



# The Brazilian Journal of INFECTIOUS DISEASES

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## Original article

# Top 10 evidence-based recommendations from the Brazilian Society of Infectious Diseases for the Choosing Wisely Project



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## ARTICLE INFO

### Article history:

Received 26 July 2019

Accepted 16 August 2019

Available online 25 September 2019

### Keywords:

Choosing wisely

Quality

Safety

Infectious diseases

Microbiology

Diagnostic tests

Healthcare administration

## ABSTRACT

The Choosing Wisely Initiative aims to collect statements from medical societies all over the world on medical interventions that result in no benefit to patients, with the potential to cause harm. In this article we present the views of the Diagnostic Laboratory Group at the Brazilian Society of Infectious Diseases (SBI). Ten experts from SBI were asked to list 10 diagnostic tests that were perceived as unnecessary in the field of infectious diseases. After voting for the more relevant topics, a questionnaire was sent to all SBI members, in order to select for the most important items. A total of 482 votes were obtained, and the top 10 results are shown in this manuscript. The Choosing Wisely statements of SBI should facilitate clinical practice by optimizing the use of diagnostic resources in the field of infectious diseases.

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<https://doi.org/10.1016/j.bjid.2019.08.004>

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## Introduction

Overuse of low-value or unnecessary health care resources is a global problem, and a growing body of evidence demonstrates its prevalence and harms.<sup>1</sup> Choosing Wisely Initiative is a front-line healthcare professional-led campaign to address overuse<sup>2,3</sup> associated with negative impact on patient safety and increased health care costs without proven benefits. The campaign first started in the United States in 2012 and was led by the American Board of Internal Medicine (ABIM) Foundation. With partners including national medical societies, hospitals and universities, the campaign is now active in more than 20 countries (<https://www.commonwealthfund.org/series/choosing-wisely>). Different groups have joined the campaign by releasing lists of evidence-based recommendations of tests, treatments, and procedures that are overused, clinically unnecessary, and/or with the potential for causing harm. After the lists are created, a debate is usually started involving healthcare professional and the lay community.

Choosing Wisely Brazil emerged in 2015 and has now 10 national medical societies recognized by the Brazilian Medical Association (AMB) that released recommendations, besides five hospitals and the Bahia School of Medicine and Public Health. This article aims to summarize the list of the top 10 recommendations developed by the Brazilian Society of Infectious Diseases (SBI) for the Choosing Wisely project.

## Methods

A group of 10 infectious diseases physicians, led by the chair of the Diagnostic Laboratory Group at SBI (Pasqualotto AC), were invited to participate in this project. In addition, the group also consisted of the SBI president (Cimerman S), a representative of Choosing Wisely Brazil (Barcellos GB), and an undergraduate medical student (Almeida CS). The group was informed about the principles of the Choosing Wisely project and invited to submit 10 topics each of laboratory-related topics that could fit in the Choosing Wisely project. The next step involved a discussion with the steering group, for the selection of the 10 most relevant recommendations based on current strength of evidence from each item. Afterwards, this list was submitted to public consultation. Based on a 95% confidence interval and an alpha level of 5%, a sample of 292 participants would be necessary. Members of SBI received a link from an online survey tool "SurveyMonkey" website through e-mail and "WhatsApp". They were asked to select, among these 10 topics, the five most relevant ones. The survey link was also published on the "SBI Facebook's page". The top-5 recommendations were published in Portuguese in the Choosing Wisely Brazil website.

The Choosing Wisely manuscript list of the top-10 recommendations by SBI were organized based on the number of votes received, from the most relevant to the less voted items.

## Results

A total of 106 recommendations were received from the steering committee group. Among these questions, 32 were selected after excluding redundant and non-appropriate topics. The group voted for the 10 most relevant questions. These questions were sent for voting to around 1600 individuals via Facebook, WhatsApp and e-mail. These people included SBI members and the general medical community. The total number of responders reached 482 physicians, and the list of topics ordered by the number of votes is presented below. A summary of these recommendations is shown in Table 1.

- 1 Do not use swab cultures for microbiological diagnosis of ulcers.

(67.8% of votes; n = 327)

The use of microbiology swabs for culturing ulcerated skin diseases commonly reflects contamination with skin microbiota. Furthermore, the superficial swabs do not reflect the microbiology of the deeper tissue, and so these cultures that do not correlate with the pathogenic bacteria involved with the disease.<sup>4,5</sup> Swab sampling may provide misleading results; therefore, we recommend using tissue biopsy to confirm the diagnosis of infected ulcers since it is unlikely to represent superficial contamination.<sup>4,6,7</sup>

- 2 Do not order urine cultures for asymptomatic patients, except for pregnant women and patients undergoing urological surgery.

