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Major Adverse Cardiac Events and Mortality Associated with Electroconvulsive Therapy

A Systematic Review and Meta-analysis

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ABSTRACT

Background: Cardiac events after electroconvulsive therapy have been reported sporadically, but a systematic assessment of the risk is missing. The goal of this study was to obtain a robust estimate of the incidence of major adverse cardiac events in adult patients undergoing electroconvulsive therapy.

Methods: Systematic review and meta-analysis of studies that investigated electroconvulsive therapy and reported major adverse cardiac events and/or mortality. Endpoints were incidence rates of major adverse cardiac events, including myocardial infarction, arrhythmia, pulmonary edema, pulmonary embolism, acute heart failure, and cardiac arrest. Additional endpoints were all-cause and cardiac mortality. The pooled estimated incidence rates and 95% CIs of individual major adverse cardiac events and mortality per 1,000 patients and per 1,000 electroconvulsive therapy treatments were calculated.

Results: After screening of 2,641 publications and full-text assessment of 284 studies, the data of 82 studies were extracted (total n = 106,569 patients; n = 786,995 electroconvulsive therapy treatments). The most commonly reported major adverse cardiac events were acute heart failure, arrhythmia, and acute pulmonary edema with an incidence (95% CI) of 24 (12.48 to 46.13), 25.83 (14.83 to 45.00), and 4.92 (0.85 to 28.60) per 1,000 patients or 2.44 (1.27 to 4.69), 4.66 (2.15 to 10.09), and 1.50 (0.71 to 3.14) per 1,000 electroconvulsive therapy treatments. All-cause mortality was 0.42 (0.11 to 1.52) deaths per 1,000 patients and 0.06 (0.02 to 0.23) deaths per 1,000 electroconvulsive therapy treatments. Cardiac death accounted for 29% (23 of 79) of deaths.

Conclusions: Major adverse cardiac events and death after electroconvulsive therapy are infrequent and occur in about 1 of 50 patients and after about 1 of 200 to 500 electroconvulsive therapy treatments.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- The incidence of major adverse cardiac events after electroconvulsive therapy is not known

What This Article Tells Us That Is New

- Major adverse cardiac events and death after electroconvulsive therapy are infrequent and occur in about 1 of 50 patients and after about 1 of 200 to 500 electroconvulsive therapy treatments

Electroconvulsive therapy provides a potentially life-saving option for severe psychiatric conditions.[1] Electroconvulsive therapy is generally considered safe.[2] Nevertheless, the brief, yet intense, hemodynamic stress caused by seizure initiation during electroconvulsive therapy may increase the risk of cardiovascular events, especially in patients with preexisting cardiovascular conditions.[3,4]

Major adverse cardiovascular events after electroconvulsive therapy, such as acute myocardial infarction or acute heart failure, have been reported sporadically in individual case reports[5,6] or case series.[7] Retrospective cohort studies[8–10] have aimed to assess the risk of major adverse cardiac events after electroconvulsive therapy, but the infrequent occurrence of these complications rendered it difficult to obtain good population-level estimates about true incidence rates.[11,12] To obtain a more robust estimate about the incidence of major adverse cardiac events and mortality after electroconvulsive therapy, we therefore conducted a systematic review and meta-analysis.

Materials and Methods

Data Sources

PubMed, PsycINFO, Scopus, Cochrane CENTRAL, Cochrane Database of Systematic Reviews, and Current Content were searched with cutoff date of November 12, 2016. In addition, bibliographies of articles included in data extraction and of pertinent books were hand-searched. Articles reporting cardiac morbidity and mortality in the context of electroconvulsive therapy published from

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January 1, 1980, to November 12, 2016, were identified using indexed terms and text words (see supplemental digital content, http://links.lww.com/ALN/B797).

Study Selection

After screening of 2,641 publications by two independent investigators, 284 studies were assessed in full text for eligibility. Interventional, retrospective and prospective observational studies, and surveys that investigated electroconvulsive therapy and reported major adverse cardiac events and/or mortality were included for data extraction. Exclusion criteria were electroconvulsive therapy performed in children (age 18 yr or younger) or pregnant women, electroconvulsive therapy performed without general anesthesia, or reports in any language other than English or German. Studies that mentioned neither the absence nor the occurrence of adverse events were excluded from data extraction (qualitative analysis).

