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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 (ECT) 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 ECT.

Methods: Systematic review and meta-analysis of studies that investigated ECT 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. We calculated pooled estimated incidence rates and 95% confidence intervals (CI 95) of individual major adverse cardiac events and mortality per 1,000 patients and per 1,000 ECT treatments.

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

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Summary Statement: Major adverse cardiac events and death after ECT are infrequent and occur in about one in 50 patients and after about one in 200 – 500 ECT treatments

and 0.06 [0.02 – 0.23] deaths per 1,000 ECT treatments. Cardiac death accounted for 29% (23/79) of deaths.

Conclusions: Major adverse cardiac events and death after ECT are infrequent and occur in about one in 50 patients and after about one in 200 – 500 ECT treatments.

Introduction

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

Major adverse cardiovascular events after ECT, such as acute myocardial infarction or acute heart failure, have been reported sporadically in individual case reports[2] or case series. Retrospective cohort studies[3–5] have aimed to assess the risk of major adverse cardiac events after ECT, but the infrequent occurrence of these complications rendered it difficult to obtain good population-level estimates about true incidence rates.[1] To obtain a more robust estimate about the incidence of major adverse cardiac events and mortality after ECT we therefore conducted a systematic review and meta-analysis.

Methods

Data Sources

PubMed, PsychInfo, Scopus, Cochrane CENTRAL, Cochrane SysReviews and Current Content were searched with cut-off date of November 12, 2016. Additionally, bibliographies of articles included in data extraction and of pertinent books were hand searched. Articles reporting cardiac morbidity and mortality in the context of ECT published from January 1, 1980 to November 12, 2016 were identified using indexed terms and text words (see supplemental digital content, S1. Search terms and engines).

Study Selection

After screening of 2641 publications by two independent investigators, 284 studies were assessed in full text for eligibility. Interventional, retrospective and prospective observational studies and surveys that investigated ECT and reported major adverse cardiac events and/or mortality were included for data extraction. Exclusion criteria were ECT performed in children (age 18 years or younger) or pregnant women, ECT 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. Ten percent of selected articles were captured by two independent investigators to test the feasibility of prespecified criteria and to develop a data extraction plan (see supplemental digital content; S2. Items extracted and risk of bias

assessment at study-level). The criteria were discussed and a database developed on consensus of all investigators that allowed uniform capture of data extraction. Three investigators (AD, MM, BP) retrieved 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, the number of ECT treatments, frequency of reported major adverse cardiac events, cardiac death and all-cause mortality, the design, information about the population's cardiovascular health status at inclusion, duration of follow-up and the quality of harms reporting. Extracted components of major adverse cardiac events were myocardial infarction, arrhythmia, pulmonary edema, pulmonary embolism, acute heart failure, and cardiac arrest. Supplemental digital content (S3. Definition of Major Adverse Cardiac Events and Death) provides the definition used for each component of MACE and mortality. Most studies did only report 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; S2. Items extracted and risk of bias assessment at study-level). Finally, extraction and adjudication of outcome data included in the meta-analysis was repeated by a second investigator and differences compared to the first investigator 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, 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 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 ECT. 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. Additionally, we report incidence rates of all-cause mortality and cardiac death. For each individual study, probability and the Jeffrey's confidence interval were calculated. We estimated the pooled probabilities and 95% confidence interval (CI 95) 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 beta distribution based method for zero event studies. The other analysis was a random effects Poisson model.

Each of the methods involves certain assumptions. In our context, the DerSimonian and Laird (D&L) 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 δi 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 beta distribution-based method as noted above.

In the Poisson modelling (Poi) approach, the number of adverse events observed in study i is assumed to arise from a Poisson distribution with mean μ_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 modelling assumptions and the computational techniques that go with them can lead to different pooled estimates and confidence intervals. As neither method has been proven superior but 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, Poi-based estimates. Data are presented as incidence rate per 1,000 patients and per 1,000 ECT treatments. For each investigated outcome, Forest plots were produced using GraphPad Prism (version 6.07; La Jolla, CA). Microsoft Access, Microsoft Excel (Microsoft, Redmond, WA) and Stata (version 14.1; College Station, TX) 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; 4 surveys) were extracted (total n=106,569 patients; n=786,995 ECT treatments; Figure 1). Most studies reported only a subset of major adverse cardiac events and/or deaths. Incidence rates of major adverse cardiac events after ECT could be extracted from 54/82 studies, and mortality data from 43/82 (see supplemental digital content, S4. List of studies included in the meta-analysis). Sample sizes for extracted individual major adverse cardiac events (denominators) ranged from n=375 patients (acute heart failure) to n=51,291 patients (cardiac arrest), or n=1,457 ECT treatments (pulmonary embolism) to n=297,624 ECT treatments (cardiac arrest). Sample sizes for mortality were n=75,587 patients and n=688,525 ECT treatments. Considerable heterogeneity (I^2 > 50 %) was observed in the incidence rates of arrhythmia (I^2 = 81.2 % - 88.8 %), cardiac arrest (I^2 = 74.8 % - 75.8 %), and all-cause mortality (sensitivity analysis) (I^2 = 71.6% - 79.3%).

