***eLife’s* transparent reporting form**

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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
* You should state the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

The sample size threshold was calculated as follows:

where is the sample size threshold, is the z-score for the level of confidence (95%), is the standard deviation (assumed to be 3 log10 copies/ml, a fourth of the full range of rVLs) and is the marginal error (assumed to be 1 log10 copies/ml, based on the minimum detection limit for qRT-PCR across studies). This item was met if ≥75% of the included DFSO had ≥46 specimen measurements. This is described in the Appendix.

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
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* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

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The number of studies, specimen numbers or case numbers are described in the results section, in a plot, its figure caption or a table (main body or appendix) in our study.

**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

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The statistical tests used in each figure are described in the caption. Greater detail on these statistical tests is described in the Methods section. Exact P-values above 0.001 are reported. Raw data in the meta-regression was presented in each of the plots (see main body figures and figure supplements). 95% CIs are specified throughout the results section, in figures, in figure supplements or appendix tables. Sample numbers are described throughout the results section, in figures, in figure supplements, tables or appendix tables.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
* Indicate if masking was used during group allocation, data collection and/or data analysis

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

Case definitions were defined in the Methods section. As our study was based on a systematic review and meta-analyses, there was no experimental groups or randomization.

**Additional data files (“source data”)**

* We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
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Please indicate the figures or tables for which source data files have been provided:

This manuscript includes a Data Availability statement, which reads “The systematic dataset and model outputs from this study can be download from a public repository (http://doi.org/10.5281/zenodo.4770611). The systematic review protocol was prospectively registered on PROSPERO (registration number, CRD42020204637).