Data Extraction and Synthesis

The PRISMA guidelines were followed to extract data. Quality of harms assessment and reporting was based on the McMaster tool.[13] Of the selected articles, 10% were captured by two independent investigators to test the feasibility of prespecified criteria and to develop a data extraction plan (see supplemental digital content, http://links.lww.com/ALN/B797). The criteria were discussed, and a database was developed on consensus of all investigators that allowed uniform capture of data extraction. Three investigators (A.D., M.M., B.P.) retrieved the data of a randomly chosen subset of studies. Of each study included in the qualitative analysis, a single investigator extracted the number of included patients; number of electroconvulsive therapy treatments; frequency of reported major adverse cardiac events, cardiac death, and all-cause mortality; design; information about the population's cardiovascular health status at inclusion; duration of follow-up; and the quality of harms reporting. The extracted components of major adverse cardiac events were myocardial infarction, arrhythmia, pulmonary edema, pulmonary embolism, acute heart failure, and cardiac arrest. The supplemental digital content (http://links.lww.com/ALN/B797) provides the definition used for each component of major adverse cardiac events and mortality. Most studies only reported a subset of major adverse cardiac events and/or mortality.

Risk of bias was assessed based on study design, cardiovascular health status at inclusion, duration of follow-up, and the quality of harms reporting (see supplemental digital content, http://links.lww.com/ALN/B797). Finally, extraction and adjudication of outcome data included in the meta-analysis was repeated by a second investigator, and differences from the first investigator were discussed and corrected. The meta-analysis of each component of major adverse cardiac events included studies that reported the occurrence or absence of the investigated component of major adverse cardiac events. In 28 of 82 studies, the authors reported that there were "no adverse events" but did not report what type of adverse events were assessed. Those studies were not included to calculate the incidence rate of major adverse cardiac events, because the risk that such events may have been missed was deemed too high. However, it appeared unlikely that authors missed deaths, and therefore, these 28 studies were included in the calculation of mortality incidence. The meta-analysis of all-cause mortality and cardiac death included studies that reported the occurrence of death or absence of any adverse event within 30 days after electroconvulsive therapy. In a sensitivity analysis of mortality, we excluded studies that reported the absence of any adverse events.

Statistical Analysis

Incidence rates of major adverse cardiac events, which included acute myocardial infarction, arrhythmia, pulmonary edema, pulmonary embolism, acute heart failure, and cardiac arrest, are reported. In addition, we report incidence rates of all-cause mortality and cardiac death. For each individual study, probability and the Jeffrey's CI were calculated.[14] We estimated the pooled probabilities and 95% CI using two different methods that were considered equally appropriate for a meta-analysis of rare or zero events studies. One analysis was a random effects model based on the method of DerSimonian and Laird with the estimate of heterogeneity from the Mantel–Haenszel model and standard error by Jeffrey's β distribution based method for zero event studies. The other analysis was a random effects Poisson model.[15]

Each of the methods involves certain assumptions. In our context, the DerSimonian and Laird method assumes that the observed adverse event rate in each study can be partitioned into two additive components, a true rate for study i, denoted θ_i, and sampling error. The studies are assumed to be a sample from a hypothetical population of studies, so that $\theta_i = \mu + \delta_i$, where μ is the population mean and δ_i is the deviation of the i^{th} study's rate from the population mean. The pooled estimate of μ is obtained by taking a weighted average of the observed rates across the different studies, where the weights depend on the sampling error for each study plus a second parameter that represents the between-study variation in the $\theta_i's$. An added complication arises when estimating the sampling error for studies in which no adverse events occur, and for this we used Jeffrey's β distribution–based method.

In the Poisson modeling approach, the number of adverse events observed in study i is assumed to arise from a Poisson distribution with mean θ_i, where the μ_i, in turn, are assumed to have been drawn from a distribution of values across a hypothetical population of similar studies. This model directly accommodates studies in which no event occurs but makes the

further assumption that the random, study-specific deviations are normally distributed. These different modeling assumptions and the computational techniques that go with them can lead to different pooled estimates and CIs. Because neither method has been proven superior, and the methods handle zero events, heterogeneity, and between-study variability differently, we decided to present the estimates from both models, although in the abstract we present only the generally higher, Poisson modeling–based estimates. The data are presented as incidence rate per 1,000 patients and per 1,000 electroconvulsive therapy treatments. For each investigated outcome, Forest plots were produced using GraphPad Prism (version 6.07; USA). Microsoft Access (Microsoft, USA), Microsoft Excel (Microsoft, USA), and Stata (version 14.1; USA) were used for data management and statistical analyses.

