressed in terms of

adherence to, or concordance with the guidelines). The demonstration of the efficacy of

practice guidelines seen as an intervention is often not carried out, based on the assumption

that they are based on the best available evidence and hence their efficacy already proven. In

most studies, implementation of guidelines is investigated retroactively through

questionnaires to users [1,2] or group discussions involving case-scenarios (3). Another

method used is the analysis of the variation in prescription practices based on administrative

records [4,5] . Prospective evaluations, however, are rarely undertaken.

The internet has recently emerged as an efficient tool for guidelines dissemination, as well as

implementation into medical practice [6-8] . A recent meta-analysis showed four features of

decision support systems to improve clinical practice: i) automatic provision of decision

support as part of the clinical workflow, ii) provision of recommendations rather than just

assessments, iii) provision of decision support at the time and location of decision-making, iv)

computer based decision support system [9]. The World Wide Web is also becoming a

research medium to conduct studies, from experimental research [10] to randomised

controlled trials [11], questionnaire surveys [12,13] and feasibility studies [14]. Internet use

allows rapid recruitment, shortens study duration, and potentially reduces costs. Moreover, it

allows access to a large range of demographical and cultural diversity, and reduces both time

constraints and organizational problems.

Following these encouraging experiences, both in guideline dissemination and research

conduct, we developed practice guidelines for the evaluation of fever in travellers and

migrants returning from tropical/subtropical countries, according to standardized methods

5

complying with evidence-based medicine [15], and using modern computerized technologies

both for dissemination as well as evaluation. We describe here the results of a prospective

online evaluation aimed at assessing the feasibility and validity of these practice guidelines in

the clinical context they had been designed for.

Methods:

Decision tree

Guideline development was based on an evidence-based approach complemented by an

explicit international expert opinion process. The content of these recommendations has been

previously published [16]. Briefly, the decision tree can be summarized in four steps (see

figure 1). First, the characteristics of the patient's travel (destination and time of travel) are

recorded, in order to later restrict the differential diagnosis based on the known incubation

times and endemic areas of specific diseases. Secondly, a series of closed questions aims at

identifying items in the history or in the clinical examination that could be rapidly fatal and

might require immediate action ("life-threatening conditions"). Thirdly, questions about key

features of the patient's history, clinical examination, and eosinophil count are asked, each

feature corresponding to a specific figure where possible diagnoses and approaches are

suggested. The physician can then navigate through to selected figures (fourth step) and

construct his/her differential diagnosis. Since the beginning of the development process, care

was taken to design the guidelines in a format that could accommodate their computerization

in order to maximize their wide accessibility. The guidelines were made freely available on

the internet in 2003 (www.fevertravel.ch), and the website has been further refined to improve

interactivity and ease of use.

6

Study objectives

As the evidence used to construct the guidelines was considered to be of rather low quality

(mainly expert opinion), further research was needed in order to validate their content.

Therefore, in parallel with the development of the website, we designed an online study

prototype aiming at the prospective evaluation of various aspects of the guidelines. The study

objectives were i) to evaluate physicians' adherence to the recommendations, ii) to investigate

the reasons for non-adherence, and iii) to ensure the safety of the recommendations for the

targeted patients. The ultimate goal was to improve the quality of the guidelines, in particular

to tailor them for the precise needs and wishes of the target audience.

Study website

The technical features of the website have been detailed extensively elsewhere [17]. In

summary, the research part of the website contains additional features superimposed on the

basic structure of the decision tree, which enable the investigators to collect data online.

These features include: (i) an online registration form for physicians, (ii) a personal member

page, where all cases included by this user are listed, (iii) for each patient, a page recording

basic patient demographic characteristics (sex, year of birth, country of origin) and symptoms

suggesting fever, (iv) a window requesting the working diagnosis after the first consultation,

and suggesting a clinical management strategy for the following days, (v) a "final box", where

follow-up information about final diagnosis and outcome as well as a satisfaction

questionnaire are recorded 14 days after the first consultation, and (vi) "non-adherence" pop-

up windows that appear on the screen every time the physician chooses not to follow the

recommendations. In this window, he is invited to detail whether his reasons for non-

adherence was due to an alternative documented diagnosis or another reason that would be

explained in a blank text field.