The most commonly reported major adverse cardiac event was acute arrhythmia (n=39 studies) with an estimated incidence rate of 14.82 [8.63 – 21.02] using the DerSimonian and Laird model and 25.83 [14.83 – 45.00] per 1,000 patients using the Poisson model or 0.87 [0.38 – 1.37] and 4.66 [2.15 – 10.09] per 1,000 ECT 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 – 34.11] (DerSimonian and Laird model) and 24 [12.48 – 46.13] (Poisson model) per 1,000 patients or 2.08 [0.61 – 3.55] (DerSimonian and Laird model) and 2.44 [1.27 – 4.69] (Poisson model) per 1,000 ECT treatments. Acute pulmonary edema (n=4 studies), which could be of cardiac or non-cardiac origin, had an incidence rate of 7.59 [0.00 – 20.09] (DerSimonian and Laird model) and 4.92 [0.85 – 28.60] (Poisson model) per 1,000 patients or 1.22 [0.22 – 2.23] (DerSimonian and Laird model) and 1.50 [0.71 – 3.14] (Poisson model) per 1,000 ECT treatments. All-cause mortality (n=41 studies) was 0.13 [0.00 – 0.27] (DerSimonian and Laird model) and 0.42 [0.11 – 1.52] (Poisson model) per 1,000 patients or 0.05 [0.01 – 0.08] (DerSimonian and Laird model) and 0.06 [0.02 – 0.23] (Poisson model) per 1,000 ECT 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 – 0.64] (DerSimonian and Laird model) and 0.75 [0.17 – 3.24] (Poisson model) per 1,000 patients or 0.06 [0.02 – 0.11] (DerSimonian and Laird model) and 0.10 [0.02 – 0.42] (Poisson model) per 1,000 ECT treatments. Cardiac death accounted for 29% (23 of 79 deaths) of deaths.

To determine whether the risk of cardiac events after ECT may be higher in patients with pre-existing cardiovascular disease, we performed several subgroup analyses that were restricted to patients with (or without) known cardiovascular disease (Tables 3 and 4).

Discussion

Results of this systematic review and meta-analysis show that an estimated 25.83 [14.83 – 45.00] per 1,000 patients (approximately 1 in 50 patients) develop major adverse cardiac events after ECT (2%). The risk based per ECT treatment is 4.66 [2.15 – 10.09] per 1,000 ECTs (approximately 1 MACE in 200 ECT treatments). These estimates are based on the Poisson model, which yield higher values in this case and wider confidence intervals. The reason why the risk per patient is proportionally higher than per ECT treatment is that most patients undergo a series of ECT 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 ECT. 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 – since we assessed the risk of having missed a death to be low –, but not in the meta-analysis for individual major adverse cardiac events, since we deemed the risk too high. The sensitivity analysis was restricted to studies 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 ECT 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 ECT 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. Sample size of that magnitude provide robust estimates that approximate population-level incidence rates. Indeed, a recent population based study determined an all-cause mortality rate of 0.04 and 0.24 per 1,000 ECTs within 1 and 7 days of an ECT treatment similar to our finding of 0.04 – 0.10 per 1,000 ECTs. Also, they determined an event rate of about 0.05 for arrhythmia and 0.1 for myocardial infarction per 1,000 ECTs corresponding to the 0.87 and 0.77 we found in the D&L models.

Clinical implications

Despite the low frequency of major cardiac events after ECT, the question should be addressed if these events may be preventable or not. In two prospective cohort studies, Duma and colleagues and Martinez and colleagues showed that in about 5 – 10% of ECT treatments, patients develop cardiac troponin elevation, which indicates myocardial cell damage.[9] Cardiovascular stress during ECT is of short duration and may be prevented by administration of short-acting drugs, such as beta-blockers.[9–11]

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 pre-existing cardiovascular disease. Therefore, the results of this study may over- or underestimate the true incidence rate of cardiac events after ECT. Second, deaths may occur after ECT due to many other factors and may only be temporally observed but not causally related to the ECT treatment. Third, risk of selection bias due to 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 2850 ECT treatments. This was 0.6% (620/106,569 patients) and 0.4% (2850/786,995 ECT treatments) of our analyzed population and therefore bears a low risk of selection bias. Finally, the per ECT treatment analyses effectively assume that repeated measurements (trials) on the same subject are independent. That may or may not be true, and since we did not have patient-level data, we cannot evaluate that assumption.