Results

Of 2,641 screened publications, 284 were assessed in full text, of which data of 82 studies (32 interventional studies, 46 observational studies, and 4 surveys) were extracted (total n = 106,569 patients; n = 786,995 electroconvulsive therapy treatments; fig. 1). Most studies reported only a subset of major adverse cardiac events and/or deaths. Incidence rates of major adverse cardiac events after electroconvulsive therapy could be extracted from 54 of 82 studies, and mortality data could be extracted from 43 of 82 studies (see supplemental digital content, http://links.lww.com/ALN/B797). Sample sizes for extracted individual major adverse cardiac events (denominators) ranged from 375 patients (acute heart failure) to 51,291 patients (cardiac arrest) or 1,457 electroconvulsive therapy treatments (pulmonary embolism) to 297,624 electroconvulsive therapy treatments (cardiac arrest). Sample sizes for mortality were 75,587 patients and 688,525 electroconvulsive therapy treatments. Considerable heterogeneity (I^2 greater than 50%) was observed in the incidence rates of arrhythmia (I^2 = 81.2% to 88.8%), cardiac arrest (I^2 = 74.8% to 75.8%), and all-cause mortality (sensitivity analysis) (I^2 = 71.6 to 79.3%).

The most commonly reported major adverse cardiac event was acute arrhythmia (n = 39 studies) with an

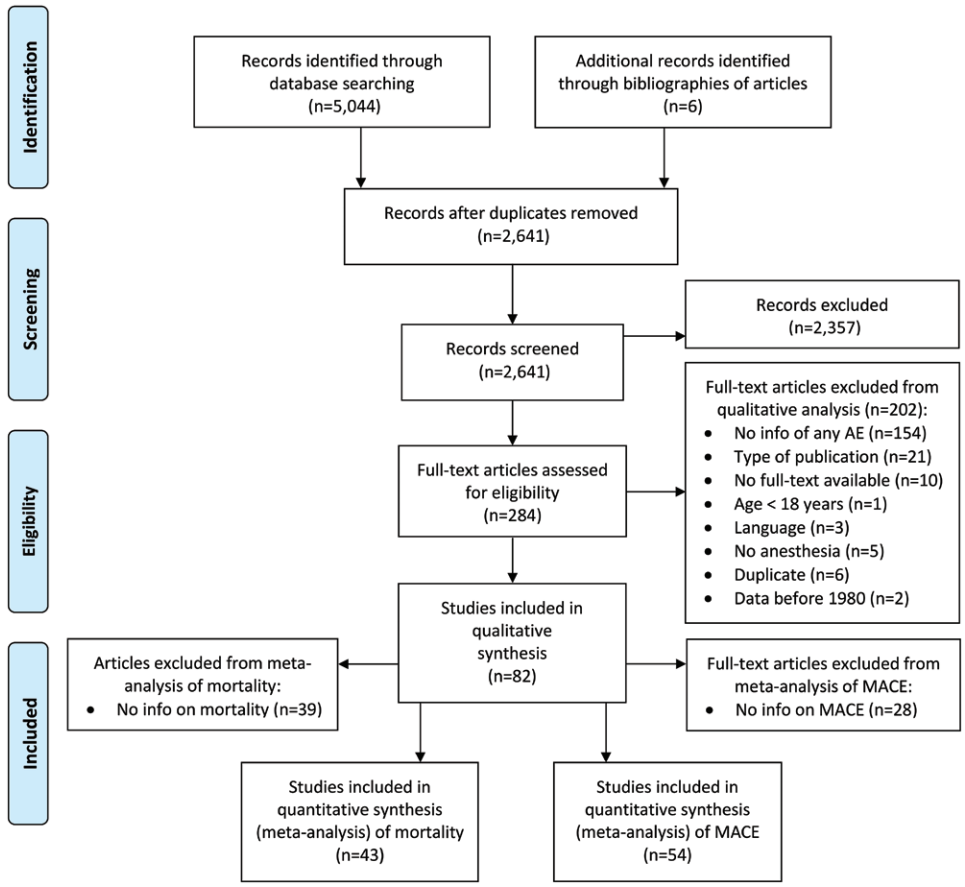

Fig. 1. PRISMA flowchart. The process from identification to inclusion of reports is shown. AE, adverse events; MACE, major adverse cardiac events.