Setting

The recruitment of the cases occurred in two steps. First, we conducted a pilot-study in the Department of Ambulatory Care and Community Medicine, University of Lausanne, Switzerland. This clinic serves as a teaching centre for physicians training in general medicine. It also serves as a reference centre in travel/tropical medicine for the area. Travellers coming back with a history of fever or with raised temperature were asked whether they were willing to be managed according to the computerized practices guidelines. After informed consent (recorded online), the pair physician/patient was recruited and the pathway followed by the physician in the decision tree automatically recorded. After the pilot-study, recruitment was freely accessible to anyone logging into the website (www.fevertravel.ch) and who agreed to participate to the study component. Again both physicians and patients needed to agree and state so before proceeding to the decision chart.

Data analysis

The dataset consisted of the cases recorded online. Data were recorded online into a MySql relational database. For day-to-day follow-up of the study, we used phpMyAdmin as an administration tool of the database. For data analysis, a script was created that translated the relational database into a linear database that could then be analysed using the Intercooled Stata 9 software. Data analysis was aimed at assessing adherence at two levels: first the proportion of patient/physician pairs that did not follow a specific recommendation, and second, the proportion of patient/physician pairs that did not follow all recommendations pertaining to a specific symptom or sign (corresponding to one entire figure, i.e. "figure-specific adherence"). Total adherence" refers to the sum of the figure-specific adherence results. "Adherence per patient/physician pair" refers to the results pooled by patient/physician pair. Reasons for non-adherence were then examined. If the reason for not-adhering to a recommendation was that the physician already had an alternative documented

8

diagnosis, the case was reclassified as adherent. The other reasons were further classified as

reasonable or unreasonable, as assessed by the subjective judgment of the investigators on the

basis of predefined criteria. By "reasonable diversions", we meant attitudes that did not put

the patient at increased risk (e.g. prescribing moxifloxacine for the treatment of atypical

pneumonia instead of a macrolide as suggested by the guidelines), or attitudes based on a

more thorough judgment than what was available in the guidelines (e.g. a patient that

travelled to a location where a disease was not endemic, although it was in another part of the

country) (see figure 3).

Final diagnoses were grouped in pre-defined categories, and the proportion of documented

diagnoses was given for each category. Information about follow-up was expressed in terms

of proportion of complications and proportion of patients admitted in the hospital. Final

outcome was categorized as recovered, dead, sequelae, or lost to follow-up. Qualitative

questions were asked for each patient/physician pair: help for reaching the final diagnosis,

number of investigations done, consultation of a tropical/travel medicine specialist. Blank text

fields were available, where the physician could record the worst and the best thing about the

guidelines.

Results:

Users

Overall, 539 patient/physician pairs were included in the study between February 2003 and

July 2007. The 539 cases were recorded by 116 different internet users; 85 (73%) of them

were general practitioners or internal medicine practitioners, 14 (12%) travel and/or tropical

medicine specialists, 8 (7%) infectious disease specialists, and 8 (7%) practising another

specialty. 399 cases (74%) were recruited in an outpatient setting, 130 (24%) in a hospital,

and 9 (2%) in a private practice. Cases included in Lausanne represented 62% of the total. 465

cases (86%) were included in European reference centres (Department of Ambulatory Care

and Community Medicine, Lausanne, Switzerland; Outpatient Clinic, Geneva University

Hospital, Switzerland; Institute of Tropical Medicine, Antwerp, Belgium; Leiden University

Medical Centre, Netherlands; Centre for International Health, University of Barcelona,

Spain).

