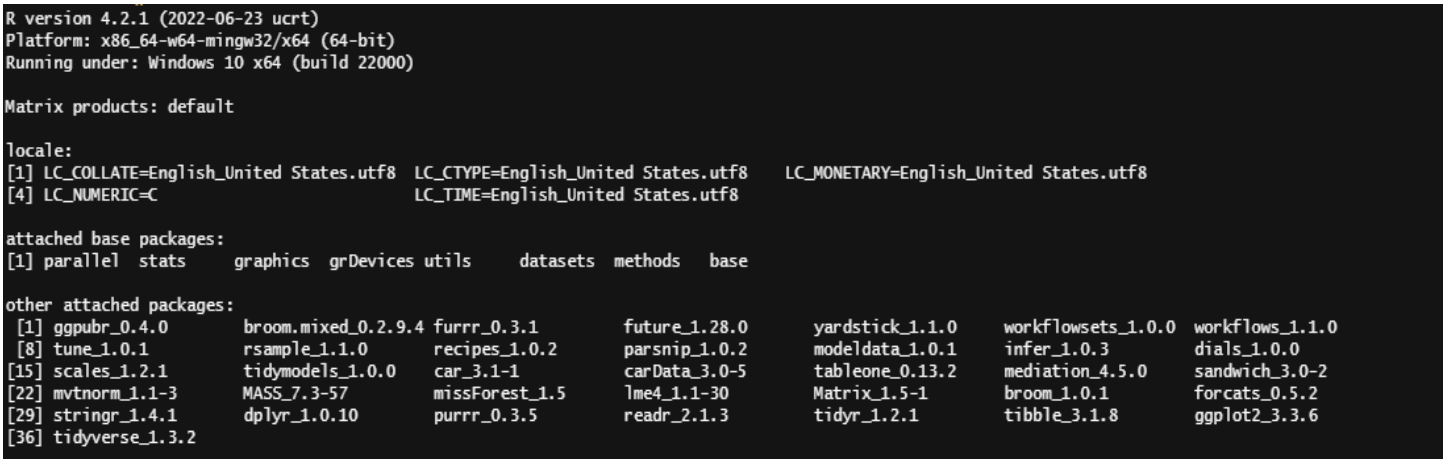
Supplement for Nikolla DA, et al. Anatomically and Physiologically Difficult Airways
(Supplemental Digital Content File)