Table 1. Incidence of Major Adverse Cardiac Events after Electroconvulsive Therapy

	Patients				Electroconvulsive Therapy Treatments			
Adverse Events	No. of Studies	No. of Events/ Patients	Model	Incidence [95% CI] per 1,000 Patients	No. of Studies	No. of Events/ Treatments	Model	Incidence [95% CI] per 1,000 Treatments
Myocardial infarction	9	12/3,827	DerSimonian and Laird Poisson	1.11 [0.00–2.58] 6.10 [2.06–18.08]	9	12/25,529	DerSimonian and Laird Poisson	0.77 [0.00–1.58] 0.97 [0.34–2.75]
Life-threatening arrhythmia	39	146/7,754	DerSimonian and Laird Poisson	14.82 [8.63–21.02] 25.83 [14.83–45.00]	41	252/132,138	DerSimonian and Laird Poisson	0.87 [0.38–1.37] 4.66 [2.15–10.09]
Acute pulmonary edema	4	7/1,783	DerSimonian and Laird Poisson	7.59 [0.00–20.09] 4.92 [0.85–28.60]	4	7/4,675	DerSimonian and Laird Poisson	1.22 [0.22–2.23] 1.50 [0.71–3.14]
Pulmonary embolism	2	1/1,447	DerSimonian and Laird Poisson	0.70 [0.00–2.06] 0.69 [0.10–4.91]	2	1/1,457	DerSimonian and Laird Poisson	0.70 [0.00–2.06] 0.69 [0.10–4.87]
Acute heart failure	3	9/375	DerSimonian and Laird Poisson	19.98 [5.85–34.11] 24 [12.48–46.13]	3	9/3,687	DerSimonian and Laird Poisson	2.08 [0.61–3.55] 2.44 [1.27–4.69]
Cardiac arrest	8	56/51,291	DerSimonian and Laird Poisson	0.95 [0.00–1.89] 4.23 [0.69–25.84]	8	56/297,624	DerSimonian and Laird Poisson	0.15 [0.01–0.28] 0.56 [0.10–3.23]

Incidence [95% CI] was determined per 1,000 patients and per 1,000 electroconvulsive therapy treatments using two random effects models.

estimated incidence rate of 14.82 (8.63 to 21.02) using the DerSimonian and Laird model and 25.83 (14.83 to 45.00) per 1,000 patients using the Poisson model or 0.87 (0.38 to 1.37) and 4.66 (2.15 to 10.09) per 1,000 electroconvulsive therapy treatments (table 1). Acute heart failure was reported in a smaller number of studies (n = 3) but had a higher incidence rate: 19.98 (5.85 to 34.11) (DerSimonian and Laird model) and 24 (12.48 to 46.13) (Poisson model) per 1,000 patients or 2.08 (0.61 to 3.55) (DerSimonian and Laird model) and 2.44 (1.27 to 4.69) (Poisson model) per 1,000 electroconvulsive therapy treatments. Acute pulmonary edema (n = 4 studies), which could be of cardiac or noncardiac origin, had an incidence rate of 7.59 (0.00 to 20.09) (DerSimonian and Laird model) and 4.92 (0.85 to 28.60) (Poisson model) per 1,000 patients or 1.22 (0.22 to 2.23) (DerSimonian and Laird model) and 1.50 (0.71 to 3.14) (Poisson model) per 1,000 electroconvulsive therapy treatments. All-cause mortality (n = 41 studies) was 0.13 (0.00 to 0.27) (DerSimonian and Laird model) and 0.42 (0.11 to 1.52) (Poisson model) per 1,000 patients or 0.05 (0.01 to 0.08) (DerSimonian and Laird model) and 0.06 (0.02 to 0.23) (Poisson model) per 1,000 electroconvulsive therapy treatments (table 2). In a sensitivity analysis, where we excluded studies (n = 13 studies) that reported simply that no adverse events occurred, but without giving any details, the estimated all-cause mortality rate was 0.33 (0.01 to 0.64) (DerSimonian and Laird model) and 0.75 (0.17 to 3.24) (Poisson model) per 1,000 patients or 0.06 (0.02 to 0.11) (DerSimonian and Laird model) and 0.10 (0.02 to 0.42) (Poisson model) per 1,000 electroconvulsive therapy treatments. Cardiac death accounted for 29% (23 of 79 deaths) of deaths. To determine whether the risk of cardiac events after electroconvulsive therapy may be higher in patients with preexisting cardiovascular disease, we performed several subgroup analyses that were restricted to patients with (or without) known cardiovascular disease (tables 3 and 4).

