Supplementary Data

Table S1: Four basic techniques are used to evaluate the relationship between sevoflurane and adverse events.

Algorithms	Formula	Signal standard
PRR	PRR = a(c+d)/c/(a+b) $\chi 2$ = [(ad-bc)^2](a+b+c+d)/[(a+b)(c+d)(a+c)(b+d)]	PRR≥2, $\chi 2 \geq 4$, N ≥ 3
ROR	ROR = ad/b/c 95%CI = $e^{\ln(ROR)\pm 1.96(1/a+1/b+1/c+1/d)^{0.5}}$	lower limit of 95% CI > 1, N ≥ 3
MGPS	EBGM = a(a+b+c+d)/(a+c)/(a+b) 95%CI = $e^{\ln(EBGM)\pm 1.96(1/a+1/b+1/c+1/d)^{0.5}}$	EBGM05 > 2
BCPNN	$IC = \log_2 \frac{a(a+b+c+d)}{(a+b)(a+c)}$ $E(IC) = \log_2 \frac{(a+\gamma 11)(a+b+c+d+\alpha)(a+b+c+d+\beta)}{(a+b+c+d+\gamma)(a+b+\alpha 1)(a+c+\beta 1)}$ and $\gamma = \gamma 11 \frac{(a+b+c+d+\alpha)(a+b+c+d+\beta)}{(a+b+\alpha 1)(a+c+\beta 1)}$ $IC - 2SD = E(IC) - 2\sqrt{V(IC)}$	IC025 > 0

The READUS-PV checklist for abstracts

Section and topic	Item #	Checklist item	Location where item is reported
Background	1a	State the aim/rationale for performing the study.	Page 1, background
	1b	Specify the adverse event(s) and/or the drug(s) under study, when applicable.	Page 1, background
	1c	Specify the specific population or setting, when applicable.	Not applicable
Methods	2a	Identify the study as a "disproportionality analysis" and specify the type of data used.	Page 1, methods
	2b	Specify the name of the database(s) used and the type of access.	Page 1, objectives
	2c	Specify the timeframe and geographical region, when applicable.	Page 1, objectives
	2d	Specify the disproportionality measure(s) used and their statistical significance threshold(s).	Not applicable
	2e	Specify if a case-by-case analysis is performed.	Not applicable
Results	3	Report main findings including their precision (e.g., 95% confidence intervals), together with a short summary of the case-by-case analysis.	Page 1, results
Conclusion	4a	Clearly report key conclusions.	Page 1, conclusion
	4b	Acknowledge that the disproportionality analysis is a hypothesis generating or refinement approach.	Page 1, conclusion
	4c	State the implications and clinical relevance of the findings.	Page 1, conclusion

The READUS-PV checklist

Section and topic	Item #	Checklist item	Location where item is reported
Title			
	1a	If disproportionality analyses are a prominent component of the published study, the study should be identified as a "disproportionality analysis". The type of data and name of the database(s) should be specified.	Pages 1, title
	1b	Report the name of adverse event(s) and/or drug(s) under study, when applicable.	Pages 1, title
Introduction			
Background	2a	Describe the drug(s) and its utilization, the nature of the adverse event(s) under study and its frequency, and the existing knowledge on the drug-event combination.	Pages 1, introduction
	2b	Specify the rationale for performing the analysis, e.g., as part of routine pharmacovigilance, to investigate an overall safety profile, or to assess a pre-specified hypothesis.	Pages 1, introduction
	2c	Explain why ICSR databases and disproportionality analysis are suitable to fill the knowledge gap.	Pages 1-2, introduction
Objectives	3	State specific objectives, identifying the adverse event(s), the drug(s), and the reference group, including any pre-specified hypothesis, if applicable.	Pages 2, methods
Methods			
Study design	4a	Identify the study (i.e., "disproportionality analysis") and the type of data used (e.g., "individual case safety reports").	Pages 2, methods
	4b	Provide an outline of the entire study design, including primary and sensitivity analyses performed, and other designs such as case-by-case analysis or literature review.	Pages 2, methods
Data description, access, and pre-processing	5a	Specify the name of the database(s), the database(s) custodian, and the coverage. Specify the type/number of drugs included within the database and the thesaurus, taxonomies, or ontologies used for coding drugs and events.	Pages 2, methods
	5b	Specify the extraction dates and describe and justify all choices used for data pre-processing, including any data transformation or exclusion, if appropriate.	Pages 2, methods
Variables definition	6a	Describe the study population, including any restriction.	Not applicable

	6b	Describe the nature and the meaning of key variables assessed in the work.	Pages 2, methods
	6c	Specify and justify any grouping of drugs or events. For drugs, specify and justify whether active ingredients/trade names/salts were considered and/or the selected role.	Pages 2, methods
	6d	Describe any additional data source used, the type of data, and how they interact with ICSRs.	Not applicable
Statistical methods	7a	Present any descriptive analysis performed, specifying variables investigated, statistical tests, and significance thresholds.	Pages 10, Supplementary Data
	7b	Describe the measure(s) selected for the disproportionality analysis including any threshold used to identify signals of disproportionate reporting. Explain the reason for this choice if applicable.	Pages 10, Supplementary Data
	7c	Clearly describe any sensitivity analysis and any tool to control confounding, including any restriction, subgroup, stratification, adjustment, or interaction.	Pages 2, methods
	7d	Specify the variables and methods used for the case-by-case analysis, including any algorithm or criteria used to assess causality, if performed.	Not applicable
	7e	Specify any statistical methods used for other data sources.	Not applicable
Results			
Participants	8a	Specify the number of individual case safety reports included at each stage, including reasons for exclusion.	Pages 2, results
	8b	Provide key demographic and clinical characteristics of cases, if possible comparing cases with any appropriate reference group.	Pages 2, results
Disproportionality analysis	9	Present all results including confidence intervals. Present also results of sensitivity analyses, if performed.	Pages 2-3, results
Case-by-case analysis	10	Present the case-by-case analysis of key variables. Present the causality assessment, if applicable.	Pages 2-3, results
Discussion			
Key results	11	Discuss key results with reference to study objectives and contextualize them within the current literature and other consulted sources. Clearly discriminate between expected reactions and emerging safety signals.	Pages 6, discussion
External validity	12a	Discuss the external validity of the results to the general population.	Pages 7, discussion
	12b	Discuss the potential relevance of results in clinical practice	Pages 7, discussion
	12c	Propose further study designs if applicable	Pages 8, discussion
Limitations	13	Present general limitations, making clear that disproportionality analysis alone cannot prove causation or measure incidence, and specific limitations, including confounding and reporting bias and efforts to mitigate them.	Pages 8, discussion
Declarations			
	14a	Provide the source of funding/sponsorship and the role of the funders/sponsors for the present study and for any original study on which the present article is based.	Pages 8
	14b	Clearly identify potential commercial and intellectual conflicts of interest (e.g., link to any drug/event investigated, whether financial, legal action, or software used).	Pages 8
	14c	Declare any institutional approval needed or granted in the investigation.	Pages 8
	14d	Include a statement on data availability, code availability (including the version of the statistical software used), and protocol registration.	Pages 8