SUPPLEMENT FIGURES

Supplemental Figure 1. R Version and Packages



```
R version 4.2.1 (2022-06-23 ucrt)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows 10 x64 (build 22000)

Matrix products: default

locale:
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[4] LC_NUMERIC=C                           LC_TIME=English_United States.utf8

attached base packages:
[1] parallel  stats     graphics  grDevices utils     datasets  methods   base

other attached packages:
 [1] ggpubr_0.4.0        broom.mixed_0.2.9.4 furrr_0.3.1         future_1.28.0       yardstick_1.1.0     workflowsets_1.0.0  workflows_1.1.0
 [8] tune_1.0.1          rsample_1.1.0       recipes_1.0.2       parsnip_1.0.2       modeldata_1.0.1     infer_1.0.3         dials_1.0.0
[15] scales_1.2.1        tidymodels_1.0.0    car_3.1-1           carData_3.0-5       tableone_0.13.2     mediation_4.5.0     sandwich_3.0-2
[22] mvtnorm_1.1-3       MASS_7.3-57         missForest_1.5      lme4_1.1-30         Matrix_1.5-1        broom_1.0.1         forcats_0.5.2
[29] stringr_1.4.1       dplyr_1.0.10        purrr_0.3.5         readr_2.1.3         tidyr_1.2.1         tibble_3.1.8        ggplot2_3.3.6
[36] tidyverse_1.3.2
```
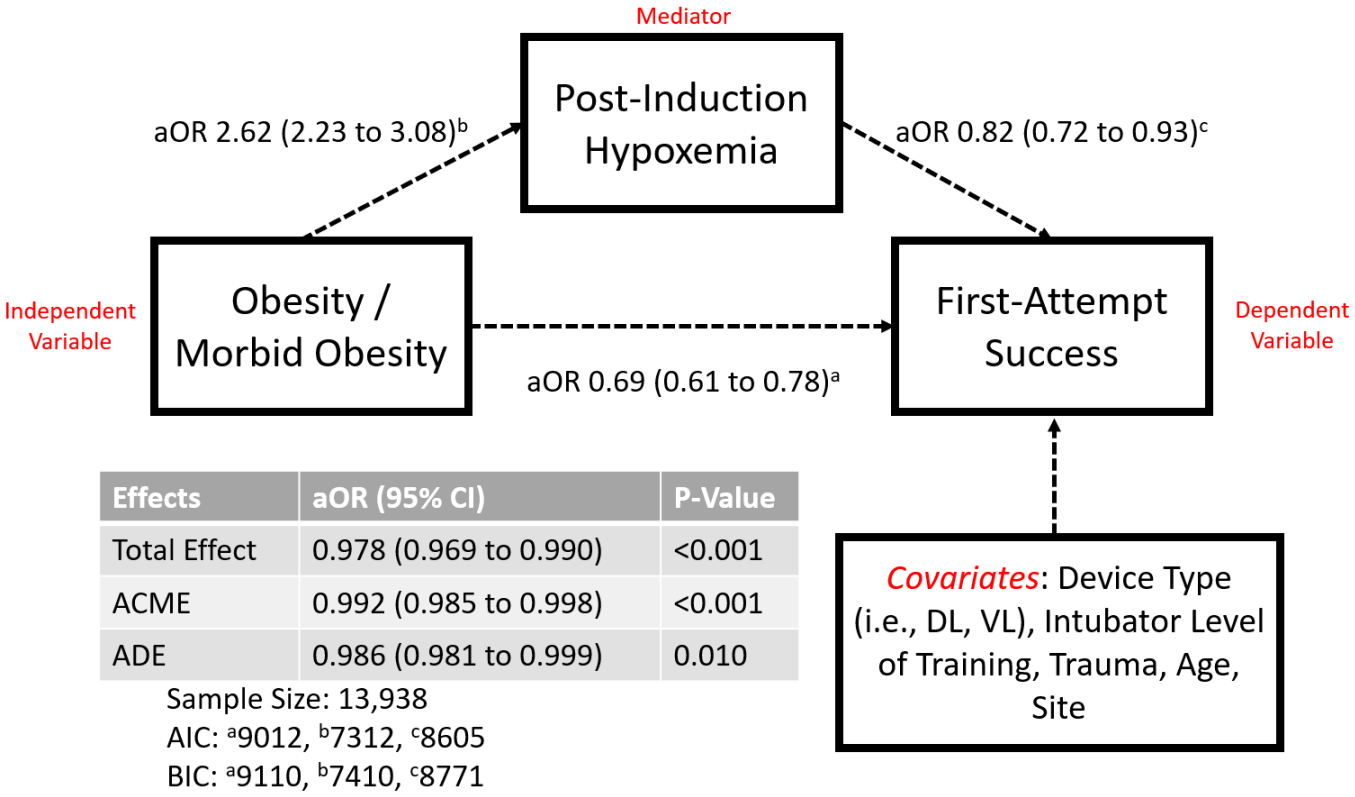

Supplemental Figure 1. The analysis was performed with R (Version 4.2.1 2022-06-23, R Foundation for Statistical Computing, Vienna, Austria) with displayed packages.

Supplemental Figure 2. Causal Diagram of the Effect of Obesity / Morbid Obesity on First-Attempt Success via Post-Induction Hypoxemia by Mediation Analysis



Effects	aOR (95% CI)	P-Value
Total Effect	0.978 (0.969 to 0.990)	<0.001
ACME	0.992 (0.985 to 0.998)	<0.001
ADE	0.986 (0.981 to 0.999)	0.010