Discussion

The results of this systematic review and meta-analysis show that an estimated 25.83 (14.83 to 45.00) per 1,000 patients (approximately 1 in 50 patients) develop major adverse cardiac events after electroconvulsive therapy (2%). The risk based per electroconvulsive therapy treatment is 4.66 (2.15 to 10.09) per 1,000 electroconvulsive therapies (approximately 1 major adverse cardiac event in 200 electroconvulsive therapy treatments). These estimates are based on the Poisson model, which yields higher values in this case and wider CI. The reason why the risk per patient is proportionally higher than per electroconvulsive therapy treatment is that most patients undergo a series of electroconvulsive therapy treatments, and the procedure is likely terminated once a serious adverse event occurs.

The primary goal of this study was to capture all available published data reporting on cardiac events after electroconvulsive therapy. We scanned the published literature from 1980 to the end of 2016 and retrieved 82 studies of varying degrees of quality and bias risk. Studies ranged from surveys that were sent out to practitioners to rigorous prospective cohort studies. We decided *a priori* to exclude studies that did not mention adverse events at all (neither absence nor presence). If studies mentioned that no adverse events occurred, they were included in the meta-analysis for mortality—because we assessed the risk of having missed a death to be low—but not in the meta-analysis for individual major adverse cardiac events, because we deemed the risk too high. The sensitivity analysis was restricted to studies

Table 2. Incidence of Mortality after Electroconvulsive Therapy

	Patients				ECT treatments			
Mortality	No. of Studies	No. of Events/ Patients	Model	Incidence [95% CI] per 1,000 Patients	No. of Studies	No. of Events/ Treatments	Model	Incidence [95% CI] per 1,000 Treatments
Studies reporting no adverse events included								
All-cause mortality	41	49/75,587	DerSimonian and Laird	0.13 [0.00–0.27]	43	79/688,525	DerSimonian and Laird	0.05 [0.01–0.08]
			Poisson	0.42 [0.11–1.52]			Poisson	0.06 [0.02–0.23]
Cardiac deaths	37	15/45,568	DerSimonian and Laird	0.04 [0.00–0.15]	39	23/525,419	DerSimonian and Laird	0.01 [0.00–0.03]
			Poisson	0.12 [0.01–1.15]			Poisson	0.02 [0.00–0.12]
Studies reporting no adverse events excluded (sensitivity analysis)								
All-cause mortality	13	49/74,128	DerSimonian and Laird	0.33 [0.01–0.64]	15	79/680,802	DerSimonian and Laird	0.06 [0.02–0.11]
			Poisson	0.75 [0.17–3.24]			Poisson	0.10 [0.02–0.42]
Cardiac deaths	9	15/44,109	DerSimonian and Laird	0.18 [0.00–0.46]	11	23/517,696	DerSimonian and Laird	0.02 [0.00–0.05]
			Poisson	0.19 [0.02–2.4]			Poisson	0.02 (0.00–0.17)

Incidence [95% CI] was determined per 1,000 patients and per 1,000 electroconvulsive therapy treatments using two random effects models. Studies reporting no adverse events stated that no adverse events occurred.

that definitively reported individual major adverse cardiac events and excluded 13 studies that mentioned only that no adverse events occurred. The mortality rate per patient in the sensitivity analysis increased 3-fold but was similar when analyzed per electroconvulsive therapy treatment.

Our analysis obtained robust sample sizes that ranged from several hundred patients to more than 50,000 and from a few 1,000 to nearly 300,000 electroconvulsive therapy treatments for individual major adverse cardiac events. For mortality estimates, pooled sample sizes included more than 75,000 patients and more than 680,000 treatments. A sample size of that magnitude provide robust estimates that approximate population-level incidence rates. Indeed, a recent population-based study[11] determined an all-cause mortality rate of 0.04 and 0.24 per 1,000 electroconvulsive therapies within 1 and 7 days of an electroconvulsive therapy treatment similar to our finding of 0.04 to 0.10 per 1,000 electroconvulsive therapies. In addition, they determined an event rate of about 0.05 for arrhythmia and 0.1 for myocardial infarction per 1,000 electroconvulsive therapies corresponding to the 0.87 and 0.77 we found in the DerSimonian and Laird models.