(65.1% of votes; n = 314)

Urinary growth of bacteria is commonly seen in asymptomatic patients and its prevalence varies with age, sex, and the presence of genitourinary abnormalities. Asymptomatic bacteriuria is generally present in 3–5% of young women and diabetic patients, and its frequency may increase up to 18% in the elderly population.<sup>8,9</sup> Due to its high frequency of occurrence, screening for asymptomatic bacteriuria is not recommended, except in cases when adverse outcomes can be prevented by antimicrobial therapy – e.g., in pregnancy and before urological surgery. In pregnancy, screening and treatment reduce the incidence of pyelonephritis, preterm delivery, and low birth weight whereas in pre-operative urological context, screening and treatment decreases the rates of postoperative fever and sepsis.<sup>10–12</sup>

- 3 Do not use treponemal tests in the follow-up of patients treated for syphilis.

(64.7% of votes; n = 312)

There are two types of serological test to diagnose syphilis: non-treponemal (NNT) and treponemal tests (TT).<sup>13</sup> Both types of test are required to confirm a diagnosis of syphilis.<sup>14</sup> TT, such as the FTA-Abs, are more specific, since they detect *T. pallidum* antigens. Therefore, they are used to confirm the diagnosis of syphilis in patients with positive NNT, as well

**Table 1 – Summary of the Brazilian Society of Infectious Diseases recommendations for the Choosing Wisely Initiative.**

| Condition                              | Recommendation                                                                                                          | Reason                                                                                                                                         |
|----------------------------------------|-------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| Ulcerated skin infection               | Swab sampling should not be used for determine microbiological etiology                                                 | Swab sampling usually represent contamination from skin microbiota                                                                             |
| Urinary tract infection                | Do not ordinarily order urine cultures for asymptomatic patients                                                        | Urinary growth of bacteria is commonly seen in asymptomatic patients                                                                           |
| Syphilis                               | Do not use treponemal tests in the follow-up of patients treated for syphilis                                           | Treponemal tests may remain positive during lifetime after syphilis is treated                                                                 |
| Toxoplasmosis                          | Do not repeat anti- <i>Toxoplasma</i> IgG antibody tests in patients known to be IgG positive                           | IgG antibodies against <i>Toxoplasma</i> remain positive during life in patients with previous IgG tests                                       |
| Herpes simplex infection               | Do not use antibody detection to diagnose or screen for herpes simplex infection                                        | The detection of anti-herpes simplex antibodies is of limited clinical use, mainly due to the high seroprevalence of such infections           |
| <i>Clostridium difficile</i> infection | Do not test for <i>Clostridium difficile</i> in patients without diarrhea                                               | Many patients are simply colonized by <i>C. difficile</i>                                                                                      |
| HIV infection                          | Do not routinely repeat CD4 measurements in patients with prolonged viral load suppression                              | CD4 monitoring offers no clinical benefit in patients who have suppresses viral loads and CD4 counts >300 cells/mm <sup>3</sup> after 48 weeks |
| Hepatitis C virus (HCV) infection      | Do not measure HCV viral load for monitoring patients who have reached sustained virologic response following treatment | HCV viral monitoring has reduced importance nowadays since novel therapies offer similar antiviral potency, regardless of baseline viral load  |
| Leishmaniasis                          | Do not use serological tests as the sole basis to diagnose leishmaniasis                                                | Asymptomatic individuals can present with positive serology for <i>Leishmania</i> species with no association with disease in endemic areas    |
| Invasive aspergillosis                 | Do not test for <i>Aspergillus</i> galactomannan in serum samples in non-neutropenic patients                           | Sensitivity of serum galactomannan testing is markedly reduced in non-neutropenic individuals                                                  |

as in cases where NNT have recognized low sensitivity, as in late syphilis. However, treponemal antibody titers correlate poorly with the disease activity as it may remain positive for the patients' lifetime.<sup>13,15,16</sup> As a result, TT should not be used for monitoring serological activity and treatment outcomes in patients previously treated for syphilis.

- 4 Do not use *Toxoplasma* IgG test for the follow-up in immunocompetent patients and do not repeat anti-*T. gondii* IgG in patients with a previous positive IgG test.

(51.7% of votes; n = 249)

Due to the high seroprevalence of *T. gondii* infection in the overall population is not recommended to repeat IgG in immunocompetent patients that already have a positive test neither to repeat tests for serological follow-up. The prevalence of *Toxoplasma* infection varies between countries and often within a given country or between different communities in the same region depending on the environmental and the socioeconomic levels of the population.<sup>17,18</sup> In some areas in Brazil, the serological prevalence of *T. gondii* infection ranges from 50 to 80%,<sup>19</sup> including areas where Indian tribes live in relative isolated locations.<sup>20</sup> A positive IgG test confers long life protection against toxoplasmosis. Once a formed *Toxoplasma* infection is confirmed is not recommended to repeat IgG serological tests since titers of IgG remain positive life-long.

- 5 Do not use serological testing to diagnose or screen for HSV-1 and HSV-2 in general population.

(50.07% of votes; n = 239)

Due to the high prevalence of herpes simplex infection in the general population detection of antibodies against herpes

simplex 1 (HSV-1) and herpes simplex 2 (HSV-2) has very little use in clinical practice. In 2012, one study estimated that 67% of world population under the age of 50 was already infected by HSV-1. The estimated global prevalence for HSV-2, for the same age population, was 11%.<sup>21</sup> Brazilian studies have also shown elevated seroprevalence of herpes simplex infection in adults.<sup>22</sup>

- 6 Do not test for *Clostridium difficile* in patients without diarrhea.

