Supplemental Material

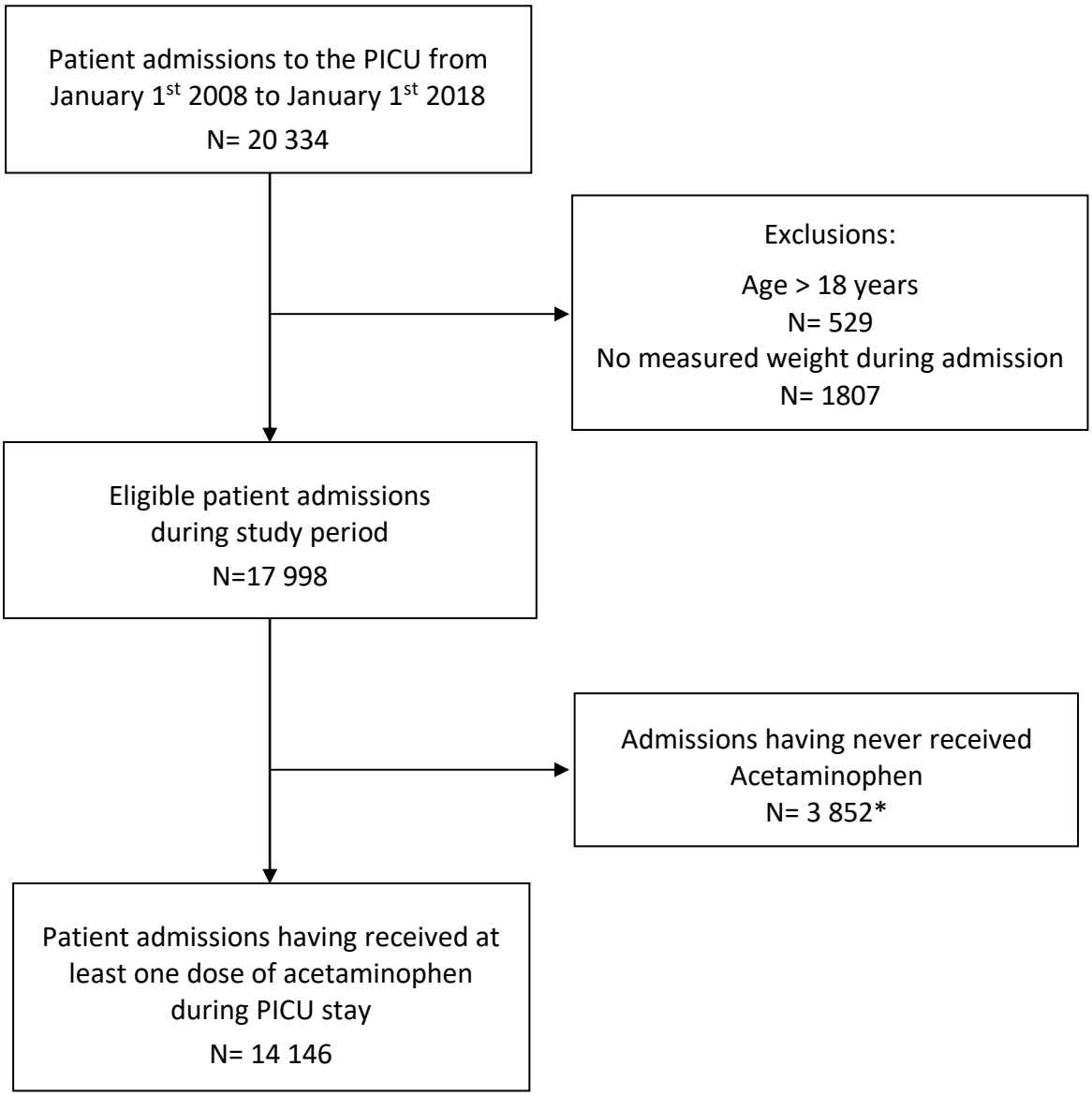
Table 1. STROBE Checklist
—Checklist of items that should be included in reports of ***cohort studies***
Page numbers as per original submission.

