

## The Rise and Fall of SARS-CoV-2 Variants

### A Ascensão e Queda das Variantes de SARS-CoV-2

**Keywords:** COVID-19; Portugal; Risk Assessment; SARS-CoV-2  
**Palavras-chave:** COVID-19; Medição de Risco; Portugal; SARS-CoV-2

Dear Editor,

As the pandemic evolves, Portugal and countries worldwide are facing the threat of the emergence of new SARS-CoV-2 variants, which represent potential game-changers in this fight. One of the most recently detected variants was the Mu variant (B.1.621). It was classified on August 30 by the World Health Organization as a variant of interest for presenting mutations that are shared with some of the variants of concern and that suggest a potential property of immunological escape.<sup>1</sup> This lineage carries several Spike protein mutations, some common with other variants of concern, while others are new. Indeed, experimental studies demonstrated that the Mu variant could escape humoral immunity acquired from infection from previous strains or vaccines.<sup>2</sup> At that point, further studies were required to assess the biological and epidemiological roles of the substitution pattern found.

However, the scientific community's interest quickly faded in parallel with the favorable epidemiological evolution of the new variant. In terms of cases sequenced, the global prevalence rate has been increasing since January, peaked in mid-July and then declined, being consistently below 0.2% (spectrum). In Portugal, it was reported firstly at the end of May, and, until now, a total of 24 cases were sequenced; a decreasing trend was observed, representing 0% of sequenced cases since August.<sup>3</sup> Thus, the Mu threat seems to have been quelled. However, its emergence reminds us that the tracking of SARS-CoV-2 variants is crucial. The first Italian cluster of the SARS-CoV-2 B.1.621 lineage was associated with a traveler from Colombia, which underlines that surveillance of SARS-CoV-2 genomic evolution is essential to limit the spread of new lineages to

different countries.<sup>4</sup>

At the moment, a new Delta sublineage (AY.4.2) is arising in England and was classified as 'variant under investigation' on October 22<sup>nd</sup> by the UK Health Security Agency.<sup>5</sup> It contains two mutations in the Spike protein, already found in other lineages and has been suggested that it might be 10% to 15% more transmissible than the original Delta variant.<sup>5</sup> The first cases emerged in late June and represent up to now less than 1% of cases sequenced worldwide.<sup>3</sup> In Portugal, nine cases were sequenced, and the respective epidemiological contexts are under investigation.<sup>3</sup> Further studies concerning the ability to escape immunity are needed.

As countries gradually resume pre-pandemic activities, risk assessments should continue to be conducted systematically, updating the global lists of variants to support priority setting for surveillance and research, and ultimately guide response strategies.

#### AUTHORS CONTRIBUTION

TPS: Conducted the research and wrote the first draft of the letter; approved the final draft of the manuscript.

AA, MP: Participated in the writing, reviewing and editing of the letter; approved the final draft of the manuscript.

RD: Conceived the idea and participated in the writing, reviewing and editing of the letter; approved the final draft of the manuscript.

#### COMPETING INTERESTS

The authors have declared that no competing interests exist.

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## Letter to the Editor Regarding the Article “Rethinking the Choosing Wisely Portugal Recommendation on Breast Cancer Screening”

### Carta ao Editor em Relação ao Artigo “Repensar a Recomendação Choosing Wisely Portugal sobre Rastreo do Cancro da Mama”

**Keywords:** Breast Neoplasms; Early Detection of Cancer; Mammography; Patient-Centered Care; Decision Making, Shared  
**Palavras-chave:** Assistência Centrada no Paciente; Detecção Precoce de Cancro; Mamografia; Neoplasia da Mama; Tomada de Decisão Compartilhada

We would like to clarify that there is an article about the “Choosing Wisely Portugal” recommendation for Breast Cancer Screening<sup>1</sup> in this journal<sup>2</sup> where the best scientific evidence (including reviews, randomized studies, meta-analyses, etc.) underlying the recommendation basis was discussed. Choosing Wisely recommendations are usually brief, and therefore it is not possible to detail all the required information and references in one or two paragraphs. The American College of Radiology has also published patient-oriented summaries about this screening among their recommendations.<sup>3</sup>

The article by Silva *et al*<sup>2</sup> does not avoid the issue of possible overdiagnosis, as it justifies the low values (0% - 5%) in adequately adjusted studies.

The argument that delaying the start of screening or increasing its intervals has an effect on the already low overdiagnosis rate does not seem legitimate to us. There is recent evidence supporting the contrary,<sup>4</sup> where it was found that there is no effect on the frequency of overdiagnosis in ‘less intensive’ screenings. Instead, the prognosis is worse for women in whom breast cancer is detected later on.<sup>5</sup>

A sensitive and serious discussion about the risks and potential harms is needed when comparing the anxiety caused by a false positive result with the one of an often-mutilating invasive cancer. The first is brief and transient in most cases, while the latter is often way more distressing, particularly when we also consider the (chemo)therapeutic aspect. Evidence exists that transient anxiety does not dissuade women from continuing their screening in the following year,<sup>6</sup> nor does it diminish the importance given to it.<sup>7</sup>

It is important to mention that the American Society of Breast Surgeons also supports the recommendation to screen annually starting at age 40.<sup>8</sup> Between 81% to 87%

of American clinicians recommend not to postpone screening to the age of 50. Moreover, 67% of them consider that screening should be continued after the age of 75.<sup>9</sup> To give even more strength to the recommendation, we agree that patients should be informed, and that is why the justification accompanying the recommendation mentions “shared decision (...) duly informed about the benefits and drawbacks”,<sup>1</sup> which is in line with the “Choosing Wisely Canada” recommendation. In the European Union, radiological tests must be subjected to informed consent in agreement with the European Council Directive 2013/59/Euratom. Therefore, the task that the radiologist who is about to perform the test has of informing patients does not seem strange, difficult or inconvenient to this specialty, quite the contrary.

Therefore, we stress that the recommendation “Choosing Wisely Portugal” for Breast Cancer Screening<sup>1</sup> takes into account the shared decision and the balance between risks and benefits and it stands in the best interest of the woman/patient or any association representing them, such as the “Associação Portuguesa de Apoio à Mulher com Cancro da Mama”, whose president is co-author of this letter and also supports the “Choosing Wisely Portugal” program. This program is tolerant, inclusive and has already given voice to similar recommendations before, also alerting to the less frequent, but no less important risks of “less can be more in the end” [see recommendations: “Choose not to postpone the referral for cryptorchidism (...)”<sup>10</sup> and “Choose not to postpone the measurement of total bilirubin (...) in a newborn”<sup>11</sup>].

#### AUTHORS CONTRIBUTION

SCN: First draft, conception, literature research.

AJ: Revision, conception.

PF: Revision, conception.

MA: Patient-centered critical review.

CFS: Literature research and analysis, and critical review of the paper with significant intellectual contribution.

#### COMPETING INTERESTS

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