(48.3% of votes; n = 233)

Asymptomatic *Clostridium difficile* carriage frequently occurs in patients on antimicrobial therapy and in hospitalized patients, especially the elderly. Colonization occurs in 5–15% of healthy adults whereas the rates increase up to 57% in residents in long-term care facilities.<sup>23</sup> For this reason, it is not clinically useful to test for *C. difficile* in asymptomatic patients without diarrhea since the presence of the pathogen in stools indicate carriage only, which should not be treated.<sup>23–25</sup> The diagnosis of *C. difficile* infection should combine clinical symptoms with laboratory tests.<sup>26</sup>

- 7 Do not routinely repeat CD4 measurements in HIV patients with prolonged (> 2 years) viral load suppression and high ( $\geq 500$  cell/mL) CD4 counts, unless virological failure occurs or an opportunistic infection develops.<sup>27–30</sup>

(43.1% of votes; n = 208)

CD4 cells monitoring can be ceased in people living with HIV/Aids (PLHIV) who are stable on antiretroviral therapy and virologically suppressed, in settings where viral load monitoring is available. In these patients, frequent CD4 cell counting is unnecessary since it rarely leads to change in

clinical management. In addition, CD4 cells remain stable over time in most patients<sup>27,28</sup> – meaningful CD4 decline is uncommon. Furthermore, CD4 count may naturally vary between measurements (<30%), in a sense that frequent sampling may only cause unnecessary anxiety to patients. Prospective studies have confirmed that CD4 monitoring offers no clinical benefit in patients who have suppressed viral load and CD4 counts >300 cells/mm<sup>3</sup> after 48 weeks of follow up.<sup>29</sup> This strategy has been recommended for virologically suppressed patients with CD4 counts between 300–500 cells/mm<sup>3</sup>, for at least 2 years.<sup>30</sup>

- 8 Do not measure HCV viral load for monitoring patients who have reached sustained virologic response post-treatment, unless there is an ongoing risk of reinfection or an unexplained hepatic dysfunction.

(29.2% of votes; n = 141)

Given the efficacy of direct-acting antiviral therapy for the treatment of chronic HCV infection, patients who achieve an undetectable HCV-RNA in serum or plasma at 12 weeks or 24 weeks after treatment are considered as having a sustained virologic response (SVR). Among patients who achieved SVR with peginterferon/ribavirin treatment, more than 99% have remained free of HCV infection when followed for five years after treatment completion.<sup>31</sup> Therefore, it is unnecessary to assess HCV recurrence or reinfection once SVR is achieved, since it is considered to be virological cure of the infection. Viral monitoring has reduced importance nowadays since novel therapies offer similar antiviral potency, regardless of baseline viral load.<sup>32</sup> Furthermore, it offers no prognostic value. It is mostly recommended to document the presence of HCV viremia. Annual viral monitoring is only recommended in patients who have ongoing risk exposure for HCV (e.g. people who inject drugs).<sup>33,34</sup>

- 9 Do not use serological tests as the sole basis to diagnose leishmaniasis in endemic areas.

(28.2% of votes; n = 136)

The prevalence of antibodies against *Leishmania* species ranges from <10% to 30% in endemic areas. Therefore, antibody detection against *Leishmania* species is of little use in the diagnosis of leishmaniasis.<sup>35,36</sup> Asymptomatic individuals, who have no history of visceral leishmaniasis (VL), can present with positive serology for *Leishmania* species with no association with disease. Furthermore, antibodies may not be detected or may be present at low levels in immunocompromised patients with VL.<sup>35–37</sup> Finally, even though serum antibody levels decrease after leishmaniasis treatment, these may remain detectable up to several years after disease control and cannot distinguish between active and previous infection. Therefore, tests for antileishmanial antibodies should not be performed as the sole diagnostic tool in patients with leishmaniasis.<sup>38</sup>

- 10 Do not test for *Aspergillus* galactomannan in serum samples in non-neutropenic patients.

(14.3% of votes; n = 69)

Invasive aspergillosis (IA) is one of the most serious fungal infections affecting immunocompromised patients. This condition is associated with high mortality, especially due to its challenging diagnosis.<sup>39,40</sup> Serum galactomannan (GM) has been extensively used to screen neutropenic patients at risk to develop IA, in association with chest computed tomography (CT). However, sensitivity of serum GM testing is much reduced in non-neutropenic individuals, including solid-organ transplant patients, patients with graft versus host disease, and other patients taking steroids. Therefore, non-neutropenic patients at risk for IA should be tested with GM in bronchoalveolar lavage samples, instead of serum samples.

## Conclusions

The top-10 Choosing Wisely statements of the Diagnostic Laboratory Group at SBI were presented in this article. These recommendations aim to reduce unnecessary and overused tests performed on patients with different sorts of infections. As a result, we expect to provide patients with a better standard of care, potentially reducing the negative impact of unnecessary tests in patients.

## Conflicts of Interest

The authors declare no conflicts of interest.

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