Patients characteristics

The demographical and clinical characteristics of the patients are shown in Table 1. The

majority were travellers, with a mean age of 37 years and a slight predominance of males over

females (310 vs. 228). On average, they had travelled for a median of 20 days, started to have

symptoms 1 day after their return and waited another 4 days prior to attending medical

consultation. The majority (54%) of the patients were returning from Africa. Final diagnoses

are shown in Table 2. The most frequently reported diagnoses were gastroenteritis (95 cases,

18%), flu-like syndrome or virosis (82 case, 15%s), and malaria (54 cases, 10%). 34% of the

diagnoses were laboratory-confirmed (data not shown). The most frequently documented

diagnoses were malaria (48 cases), bacterial gastroenteritis (32 cases), and pneumonia (28

cases).

Figures (see table 3)

Most physicians consulted one or two figures for their patient (34% and 29% of the cases,

respectively). 96 (18%) patient/physician pairs consulted no figure and 104 (19%) consulted

at least 3 figures. The figures most frequently consulted were the figures on "diarrhoea"

(consulted by 34% of the pairs), on "abdominal pain" (28%), on "cough or dyspnea" (26%),

and on "sore throat" (19%). The figure that was least frequently consulted was the one on

"jaundice" (consulted by only 5 pairs).

Adherence

The overall adherence rate was 29.7% (160/539) per case (patient/physician pair). The

proportion of non-adherent and incomplete cases were 45.1% (243/539) and 25.2% (136/539),

respectively. The figure-specific adherence varied between 13.6% for the figure on enlarged

liver and 86.1% for figure on sore throat. Table 3 describes the section-specific adherence rate

and the nature of the recommendation not followed in each figure. For details of the figures

content, you can access www.fevertravel.ch or annex 1. The adherence rate by figure

(symptom or sign or laboratory result) was 54.8%, corresponding to 776 figures adhered to

out of 1417 figures consulted. The proportion of figures not adhered to was 31.3% (444/1417)

and those incomplete 13.9% (197/1417). In absolute numbers, the recommendations that most

of the physician/patient pairs did not follow (in spite of no alternative documented diagnosis)

were: i) to repeat the malaria test after a first negative result (111/352), ii) to give presumptive

treatment with quinolones in case of febrile diarrhoea (64/153) or in case of abdominal pain

with a leucocyte count below 10G/l (46/101). These three points make up half of all figures

not adhered to. At the level of patient/physician pairs, if we exclude the non-adherences at

these three locations, the proportion of adherent, non-adherent, and incomplete pairs was

40.1%, 30.4% and 29.5%, respectively.

Reasons for non-adherence

Reasons given by the physicians for non-adherence are detailed in table 4. Out of the total of

543 diversions from the decision tree, 96 (18%) were justified by an alternative documented

diagnosis and therefore not considered as non-adherent. 463 justifications were given for the

remaining 447 diversions (more than one reason per diversion). Out of these 463, 95 (20%)

were judged to be reasonable diversions from the decision tree, based on the available

evidence, which translates into 23% of the 243 non-adherent patient/physician pairs. This

gives us a corrected adherence per case (patient/physician pair) of 40.1% (216/539) and a

corrected figure adherence rate of 61.7% (874/1417). Reasonable diversions include situations

that were not taken into account in the guidelines, such as previous investigations or

treatments, follow-up by another physician, a more detailed analysis of endemicity (defined at

country-level in the recommendations), or prescription of a broader spectrum antibiotic then

the one recommended. Diversions judged unreasonable referred often to atypical clinical

pictures for the diagnoses considered, or clinical pictures more compatible with other

unproven presumptive diagnoses, that refrained the physicians from following the given

recommendations. Some diversions were also due to the patient's non-adherence, for example

when not bringing stool for examination or not returning for the second malaria test.

