New Results

Previous

Fatal neuroinvasion of SARS-CoV-2 in K18-hACE2 mice is partially dependent on hACE2 expression

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ABSTRACT

Animal models recapitulating the distinctive features of severe COVID-19 are critical to enhance our understanding of SARS-CoV-2 pathogenesis. Transgenic mice expressing human angiotensin-converting enzyme 2 (hACE2) under the cytokeratin 18 promoter (K18-hACE2) represent a lethal model of SARS-CoV-2 infection. However, the cause(s) and mechanisms of lethality in this mouse model remain unclear. Here, we evaluated the spatiotemporal dynamics of SARS-CoV-2 infection for up to 14 days post-infection. Despite infection and moderate inflammation in the lungs, lethality was invariably associated with viral neuroinvasion and neuronal damage (including spinal motor neurons). Neuroinvasion occurred following virus transport through the olfactory neuroepithelium in a manner that was only partially dependent on hACE2. Interestingly, SARS-CoV-2 tropism was overall neither widespread among nor restricted to only ACE2-expressing cells. Although our work incites caution in the utility of the K18-hACE2 model to study global aspects of SARS-CoV-2 pathogenesis, it underscores this model as a unique platform for exploring the mechanisms of SARS-CoV-2 neuropathogenesis.

New Results

Previous

SARS-CoV-2 causes brain inflammation and induces Lewy body formation in macaques

Ingrid H.C.H.M. Philippens, Kinga P. Böszörményi, Jacqueline A. Wubben, Zahra C. Fagrouch, Nikki van Driel, Amber Q. Mayenburg, Diana Lozovagia, Eva Roos, Bernadette Schurink, Marianna Bugiani, Ronald E. Bontrop, Jinte Middeldorp, Willy M. Bogers, Lioe-Fee de Geus-Oei, Jan A.M. Langermans, Marieke A. Stammes, Babs E. Verstrepen, Ernst J. Verschoor

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Posted May 05, 2021.

Abstract

SARS-CoV-2 may cause acute respiratory disease, but the infection can also initiate neurological symptoms. Here we show that SARS-CoV-2 infection causes brain inflammation in the macaque model. An increased metabolic activity in the pituitary gland of two macaques was observed by longitudinal positron emission tomography-computed tomography (PET-CT). Post-mortem analysis demonstrated infiltration of T-cells and activated microglia in the brain, and viral RNA was detected in brain tissues from one animal. We observed Lewy bodies in brains of all rhesus macaques. These data emphasize the virus' capability to induce neuropathology in this nonhuman primate model for SARS-CoV-2 infection. As in humans, Lewy body formation is an indication for the development of Parkinson's disease, this data represents a warning for potential long-term neurological effects after SARS-CoV-2 infection.

Teaser SARS-CoV-2 causes brain inflammation and Lewy bodies, a hallmark for Parkinson, after an asymptomatic infection in macaques.

Competing Interest Statement

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Microbiology & Infectious Diseases