Clinical Implications

Despite the low frequency of major cardiac events after electroconvulsive therapy, the question of whether these events may be preventable or not should be addressed in subsequent work. In two prospective cohort studies, Duma *et al.*[16] and Martinez *et al.*[17] showed that in about 5 to 10% of electroconvulsive therapy treatments, patients develop cardiac troponin elevation, which indicates myocardial cell damage. Cardiovascular stress during electroconvulsive therapy is of short duration and may be prevented by administration of short-acting drugs, such as β-blockers.[3,18–23]

Limitations

Systematic reviews can only pool available evidence and strongly relies on the quality of the underlying data. In our study, the quality of data was mixed. Several studies were prospectively designed with rigorous outcomes assessment; other studies were either surveys or retrospective database analyses with a significant risk of missed events. Considerable heterogeneity was found in the meta-analysis of several outcomes. Possible explanations for the heterogeneity may include the differences in design and duration of follow-up, as well as uncaptured differences in patient characteristics and periprocedural management. The majority of studies were not restricted to patients with cardiac disease, so it was difficult assess a potential risk increase in patients with preexisting cardiovascular disease. Therefore, the results of this study may over- or underestimate the true incidence rate of cardiac events after electroconvulsive therapy. Second, deaths may occur after electroconvulsive therapy because of many other factors and may only be temporally observed but not causally related to the electroconvulsive therapy treatment. Third, risk of selection bias caused by the exclusion of publications other than English or German exists. The excluded Japanese, Spanish, Polish, Persian, and Chinese literature reported a total of 620 patients and 2,850 electroconvulsive therapy treatments. This was 0.6% (620 of 106,569 patients) and 0.4% (2,850 of 786,995 electroconvulsive therapy treatments) of our analyzed population and therefore bears a low risk of selection bias. Finally, the per electroconvulsive therapy treatment analyses effectively assume that repeated measurements (trials) on the same subject are independent. That may or may not be true, and because we did not have patient-level data, we cannot evaluate that assumption. In conclusion, this systematic review and meta-analysis study shows that major

Table 3. Incidence of Major Adverse Cardiac Events Associated with Electroconvulsive Therapy in Patients with Preexisting Cardiovascular Disease

		Patients					Electroconvulsive Therapy Treatments				
Adverse Events	Population	No. of Studies	No. of Events/ Patients	Incidence [95% CI] DerSimonian and Laird Model	I^2, %	Incidence [95% CI] Poisson Model	No. of Studies	No. of Events/ Treatments	Incidence [95% CI] DerSimonian and Laird Model	I^2, %	Incidence [95% CI] Poisson Model
Myocardial infarction	No cardiac disease	0	—	—	—	—	0	—	—	—	—
	General population	6	12/3,699	1.23 [0.00–3.10]	29.7	5.21 [1.35–20.05]	6	10/24,458	0.86 [0.00–1.84]	40.5	0.84 [0.25–2.86]
	Cardiac disease	3	2/128	17.77 [0.00–44.56]	0.0	15.63 [3.91–62.48]	3	2/1,071	1.46 [0.00–4.62]	0.0	1.87 [0.47–7.5]
Life-threatening arrhythmia	No cardiac disease	6	7/169	30.79 [4.90-56.69]	0.0	41.42 [19.75–86.88]	6	12/597	11.98 [2.66–21.30]	9.9	17.22 [7.57–39.17]
	General population	26	129/7,342	12.44 [5.87–19.01]	86.5	21.87 [9.93–48.12]	28	229/28,754	0.73 [0.23–1.24]	91.9	3.92 [1.33–11.58]
	Cardiac disease	7	10/243	29.83 [8.14–51.52]	0.0	41.15 [22.14–76.48]	7	11/2,787	1.93 [0.17–3.70]	4.6	4.13 [1.71–9.97]
Acute pulmonary edema	No cardiac disease	0	—	—	—	—	0	—	—	—	—
	General population	3	7/1,773	8.37 [0.00–22.64]	64.2	5.27 [0.85–32.79]	3	7/4,655	1.22 [0.22–2.23]	0.0	1.50 [0.72–3.15]
	Cardiac disease	1	0/10	0.00 [0.00-212.9]	—	—	1	0/20	0.00 [0.00–114.3]		—
Pulmonary embolism	No cardiac disease	0	—	—	—	—	0	—	—	—	—
	General population	1	1/1,437	0.70 [0.00–2.06]	—	—	1	1/1,437	0.70 [0.00–2.06]	—	—
	Cardiac disease	1	0/10	0.00 [0.00–212.9]	—	—	1	0/20	0.00 [0.00–114.3]	—	—
Acute heart failure	No cardiac disease	0	—	—	—	—	0	—	—	—	—
	General population	2	7/335	18.60 [4.15–33.05]	0.0	20.90 [9.96–43.83]	2	7/3,235	1.94 [0.42–3.45]	0.0	2.16 [1.03–4.54]
	Cardiac disease	1	2/40	50.00 [0.00–117.5]	—	—	1	2/452	4.42 [0.00–10.54]	—	—
Cardiac arrest	No cardiac disease	1	4/13	307.7 [56.80–558.6]	—	—	1	4/110	36.36 [1.38–71.35]	—	—
	General population	6	52/51,268	0.94 [0.06–1.81]	78.4	2.18 [0.45–10.67]	6	52/297,494	0.15 [0.02–0.27]	78.9	0.28 [0.07–1.17]
	Cardiac disease	1	0/10	0.00 [0.00–212.9]	—	—	1	0/20	0.00 [0.00–114.3]	—	—