Outcome

Information on outcome had to be given 14 days after the initial consultation. 77 participating

patient/physician pairs, representing 14% of the total, did not complete this section despite

repeated email reminders. 424 patients had recovered (79%); 34 cases (6%) were lost-to-

follow-up by their physician. No death was reported. 4 patients were reported to have

sequelae (persisting cough, arthralgia, HIV and oncologic treatment). Non-adherence does not

appear to have played any role in the development of sequelae. 29 cases had complications

reported, representing 5% of the patient/physician pairs. Adherence and nature of the

recommendation not followed for patient that developed sequelae and/or complications are

shown in table 5. Complications were mainly observed among patients diagnosed with

malaria, Dengue, gastroenteritis, enteric fever, and amoebic liver abscess. All complications

could be attributed to the underlying illness. None appears to be related to or aggravated by

the guidelines' use (see table 5). There was no significant difference between the proportion

of adherent cases when comparing patients with complications with the other cases (41.4% vs.

30.3%, p=0.21). Out of these, 23 required admission to hospital. Overall, 61 patients were

admitted (11% of the patient/physician pairs), for a mean of 4.4 days. The diagnoses that most

frequently led to hospital admission were malaria (19 cases), gastroenteritis (6 cases), enteric

fever, Dengue, and skin infections (5 cases each). All patients recovered, except the patient

with lymphoma. Outcome was not known for 4 admitted patients. Adherence to the guidelines

was higher among admitted patients compared to outpatients (50.8% vs. 27.8%, $p<0.001$).

Qualitative evaluation

Qualitative questions were answered by 359 patient/physician pairs, representing 67% of all

cases. 55% of these physicians found the guidelines website to help them to reach a final

diagnosis. 71% said they would have performed the same number of investigations, had they

not used the guidelines, while 10% would have performed more and 19% less. 26% of the

patient/physician pairs asked for advice to a consultant of travel/tropical medicine . When

questioned about the "worst thing" while using these guidelines, 53 out of 156 physicians

answered "nothing", 52 were critically referring to specific points of the decision chart, 21

found the use of the website rather complicated and/or had technical problems, 17 complained

of the time consumption, and another 13 made more general comments that pertained mainly

to the guidelines' rigidity, over-simplification, and to the fact that they did not help them to

manage a particular case. More specific criticisms related to the absence of a separate figure

when there was no specific symptom or sign, to the fact that cosmopolitan infections were not

taken into account and to other specific points in the decision chart. When asked about the

"best thing" of the guidelines, 19 out of 148 answered nothing, 100 made general comments

on the usefulness of the guidelines not to forget an important diagnosis, on the clarity of the

decision chart, and its sequential format. 29 made more specific comments that mainly

referred to the usefulness of the guidelines to take a relevant medical history and to consider

appropriately malaria and other specific diagnoses.

Conclusions:

Internet-based research, in our experience, was shown to be an excellent tool for research in

primary care. The Internet is widely available, and web-based tools are increasingly used as

an aid to decision-making during routine medical consultations. We integrated data collection

for the evaluation of our web-based tool into the use of the tool itself, in order to stick as

closely as possible to the real practice of physicians. This innovative design enabled us to

obtain extremely precise feedback on case management in different settings and regions of the

world. It gave a unique opportunity to bring experience from the field to the developers.

Most of the physician/patient pairs were recruited from reference centers. Still, the cases were

usually drawn from the outpatient clinic or emergency wards linked to those specialized

centres. The practices recorded reflect probably those used in settings experienced in

managing patients with fever upon return, rather than the usual practice of GPs. However,

74% of the patients included were treated as outpatients, which is in line with the target

audience of the guidelines. The relatively low proportion of malaria cases (10%) compared

with other case series [18,19] confirms that our respondents represent a rather unselected

physician population.