In conclusion, this systematic review and meta-analysis show that major adverse cardiac events after ECT are infrequent and occur in about one in 50 patients and after about one in 200 – 500 ECT treatments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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not applicable

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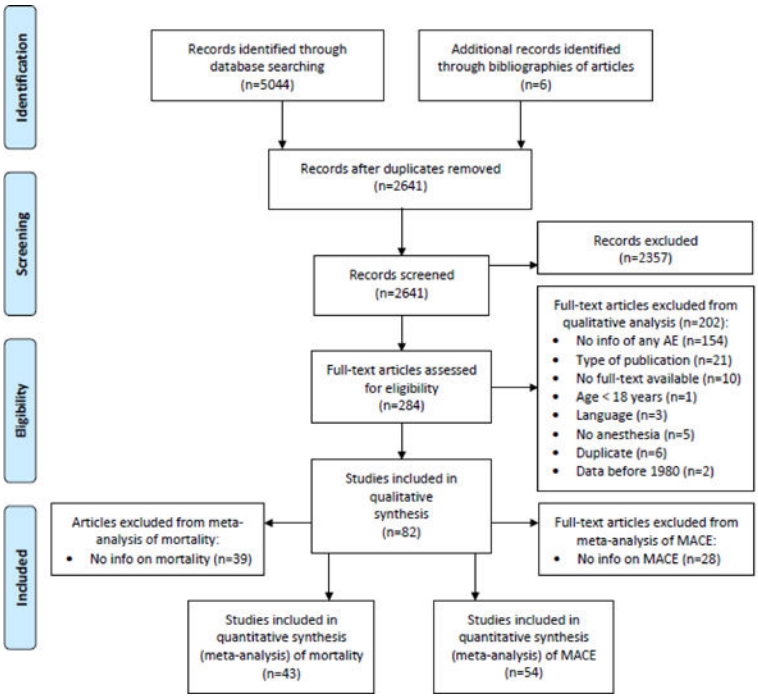

Figure 1.

PRISMA flowchart Process from identification to inclusion of reports. MACE = major adverse cardiac events

Table 1.

Incidence of major adverse cardiac events after ECT

	Patients				ECT treatments			
Adverse events	**Studies (n)**	**Events / Patients**	**Model**	**Incidence [95% CI] per 1,000 patients**	**Studies (n)**	**Events / ECTs**	**Model**	**Incidence [95% CI] per 1,000 ECTs**
Myocardial infarction	9	12 / 3,827	D&L	1.11 [0.00 – 2.58]	9	12 / 25,529	D&L	0.77 [0.00 – 1.58]
			Poi	6.10 [2.06 – 18.08]			Poi	0.97 [0.34 – 2.75]
Life-threatening arrhythmia	39	146 / 7,754	D&L	14.82 [8.63 – 21.02]	41	252 / 132,138	D&L	0.87 [0.38 – 1.37]
			Poi	25.83 [14.83 – 45.00]			Poi	4.66 [2.15 – 10.09]
Acute pulmonary edema	4	7 / 1,783	D&L	7.59 [0.00 – 20.09]	4	7 / 4,675	D&L	1.22 [0.22 – 2.23]
			Poi	4.92 [0.85 – 28.60]			Poi	1.50 [0.71 – 3.14]
Pulmonary embolism	2	1 / 1,447	D&L	0.70 [0.00 – 2.06]	2	1 / 1,457	D&L	0.70 [0.00 – 2.06]
			Poi	0.69 [0.10 – 4.91]			Poi	0.69 [0.10 – 4.87]
Acute heart failure	3	9 / 375	D&L	19.98 [5.85 – 34.11]	3	9 / 3,687	D&L	2.08 [0.61 – 3.55]
			Poi	24 [12.48 – 46.13]			Poi	2.44 [1.27 – 4.69]
Cardiac arrest	8	56 / 51,291	D&L	0.95 [0.00 – 1.89]	8	56 / 297,624	D&L	0.15 [0.01 – 0.28]
			Poi	4.23 [0.69 – 25.84]			Poi	0.56 [0.10 – 3.23]

Incidence [95% CI] was determined per 1,000 patients and per 1,000 ECT treatments using two random effects models. D&L = DerSimonian and Laird model, Poi = poisson model, ECT = Electroconvulsive therapy, n = count, CI = confidence interval.

Table 2.