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Page 1.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found. Page 4.
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported. Page 5.
Objectives	3	State specific objectives, including any prespecified hypotheses Page 5.
Methods		
Study design	4	Present key elements of study design early in the paper Page 6.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Page 6.
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 7
Bias	9	Describe any efforts to address potential sources of bias Page 8
Study size	10	Explain how the study size was arrived at N/A, Entire cohort
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. Page 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding Page 7-8.
		(*b*) Describe any methods used to examine subgroups and interactions. Page 7-8
		(*c*) Explain how missing data were addressed. Page 7
		(*d*) If applicable, explain how loss to follow-up was addressed N/A
		(*e*) Describe any sensitivity analyses Page 8.
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Page 8, Flow diagram in Supplement

		(b) Give reasons for non-participation at each stage Page 8, Flow diagram in supplement
		(c) Consider use of a flow diagram included Supplement (figure 1)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Page 8. Table 1.
		(b) Indicate number of participants with missing data for each variable of interest Table 1.
		(c) Summarise follow-up time (eg, average and total amount). N/A, closed cohort
Outcome data	15*	Report numbers of outcome events or summary measures over time. Page 9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. Page 9.
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Page 9.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses. Page 9, 10
Discussion		
Key results	18	Summarise key results with reference to study objectives. Page 10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 12.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 12
Generalisability	21	Discuss the generalisability (external validity) of the study results Page 12.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 1

*Give information separately for exposed and unexposed groups.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org

Figure 1. Flow diagram of Included admissions



*N=2 admissions had acetaminophen doses coded as 0 mg, and these were excluded from analysis

Table 2. Univariate Mixed model of the effect of dependent variables on ALT, AST and GGT (in U/L).

	ALT		**AST**		**GGT**	
	Estimate	p-value	Estimate	p-value	Estimate	p-value
Age in months	0.073	0.002	-0.0006	0.99	0.032	0.02
PRISM III score	4.63	<0.0001	9.83	<0.0001	1.99	<0.0001
Sex (Ref male)	5.85	0.07	9.81	0.17	-2.38	0.20
ICU day	-0.26	<0.0001	-0.57	<0.0001	1.34	<0.0001
Cardiac patient	-20.2	<0.0001	5.11	0.47	-16.9	<0.0001
Frequency of labs drawn in 24h to 96h post overdose window (for >82.5 mg/kg/day)	0.048	0.59	-0.17	0.50	-0.17	0.004
Acetaminophen cumulative overdose >82.5 mg/kg/day	-0.90	0.80	-12.78	0.19	-13.99	<0.0001

Table 3. Subgroup analysis by PRISM III quartile of the effect of acetaminophen cumulative overdose on ALT, AST, and GGT.

	ALT		AST		GGT	
	Estimate	p-value	Estimate	p-value	Estimate	p-value
PRISM III First Quartile (Score 0-3)						
Age in months	-0.30	0.11	-0.09	0.06	-0.05	0.005
Sex (Ref male)	-1.87	0.42	-4.49	0.46	-4.3	0.06
ICU day	-0.04	0.19	0.05	0.59	0.73	<0.0001
Cardiac patient	-8.2	0.0016	14.2	0.04	0.03	0.99
Frequency of labs drawn in 24h to 96h post overdose window	1.02	<0.0001	3.01	<0.0001	0.18	0.16
Acetaminophen cumulative overdose >82.5 mg/kg/day	-19.3	0.0004	-78.3	<0.0001	-17.5	0.0006
PRISM III Second Quartile (Score 4-7)						
Age in months	-0.08	0.10	-0.04	0.62	-0.06	0.03
Sex (Ref male)	-0.03	0.95	1.8	0.86	-4.2	0.18
ICU day	-0.22	<0.0001	-0.58	<0.0001	1.35	<0.0001
Cardiac patient	-29.2	<0.0001	14.5	0.20	-23.9	<0.0001
Frequency of labs drawn in 24h-96h post overdose window	-0.06	0.80	-0.47	0.43	-0.04	0.8
Acetaminophen cumulative overdose >82.5 mg/kg/day	-5.07	0.58	-23.0	0.32	-13.9	0.025
PRISM III Third Quartile (Score 7-11)						
Age in months	-0.08	0.14	-0.12	0.12	0.005	0.89
Sex (Ref male)	12.4	0.06	12.7	0.20	-1.5	0.72
ICU day	-0.02	0.67	-0.43	0.0002	2.64	<0.0001
Cardiac patient	-45.0	<0.0001	-19.7	0.07	-36.8	<0.0001
Frequency of labs drawn in 24h -96h post overdose window	-0.11	0.68	-0.63	0.26	0.59	0.019
Acetaminophen cumulative overdose >82.5 mg/kg/day	3.45	0.75	0.73	0.97	-23.9	0.015
PRISM III Fourth Quartile (Score >=12)						
Age in months	0.24	0.04	0.21	0.45	0.07	0.19
Sex (Ref male)	18.1	0.26	44.4	0.23	-9.15	0.19
ICU day	-0.65	<0.0001	-1.19	<0.0001	0.47	0.04
Cardiac patient	-21.6	0.22	-24.5	0.54	-45.87	<0.0001
Frequency of labs drawn in 24h- 96h post overdose window	-0.11	0.83	-0.99	0.55	0.32	0.1
Acetaminophen cumulative overdose >82.5 mg/kg/day	-3.98	0.84	10.8	0.87	-15.8	0.04