Feasibility

One of the objectives of this work was to prove the feasibility of web-based guidelines for the

evaluation of fever in travellers. Since the launching of the website in 2003 until April 2008,

31176 visits to the website were recorded, showing that the tool is used. In April 2008,

Switzerland represented 27% of the accesses, followed by the Netherlands (19%), Italy (7%),

the USA (7%), Israel (2%), and Belgium (1%). 8% of the visitors came from other countries

and another 28% could not be traced back to a specific country. The qualitative assessment

showed that the guidelines are especially appreciated for their clarity and easiness of use; they

do help the primary care physicians not to forget, or to think of specific diagnoses, including

those they might not be aware of. The vast majority of physicians found their way relatively easily through the decision chart, and completed the figures appropriately. The recurrent negative comment of not including cosmopolitan infections in the decision chart is difficult to address in future versions of the guidelines since the latter would become guidelines for the management of fever, which would be much to vast to be feasible. The specific comments will be taken into account as much as possible in the revision process of the guidelines.

Adherence

Our results showed that 29.7% of the patient/physician pairs participating in the study were adherent to all steps of the decision chart. Splitting this adherence rate by figure-specific adherence, the total adherence rate was 54.8%. The proportion of incomplete figures (25% of the patient/physician pairs) affects the low adherence observed; indeed, when those incomplete were not taken into account, the overall adherence rate was of 39.7% and the figure-specific of 63.6%. Various hypotheses can be formulated in order to explain this rather low result. The fact that most cases were included in centres experienced in travel medicine may have resulted in approaches that left more room for interpretation and specialized approaches. As previously mentioned, about one fifth of all diversions from the algorithm were considered reasonable, suggesting appropriate management that was not specifically mentioned in the guidelines. It is obvious that specialists can be more confident in their approaches since they may know better on the local disease epidemiology, defined clinical features, usefulness of a diagnostic test in a particular context etc. Specialist doctors can have personal approaches, although this is even debatable, but certainly primary care physicians need guidelines that will help them to manage cases, whatever the field is, but a fortiori one that is far from their daily practice. Since guidelines are designed to fit 'all' situations, they are by essence oversimplistic. Each situation needs therefore a refinement, which will affect full adherence. But this peculiar diversion might not mean that the guidelines were useless.

They may have been considered, and helped for the management of a particular case, even when not followed exactly. This is the reason why we integrated this concept of 'reasonable diversion'. Even what we consider 'not reasonable' may have been appropriate in a particular situation, considering the particular patient situation. This is the inherent difficulty of assessing guidelines implementation and adherence. We feel however that the recurrent diversions will need to be thoroughly reviewed, the new evidence searched for, and experts asked for their opinion to assess the appropriateness of the recommendation, or the need for a change in the revised version of the decision chart. However, some of the observed diversions, such as not repeating a malaria test with persistent fever and in the absence of an alternative diagnosis certainly, represent a clear mismanagement that needs to be addressed, as this recommendation is based on a strong level of evidence and lies on an expert consensus. As expected, a number of clinical situations differ from the ones proposed in the guidelines. The inclusion criteria were very broad, as we did not only include patients with documented fever, but also patients with fever-associated symptoms such as headache, or feelings of cold and warm. This conservative approach of the definition of fever [12] led to the inclusion of numerous mild cases. This is probably one of the reasons why physicians were often reluctant to prescribe antibiotics in case of fever with diarrhoea, although this recommendation is based on a consensus among experts [13]. Interestingly, this practice has not been associated with an increased number of negative outcomes. This observation may well deserve further solid evidence. One difficulty in designing clinical algorithms is how to include symptoms' intensity in the evaluation, a point, which is of foremost importance in decision-making. "Good general condition" is usually a subjective judgment, not based on hard figures, but it affects physicians' behaviour, for example to decide on antibiotic prescription. Unfortunately, it also affects decisions that should be unaffected by the status of the patient, e.g. to repeat a malaria test when negative. In general, the observation that the degree of severity of the

patient's condition affects physicians' adherence to the proposed recommendations dictates to

include this parameter in the next version of the practice guidelines.