COVID-19 RNA Based Vaccines and the Risk of Prion Disease

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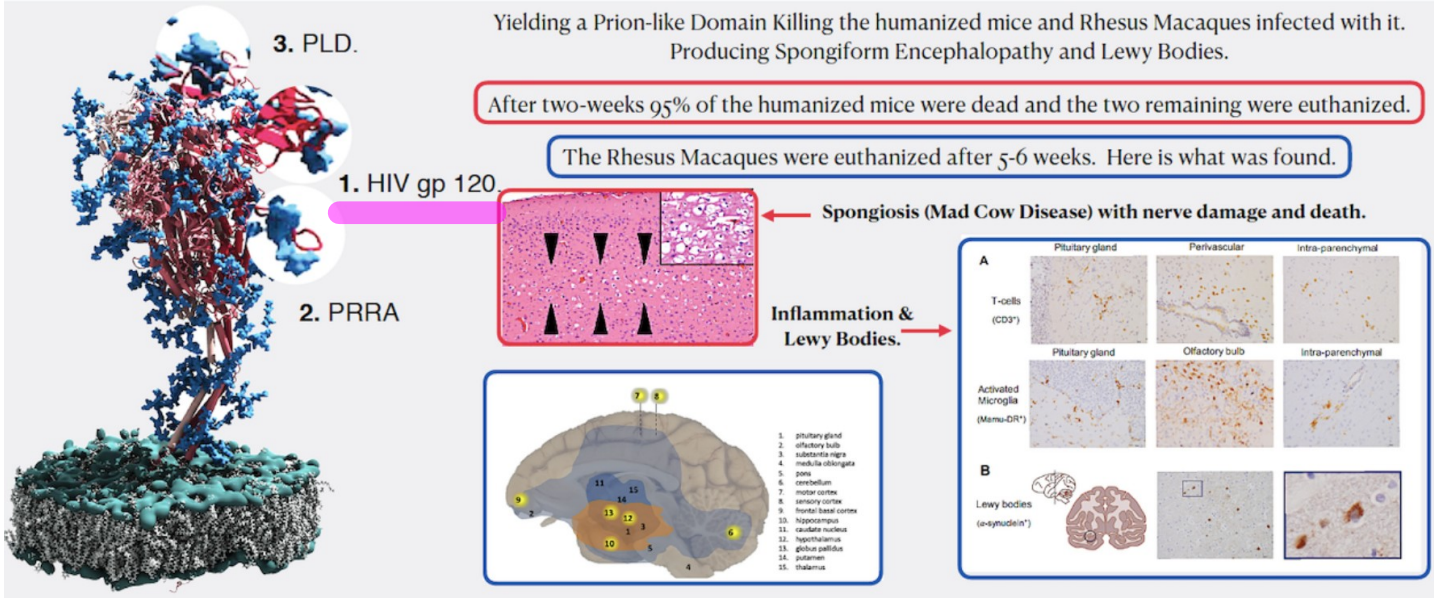
ABSTRACT

Development of new vaccine technology has been plagued with problems in the past. The current RNA based SARS-CoV-2 vaccines were approved in the US using an emergency order without extensive long term safety testing. In this paper the Pfizer COVID-19 vaccine was evaluated for the potential to induce prion-based disease in vaccine recipients. The RNA sequence of the vaccine as well as the spike protein target interaction were analyzed for the potential to convert intracellular RNA binding proteins TAR DNA binding protein (TDP-43) and Fused in Sarcoma (FUS) into their pathologic prion conformations. The results indicate that the vaccine RNA has specific sequences that may induce TDP-43 and FUS to fold into their pathologic prion confirmations. In the current analysis a total of sixteen UG tandem repeats (ΨGΨG) were identified and additional UG (ΨG) rich sequences were identified. Two GGΨA sequences were found. Potential G Quadruplex sequences are possibly present but a more sophisticated computer program is needed to verify these. Furthermore, the spike protein, created by the translation of the vaccine RNA, binds angiotensin converting enzyme 2 (ACE2), a zinc containing enzyme. This interaction has the potential to increase intracellular zinc. Zinc ions have been shown to cause the transformation of TDP-43 to its pathologic prion configuration. The folding of TDP-43 and FUS into their pathologic prion confirmations is known to cause ALS, front temporal lobar degeneration, Alzheimer's disease and other neurological degenerative diseases. The enclosed finding as well as additional potential risks leads the author to believe that regulatory approval of the RNA based vaccines for SARS-CoV-2 was premature and that the vaccine may cause much more harm than benefit.

Inform

Insertions 1 & 2 Produces Prion-Like Domain



Carossino M, et al. Fatal neuroinvasion of SARS-C 1 oV-2 in K18-hACE2 mice is partially dependent on hACE2 expression. https://doi.org/10.1101/2021.01.13.425144
Philippens I, et al. SARS-CoV-2 causes brain inflammation and induces Lewy body 1 formation in macaques. https://doi.org/10.1101/2021.02.23.432474

bioRxiv preprint doi: https://doi.org/10.1101/2020.01.30.927871

Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag

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Abstract:

We are currently witnessing a major epidemic caused by the 2019 novel coronavirus (2019-nCoV). The evolution of 2019-nCoV remains elusive. We found 4 insertions in the spike glycoprotein (S) which are unique to the 2019-nCoV and are not present in other coronaviruses. Importantly, amino acid residues in all the 4 inserts have identity or similarity to those in the HIV-1 gp120 or HIV-1 Gag. Interestingly, despite the inserts being discontinuous on the primary amino acid sequence, 3D-modelling of the 2019-nCoV suggests that they converge to constitute the receptor binding site. The finding of 4 unique inserts in the 2019-nCoV, all of which have identity /similarity to amino acid residues in key structural proteins of HIV-1 is unlikely to be fortuitous in nature. This work provides yet unknown insights on 2019-nCoV and sheds light on the evolution and pathogenicity of this virus with important implications for diagnosis of this virus.