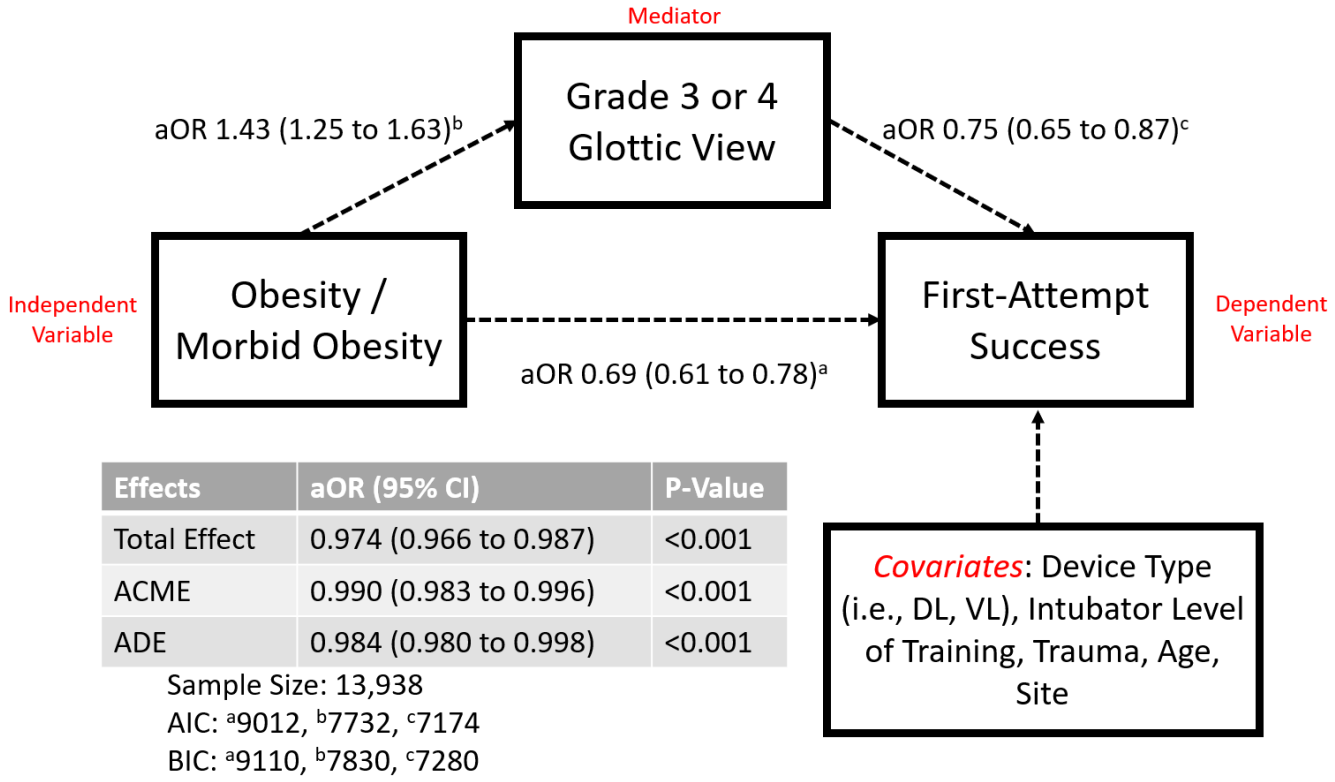
Sample Size: 13,938
AIC: [a]9012, [b]7312, [c]8605
BIC: [a]9110, [b]7410, [c]8771

aOR, adjusted odds ratio; CI, confidence interval; ACME, average causal mediation effects; ADE, average direct effects; AIC, Akaike information criterion; BIC, Bayesian information criterion; DL, direct laryngoscopy; VL, video laryngoscopy.

Supplemental Figure 2. The causal diagram illustrates adjusted odds ratios for the associations between the independent variable and the dependent variable (a), the independent variable and the mediator (b), and the mediator and the dependent variable (c). The adjusted odds ratios between obesity / morbid obesity and post-induction hypoxemia and between post-induction hypoxemia and first-attempt success were significant, with confidence intervals that do not cross one.

Using these models (detailed outputs in Supplemental Table 3), we conducted the mediation analysis. The effect of obesity / morbid obesity on first-attempt success was partially mediated via post-induction hypoxemia. The indirect effect was aOR 0.992 (95% CI 0.985 to 0.998), and the direct effect was aOR 0.986 (95% CI 0.981 to 0.999). Since both were significant, we observed partial mediation.

