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Our reference
GZB 2021 – 0181 SJ/BV/lw

Date 14 October 2021
Subject Questions on JAMA Network Open publication

Enclosure(s)
1 Appendix

Dear Mrs v. R.,

Please find enclosed our response to your question regarding the recent publication on silicone breast implants in JAMA Network Open.

Question to RIVM: Does the recent publication by Dijkman et al. in JAMA Network Open¹ change RIVM's understanding of the quality and safety of silicone breast implants?

Response: RIVM concludes that the study by Dijkman et al. brings no new insights to the existing body of knowledge on the migration of silicones. The study confirms earlier studies that show migration of silicones is a possibility and Dijkman et al. acknowledge that no correlation of their results with clinical symptoms can be made. A more elaborate review of the publication is given in the appendix.

Yours sincerely,

Dr. Susan Janssen
Hoofd Centrum voor Gezondheidsbescherming

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Summary of the paper:

The study of Dijkman et al. reports on 389 tissue samples from a pathology database collected from 1986-2020. Tissue samples were selected from women that had silicone breast implants and underwent surgery for unspecified reasons. The tissue samples were examined for the presence of silicones by visual light microscopy, sometimes supported by histological staining and in a few cases by EDX measurements. Using these methods, the authors report finding silicones in 98,8% of the tissue samples. The authors subsequently attribute tissue samples to a group of cohesive or non-cohesive gel implants and conclude they are qualitatively not statistically different. Dijkman et al. acknowledge that no correlations of silicone migration and clinical symptoms can be made.

Considerations:

RIVM concludes that this study brings no new insights since:

- The migration of silicones from silicone breast implants to surrounding tissue and lymph nodes has been broadly recognized for many years.² Silicones from all types of silicone breast implants may migrate to surrounding tissue and lymph nodes. Over time, several actions were taken to reduce the migration of silicones.³
- It has been known for many years that there are persons with silicone breast implants who report various types of health complaints. Part of the health complaints are local complications with a clear association with silicone breast implants.⁴ For the more generic systemic health complaints the research on their potential association with silicone breast implants is ongoing, also in the Netherlands.⁵ This ongoing research should lead to an understanding of whether there is an association with silicone breast implants and if so why part of the people with silicone breast implants experience health complaints, while others do not.

Methodological limitations:

JAMA Network Open has published an invited commentary together with the Dijkman paper.⁶ The authors of the invited commentary point out that the Dijkman study was performed on a set of samples from a non-representative group of women with breast implants with unknown medical history. They also mention that it is not clear if the implants were ruptured or not, and that clinical relevance of migrating silicones remains to be investigated. RIVM agrees with these remarks.

RIVM would like to add that the set of samples has an additional bias because it is solely based on a surgeons' decision to select them for pathology examination and that grouping of the samples by the authors is largely based on assumed implant history and gel-type. Results thus do not inform on the actual proportion of breast implants in which silicones migrate from either cohesive or non-cohesive gel filled breast implants. It also does not inform on the extent migration takes place from different types of implants.

Furthermore, Dijkman et al. use light microscopy, sometimes supported by histological staining and in a few cases EDX to identify silicones in human tissue. The suitability and accuracy of these methods cannot be determined as the authors do not provide validation studies for this application.

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References

1. Dijkman HBPM, Slaats I, Bult P. Assessment of Silicone Particle Migration Among Women Undergoing Removal or Revision of Silicone Breast Implants in the Netherlands. *JAMA Network Open* 2021; **4**(9): e2125381-e.
2. SCENIHR. Opinion on The safety of Poly Implant Prothèse (PIP) Silicone Breast Implants Update of the Opinion of February 2012. Luxembourg, 2014.
3. Kaderbhai A, Broomfield A, Cuss A, Shaw K, Deva A. Breast implant guide for general practice. *Australian Journal for General Practitioners* 2021; **50**: 484-90.
4. de Boer M, van Leeuwen FE, Hauptmann M, et al. Breast Implants and the Risk of Anaplastic Large-Cell Lymphoma in the Breast. *JAMA oncology* 2018; **4**(3): 335-41.
5. RIVM. Onderzoeksprogramma gezondheidsklachten van vrouwen met een siliconen borstimplantaat. 2021. <https://www.rivm.nl/medische-hulpmiddelen/siliconen-borstimplantaten/onderzoeksprogramma-gezondheidsklachten>.
6. Löfgren J, Lohmander F. Silicone Breast Implants and Disease—Many Questions Unanswered. *JAMA Network Open* 2021; **4**(9): e2128947-e.