Incidence [95% CI] was determined per 1,000 patients and per 1,000 electroconvulsive therapy treatments.

Table 4. Incidence of Mortality after Electroconvulsive Therapy in Patients with Preexisting Cardiovascular Disease

		Patients					Electroconvulsive therapy Treatments				
Adverse Events	Population	No. of Studies	No. of Events/ Patients	Incidence [95% CI] DerSimonian and Laird Model	I^2, %	Incidence [95% CI] Poisson Model	No. of Studies	No. of Events/ Treatments	Incidence [95% CI] DerSimonian and Laird Model	I^2, %	Incidence [95% CI] Poisson Model
Studies reporting no adverse events included											
All-cause mortality	No cardiac disease	13	0/889	0.00 [0.00–4.60]	0.0	—	13	0/4,926	0.00 [0.00–0.66]	0.0	—
	General population	26	49/74,653	0.25 [0.00–0.50]	40.9	0.54 [0.14–2.03]	28	79/683,066	0.06 [0.02–0.10]	60.1	0.08 [0.02–0.30]
	Cardiac disease	2	0/45	0.00 [0.00–64.26]	0.0	—	2	0/533	0.00 [0.00–4.78]	0.0	—
Cardiac deaths	No cardiac disease	13	0/889	0.00 [0.00–4.60]	0.0	—	13	0/4,926	0.00 [0.00–0.66]	0.0	—
	General population	22	15/44,624	0.04 [0.00–0.15]	0.0	0.15 [0.01–1.49]	24	23/519,960	0.01 [0.00–0.03]	0.0	0.02 [0.00–0.14]
	Cardiac disease	2	0/45	0.00 [0.00–64.26]	0.0	—	2	0/533	0.00 [0.00–4.78]	0.0	—
Studies reporting no adverse events excluded (sensitivity analysis)											
All-cause mortality	No cardiac disease	0	—	—	—		0	—	—	—	—
	General population	11	49/74,083	0.34 [0.02–0.66]	76.4	0.80 [0.18–3.59]	13	79/680,269	0.07 [0.02–0.11]	82.3	0.11 [0.02–0.47]
	Cardiac disease	2	0/45	0.00 [0.00–64.26]	0.0	—	2	0/533	0.00 [0.00–4.78]	0.0	—
Cardiac deaths	No cardiac disease	0	—	—	—	—	0	—	—	—	—
	General population	7	7/44,064	0.20 [0.00–0.52]	59.0	0.21 [0.02–2.78]	9	23/517,163	0.02 [0.00–0.05]	59.6	0.02 [0.00–0.19]
	Cardiac disease	2	0/45	0.00 [0.00–64.26]	0.0	—	2	0/533	0.00 [0.00–4.78]	0.0	—

Incidence [95% CI] was determined per 1,000 patients and per 1,000 electroconvulsive therapy treatments. Studies reporting no adverse events stated that no adverse event occurred.

adverse cardiac events after electroconvulsive therapy are infrequent and occur in about 1 in 50 patients and after about 1 of 200 to 500 electroconvulsive therapy treatments.