Safety

The assessment of guidelines safety is not easy since mortality is a rare outcome among

travellers returning with fever. By the nature of our free internet-based study, we could not

make a proper controlled trial to assess complication and mortality rates among guidelines

users and non-users. We found that adherence rate was higher for admitted cases. However,

this does not imply that the decision chart was unsafe since we have no evidence that the use

of the guidelines caused any delay in the management of patients or recognition of their

diagnosis. The higher adherence rate among admitted cases simply indicates that physicians

are more cautious when dealing with more severe cases, whereas they use their own judgment

more freely with mild cases. Furthermore, the observed complications were due to the

underlying illnesses, and could neither be related to the guidelines' use nor to non-adherence

to a specific recommendation. It is noteworthy that many physicians commented that the

guidelines helped them not to miss a particular diagnosis, which they would not have thought

of otherwise. For the majority of the physicians, the decision chart helped to reach a final

diagnosis, most often without increasing the number of investigations performed.

We insist on presenting these guidelines as an aid to decision-making, and not as a rigid

pathway to be followed. If the complexity of all clinical situations cannot be summarized in a

decision chart, we believe it offers a good start to include in the differential diagnosis the

diseases with a relatively high pre-test probability [20], or those with a high case-fatality rate.

Physicians still use their judgment and do not simply follow the guidelines as a cookbook.

While these guidelines were being implemented in our clinic, we observed that the sense of

self-efficiency felt by the physicians increased. They found particularly rewarding to make up

their own opinion, and establish a reasonable differential diagnosis, prior to calling the

registrar. Some would argue that this self-confidence could be dangerous, but we think, on the

contrary, that it is an advantage to increase the knowledge and experience of primary care

physicians in this field, especially with the steady increase of international travel and

globalization. The diffusion of important "red-flags" in travel medicine can only be of benefit

to the patients, since the primary care physicians represent the first medical recourse…. but

could also be the last if not sufficiently aware of the emergency of some clinical situations. As

much as it is important to maintain high quality care in tertiary centres, as much it is also

crucial to work upstream to ensure a correct initial evaluation, immediate treatment when

needed and appropriate referral.

Conclusion

We showed that web-based practice guidelines for the evaluation of fever in returning

travellers are feasible, that they are useful, and that they do not appear to cause increased

complication rates. Our data are limited by the proportion of missing data, and the risk of

selection bias. We believe however that our results are extremely valuable in terms of

feedback to the guideline developers, as we have now very precise information about all

diversions to the guidelines and the reasons for these diversions. There is not room in this

article to comment every one of them, but each one will now be analysed step by step and

used in combination with the updated literature review to produce a new algorithm, which

will fit better to physicians' practices. In order to fine-tune this algorithm, we will try to

include disease severity as well as pre-test probabilities. Technically, the lessons learned

during the development process of the guidelines will also help us to produce a more efficient

web-based tool.

18

Acknowledgments

Declaration of Interests

1
2
3   **References**
4
5
6
7   [1]   Finkelstein JA, Lozano P, Shulruff R, et al. Self-reported physician practices for
8
9
10   children with asthma: are national guidelines followed? Pediatrics 2000; 106: 886-96.
11
12
13   [2]   Szajewska H, Hoekstra JH, Sandhu B. Management of acute gastroenteritis in Europe
14
15   and the impact of the new recommendations: a multicenter study. The Working Group
16
17   on acute Diarrhoea of the European Society for Paediatric Gastroenterology,
18
19
20   Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2000; 30: 522-7.
21
22
23   [3]   Mol PG, Rutten WJ, Gans RO, et al. Adherence barriers to antimicrobial treatment
24
25   guidelines in teaching hospital, the Netherlands. Emerg Infect Dis 2004; 10: 522-5.
26
27
28   [4]   Chen RS, Rosenheck R. Using a computerized patient database to evaluate guideline
29
30   adherence and measure patterns of care for major depression. J Behav Health Serv Res
31
32   2001; 28: 466-74.
33
34
35
36   [5]   Marshall DA, Simpson KN, Norton EC, et al. Measuring the effect of clinical
37
38   guidelines on patient outcomes. Int J Technol Assess Health Care 2000; 16: 1013-23.
39
40
41   [6]   Rodrigues RJ. Information systems: the key to evidence-based health practice. Bull
42
43   World Health Organ 2000; 78: 1344-51.
44
45
46   [7]   Shiffman RN, Liaw Y, Brandt CA, Corb GJ. Computer-based guideline
47
48   implementation systems: a systematic review of functionality and effectiveness. J Am
49
50
51   Med Inform Assoc 1999; 6: 104-14.
52
53
54   [8]   Thomas KW, Dayton CS, Peterson MW. Evaluation of internet-based clinical decision
55
56   support systems. J Med Internet Res 1999; 1: E6.
57
58
59
60

