

Peer Review

Review of: "Syphilis: A Review of the Controversies on Its Origins and Research of Its Arrival in Quebec, Canada"

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The manuscript addresses an interesting and relevant topic. However, several points require clarification and/or revision in order to strengthen the scientific rigour and clarity of the work. Detailed comments are provided below.

Comments:

In the Results section of the abstract :

- Subspecies names are not consistently formatted. Please ensure that the genus, species, and subspecies epithets are italicised, while "subsp." remains in roman type (e.g., *T. pallidum* subsp. *pallidum*, *T. pallidum* subsp. *endemicum*).
- In paleopathology, periosteal reactions typically associated with syphilis are not specific and may be confused with several other pathological conditions, as mentioned in the final section of the review. In addition to paleopathological observations, it would therefore be useful to indicate whether paleomicrobiological and/or paleogenetic analyses have been performed on the skeletal remains.

In the Conclusions section of the abstract :

The statement "The first historical evidence of syphilis in Quebec dates to 1773" appears to be presented as a definitive conclusion. However, in the absence of any paleomicrobiological confirmation, this should be framed as a probable or tentative hypothesis rather than a certain finding.

Section « Evidence of treponematoses in pre-Columbian Europe »

Paleopathological, paleogenetic, and paleoserological evidence suggests that treponematoses existed in Europe long before the 15th century. You have already cited a medieval case of treponematoses in southern

Europe dating to the 7th and 8th centuries [<https://doi.org/10.1093/infdis/jiad248>]. In addition, the recovery of ancient *Treponema* genomes from human skeletal remains dated to the fifteenth–sixteenth centuries, corresponding to the early modern period in Europe, further supports this view [<https://doi.org/10.1016/j.cub.2020.07.058>]. Moreover, although studies published in 2025 fall outside your inclusion criteria, it is worth noting that treponematoses has very recently been confirmed by paleoserological analyses in skeletal remains from individuals dated to the thirteenth–seventeenth centuries in Central Europe [<https://doi.org/10.1038/s41598-025-12970-z>].

Therefore, as you correctly state that “today, it seems likely that syphilis originated in the Americas,” a hypothesis that is well documented, the key question regarding Europe may rather be whether the American strains introduced into Europe were truly novel or whether they replaced pre-existing local lineages that were potentially less virulent, marked by recombination events and genetic plasticity.

Section « First signs of syphilis in Quebec, Canada »

The statement indicating that « no specific mention of syphilis in Quebec was found in an early edition (eighth edition, 1915) of Sir William Osler’s textbook “*The Principles and Practice of Medicine*” should be interpreted with caution. Historically, during the first epidemics in Italy associated with the French military campaign of 1494 led by King Charles VIII, the disease was commonly referred to as *morbus gallicus* or “French disease” [<https://www.lesbelleslettres.com/livre/9782251344997/la-syphilis-ou-le-mal-francais-syphilis-sive-morbus-gallicus>, <https://doi.org/10.1093/clinids/20.5.1402>]. The term “syphilis” itself was only coined later by the physician and poet Girolamo Fracastoro in his poem *Syphilis sive morbus gallicus*, first published in 1530 [<https://www.lesbelleslettres.com/livre/9782251344997/la-syphilis-ou-le-mal-francais-syphilis-sive-morbus-gallicus>]. Consequently, the absence of the term “syphilis” in early medical texts does not necessarily indicate the absence of the disease, but may rather reflect historical variations in nomenclature.

Declarations

Potential competing interests: No potential competing interests to declare.