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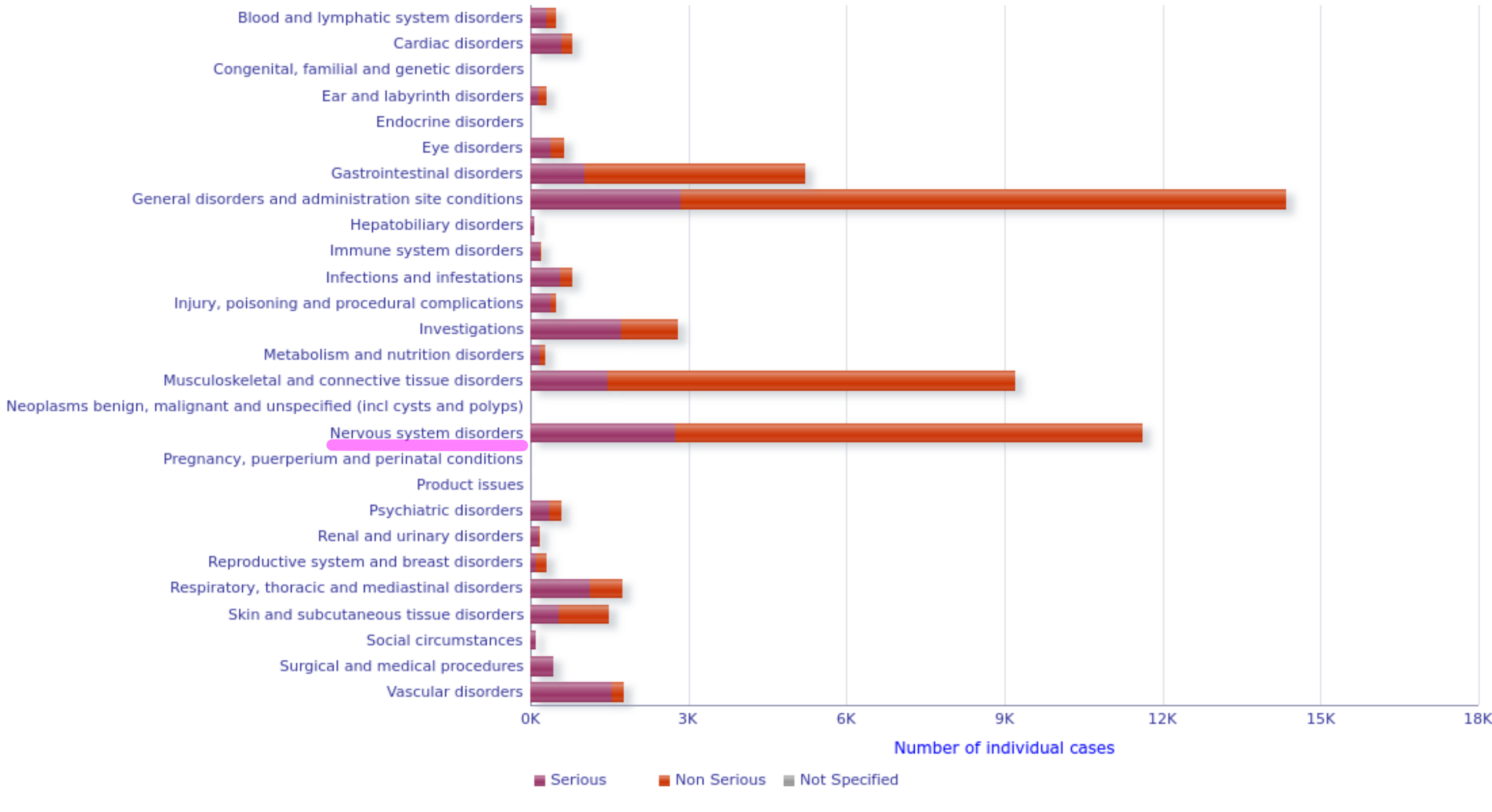
Choose how you want to see the number of individual cases identified in EudraVigilance for **COVID-19 VACCINE JANSSEN (AD26.COV2.S)** (up to 24/07/2021)