[9] Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. BMJ 2005; 330: 765.

[10] Reips UD. Standards for Internet-based experimenting. Exp Psychol 2002; 49: 243-56.

[11] McAlindon T, Formica M, Kabbara K, et al. Conducting clinical trials over the internet: feasibility study. BMJ 2003; 327: 484-7.

[12] Sinkowitz-Cochran RL, Stein GP, Keyserling HL, et al. The Internet: a practical example of the use of new technology in the assessment of vancomycin use in pediatrics. The Pediatric Prevention Network. Am J Infect Control 2000; 28: 459-64.

[13] Zehnder S, Bruppacher R, Ruppanner H, Hersberger KE. Swiss community pharmacies' on the Web and pharmacists' experiences with E-commerce: longitudinal study and Internet-based questionnaire survey. J Med Internet Res 2004; 6: e9.

[14] Jeannot JG, Scherer F, Pittet V, et al. Use of the World Wide Web to implement clinical practice guidelines: a feasibility study. J Med Internet Res 2003; 5: e12.

[15] Hayward RS, Wilson MC, Tunis SR, et al. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. A. Are the recommendations valid? The Evidence-Based Medicine Working Group. JAMA 1995; 274: 570-4.

[16] D'Acremont V, Ambresin AE, Burnand B, Genton B. Practice guidelines for evaluation of Fever in returning travelers and migrants. J Travel Med 2003 May;10 Suppl 2:S25-S52.

[17] Ambresin AE, D'Acremont V, Mueller Y, et al. www.fevertravel.ch: an online study prototype to evaluate the safety and feasibility of computerized guidelines for fever in

returning travellers and migrants. Comput Methods Programs Biomed 2007; 85: 19-

31.

[18] Bottieau E, Clerinx J, Schrooten W, et al. Etiology and outcome of fever after a stay in

the tropics. Arch Intern Med 2006; 166: 1642-8.

[19] O'Brien D, Tobin S, Brown GV, Torresi J. Fever in returned travelers: review of

hospital admissions for a 3-year period. Clin Infect Dis 2001; 33: 603-9.

[20] Bottieau E, Clerinx J, Van den EE, et al. Fever after a stay in the tropics: diagnostic

predictors of the leading tropical conditions. Medicine (Baltimore) 2007; 86: 18-25.

Figure legends

Figure 1   Architecture of the website (www.fevertravel.ch)