Research Support

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Competing Interests

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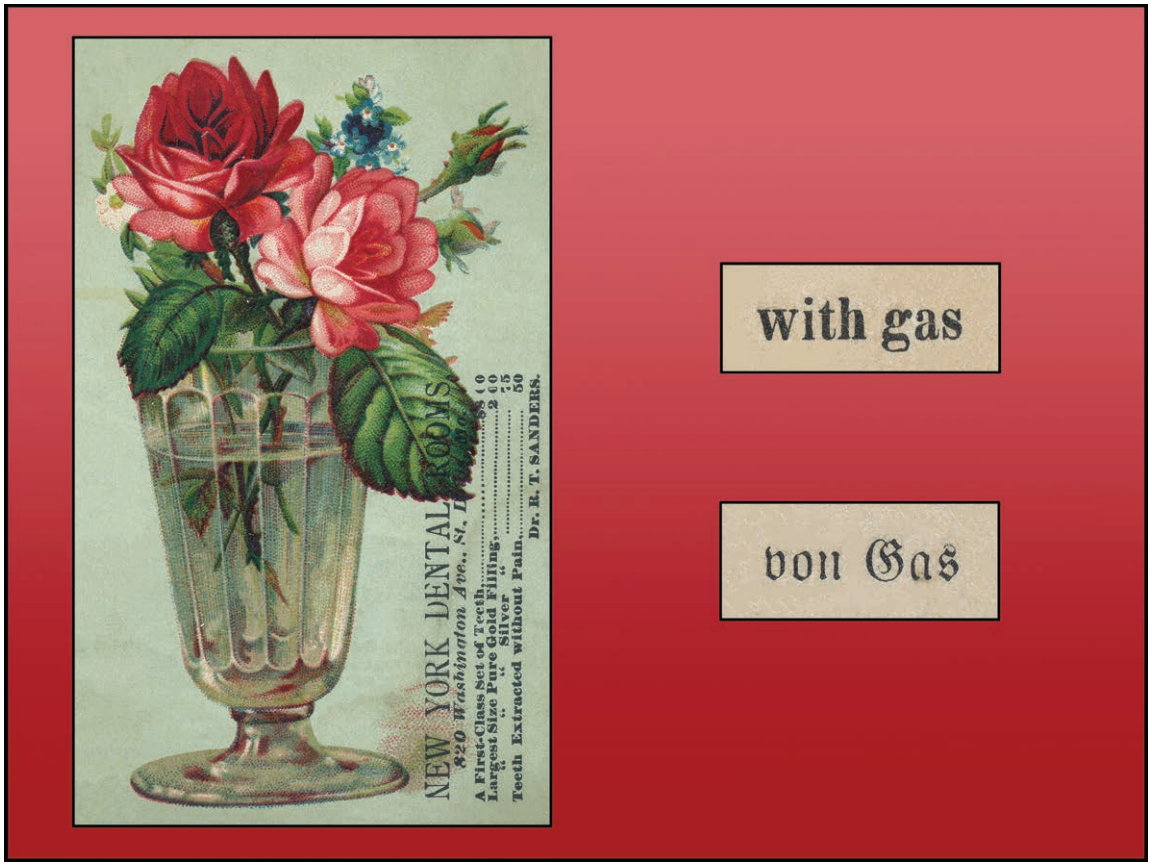
Missouri's New York Dental Rooms: Advertising Laughing Gas in English and German



Although born in Philadelphia, Dr. Robert T. Sanders (1830 to 1898) spent most of his dental career in Missouri. In 1871 he began practicing dentistry in St. Louis under his trademark of "New York Dental Rooms." As imprinted up the right side of this trade card's obverse (*left*), his office was on Washington Street. He practiced at that location from 1875 to 1888, which helps in dating this trade card. Fluent in English and German, Dr. Sanders promised, for 50 cents, painless dental extractions either "with gas" or "*von gas*" (both *right*). This made him particularly popular with the waves of German immigrants working in the city's papermaking and tobacco processing factories, flour mills, and breweries. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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