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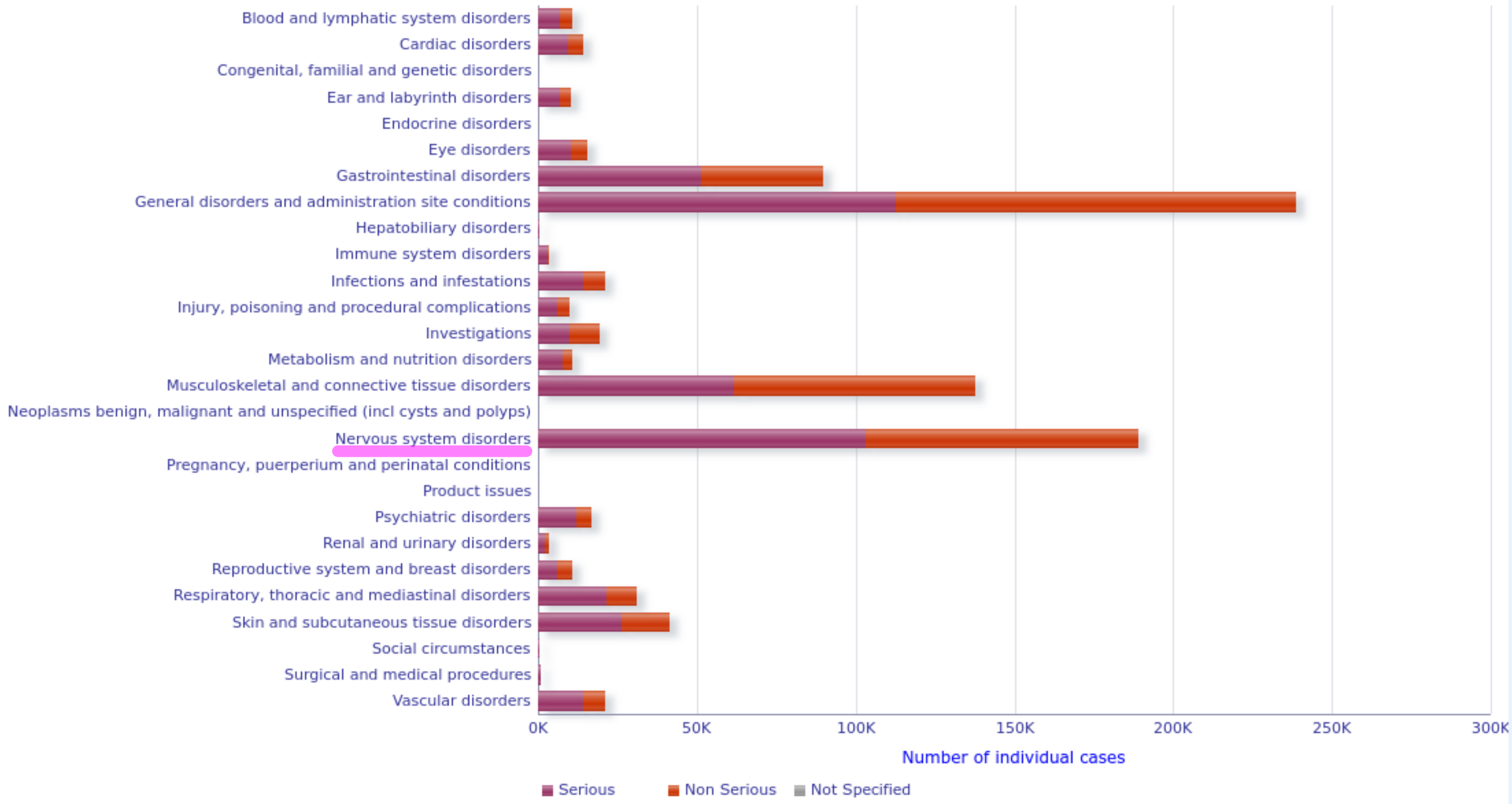