Incidence of mortality after ECT

	Patients				ECT treatments			
Mortality	**Studies (n)**	**Events / Patients**	**Model**	**Incidence [95% CI] per 1,000 patients**	**Studies (n)**	**Events / ECTs**	**Model**	**Incidence [95% CI] per 1,000 ECTs**
Studies reporting no AE included								
All-cause Mortality	41	49/ 75,587	D&L	0.13 [0.00 – 0.27]	43	79 / 688,525	D&L	0.05 [0.01 – 0.08]
			Poi	0.42 [0.11 – 1.52]			Poi	0.06 [0.02 – 0.23]
Cardiac Deaths	37	15 / 45,568	D&L	0.04 [0.00 – 0.15]	39	23 / 525,419	D&L	0.01 [0.00 – 0.03]
			Poi	0.12 [0.01 – 1.15]			Poi	0.02 [0.00 – 0.12]
Studies reporting no AE excluded (sensitivity analysis)								
All-cause Mortality	13	49 / 74,128	D&L	0.33 [0.01 – 0.64]	15	79 / 680,802	D&L	0.06 [0.02 – 0.11]
			Poi	0.75 [0.17 – 3.24]			Poi	0.10 [0.02 – 0.42]
Cardiac Deaths	9	15 / 44,109	D&L	0.18 [0.00 – 0.46]	11	23 / 517,696	D&L	0.02 [0.00 – 0.05]
			Poi	0.19 [0.02 – 2.4]			Poi	0.02 [0.00 – 0.17

Incidence [95% CI] was determined per 1,000 patients and per 1,000 ECT treatments using two random effects models. Studies reporting no AE stated that no adverse event occurred. D&L = DerSimonian and Laird model, Poi = poisson model, AE = Adverse Events, ECT = Electroconvulsive therapy, n = count, CI = confidence interval.

Table 3.

Incidence of MACE associated with ECT in patients with pre-existing cardiovascular disease

		Patients					ECT treatments				
Adverse events	**Population**	**Studies (n)**	**Events / Patients**	**Incidence [95% CI] D&L model**	**I^2**	**Incidence [95% CI] Poisson model**	**Studies (n)**	**Events / ECTs**	**Incidence [95% CI] D&L model**	**I^2**	**Incidence [95% CI] Poisson model**
Myocardial infarction	No cardiac disease	0	-	-	-	-	0	-	-	-	-
	General population	6	12 / 3699	1.23 [0.00–3.10]	29.7 %	5.21 [1.35–20.05]	6	10 / 24458	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 / 1071	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 / 7342	12.44 [5.87–19.01]	86.5 %	21.87 [9.93–48.12]	28	229 / 28754	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 / 2787	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 / 1773	8.37 [0.00–22.64]	64.2 %	5.27 [0.85–32.79]	3	7 / 4655	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 / 1437	0.70 [0.00–2.06]	-	-	1	1 / 1437	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 / 3235	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 / 51268	0.94 [0.06–1.81]	78.4 %	2.18 [0.45–10.67]	6	52 / 297494	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 ECT treatments. CI = confidence interval, D&L = DerSimonian and Laird, ECT= Electroconvulsive therapy, n = count.

Table 4.

Incidence of mortality after ECT in patients with pre-existing cardiovascular disease

		Patients					ECT treatments				
Adverse events	**Population**	**Studies (n)**	**Events / Patients**	**Incidence [95% CI] D&L model**	**I^2**	**Incidence [95% CI] Poisson model**	**Studies (n)**	**Events / ECTs**	**Incidence [95% CI] D&L model**	**I^2**	**Incidence [95% CI] Poisson model**
Studies reporting no AE included											
All-cause Mortality	No cardiac disease	13	0 / 889	0.00 [0.00–4.60]	0.0%	-	13	0 / 4926	0.00 [0.00–0.66}	0.0%	-
	General population	26	49 / 74653	0.25 [0.00–0.50]	40.9%	0.54 [0.14–2.03]	28	79 / 683066	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 / 4926	0.00 [0.00–0.66]	0.0%	-
	General population	22	15 / 44624	0.04 [0.00–0.15]	0.0%	0.15 [0.01–1.49]	24	23 / 519960	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 AE excluded (sensitivity analysis)											
All-cause Mortality	No cardiac disease	0	-	-	-		0	-	-	-	-
	General population	11	49 / 74083	0.34 [0.02–0.66]	76.4%	0.80 [0.18–3.59]	13	79 / 680269	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 / 44064	0.20 [0.00–0.52]	59.0%	0.21 [0.02–2.78]	9	23 / 517163	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 ECT treatments. Studies reporting no AE stated that no adverse event occurred. AE = Adverse Events, CI = confidence interval, D&L = DerSimonian and Laird, ECT = Electroconvulsive therapy, n = count.