Figure 2   Strategy used to classify adherence

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
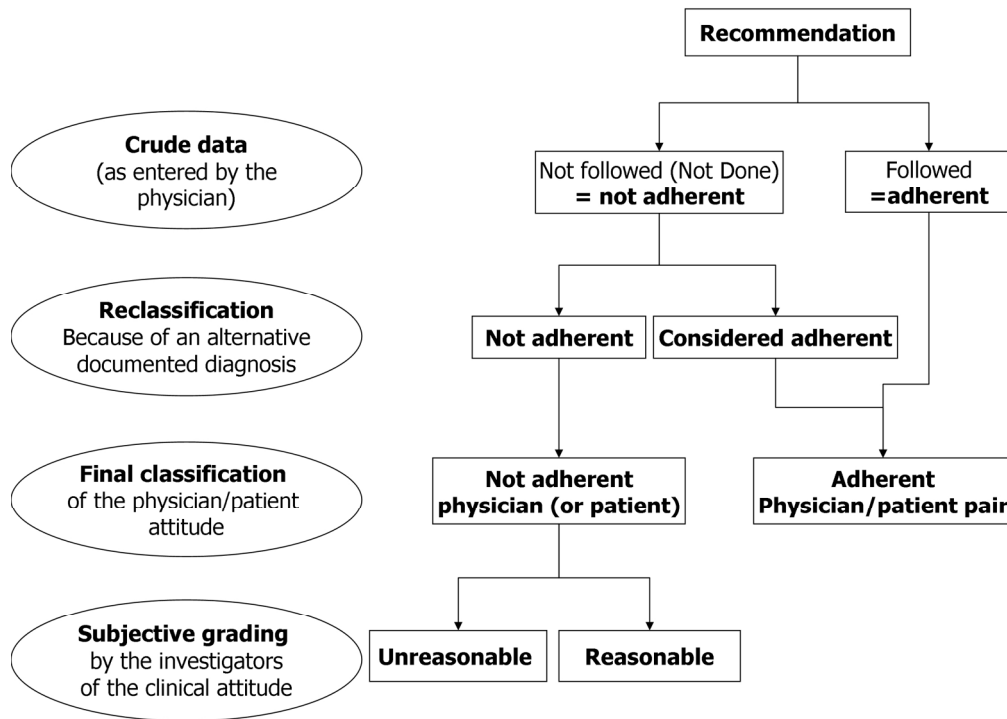43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
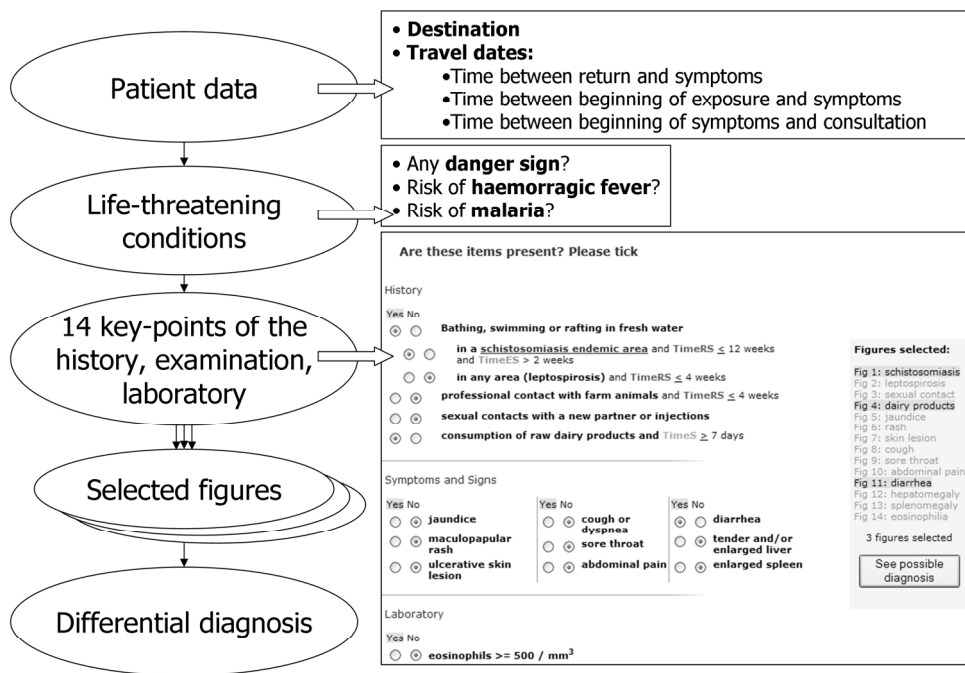
190x142mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

190x142mm (300 x 300 DPI)