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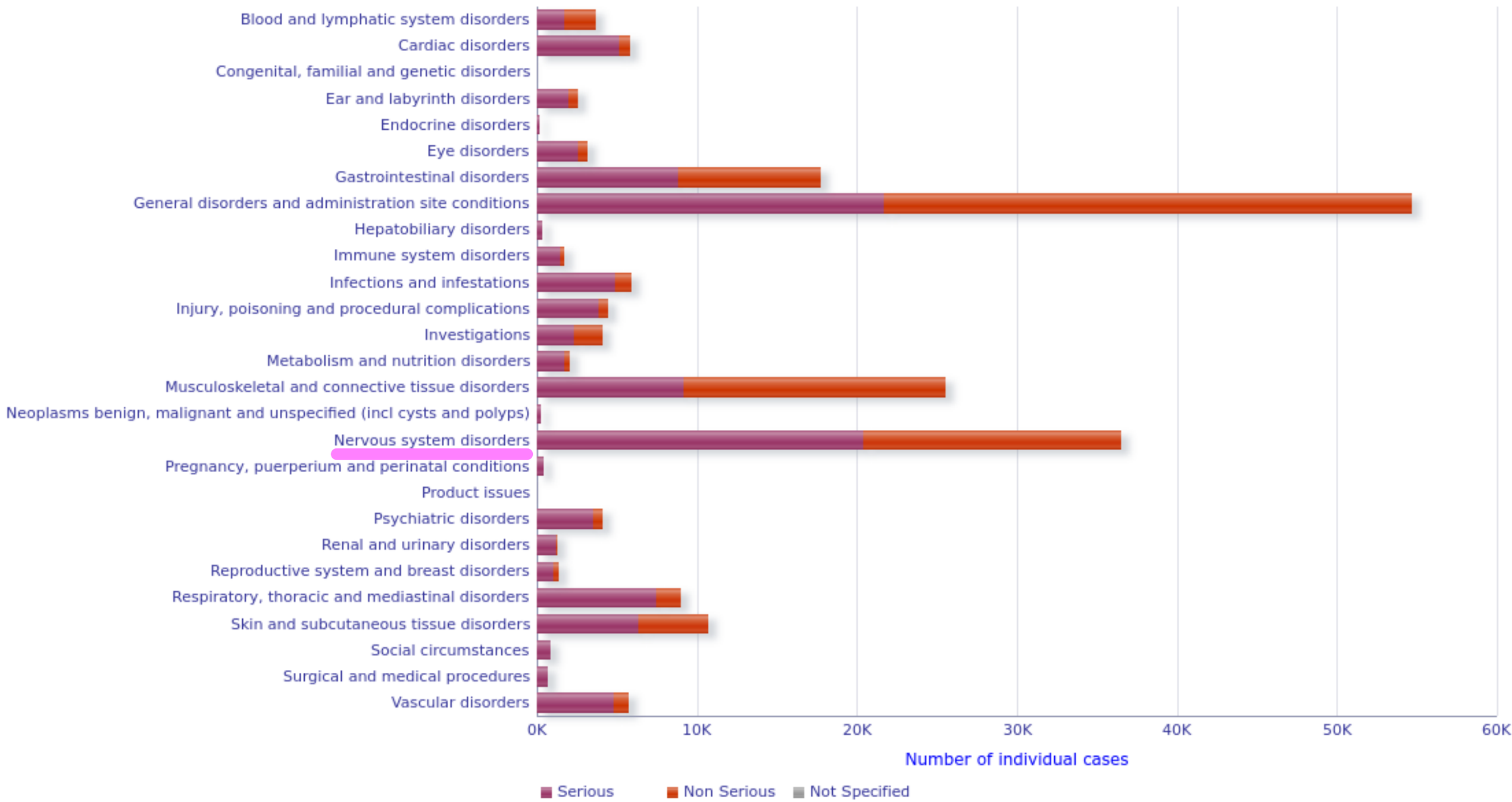

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