Supplemental Figure 3. Causal Diagram of the Effect of Obesity / Morbid Obesity on First-Attempt Success via Poor Glottic View by Mediation Analysis



Effects	aOR (95% CI)	P-Value
Total Effect	0.974 (0.966 to 0.987)	<0.001
ACME	0.990 (0.983 to 0.996)	<0.001
ADE	0.984 (0.980 to 0.998)	<0.001

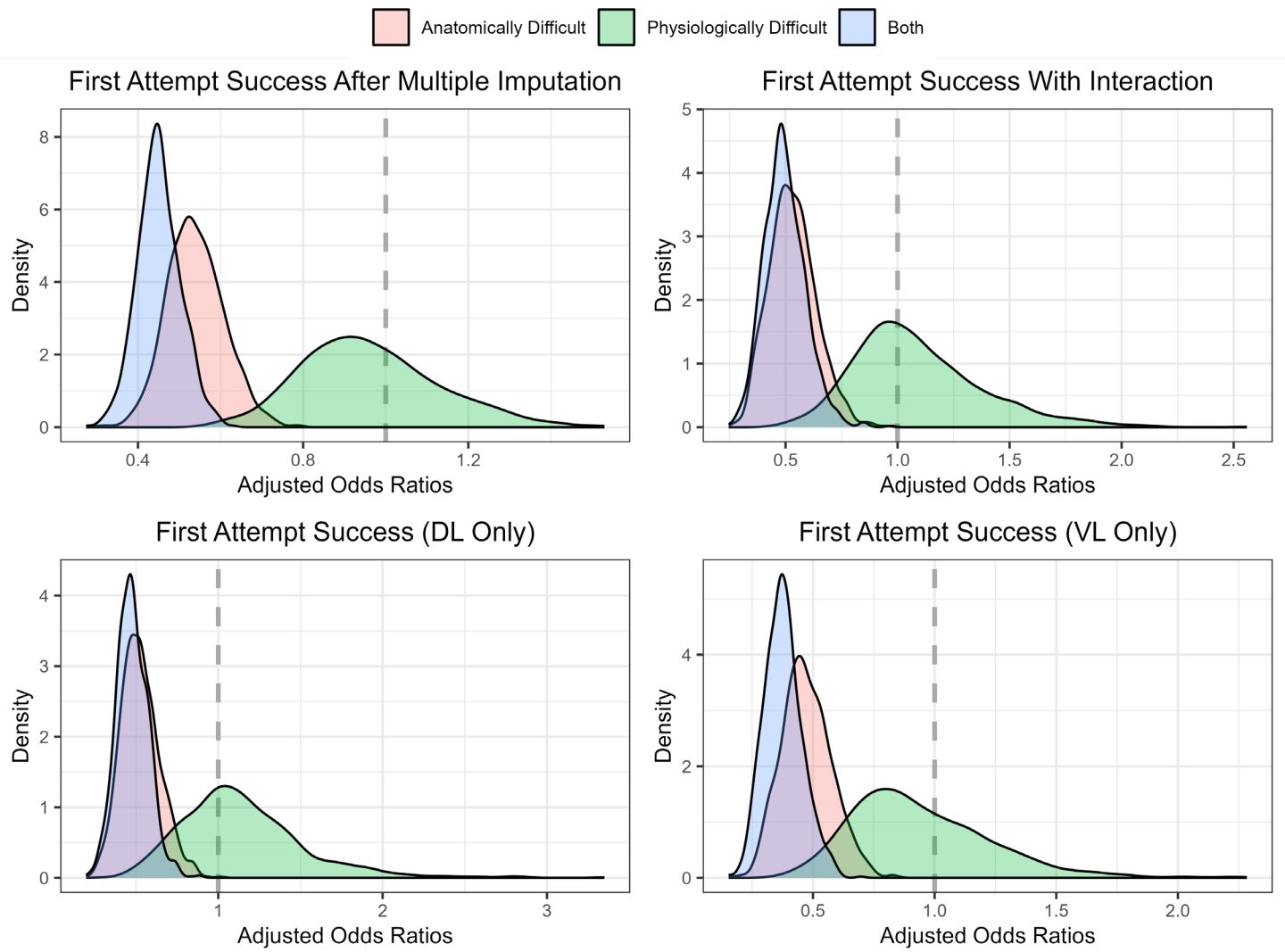
Sample Size: 13,938
AIC: a9012, b7732, c7174
BIC: a9110, b7830, c7280

aOR, adjusted odds ratio; CI, confidence interval; ACME, average causal mediation effects; ADE, average direct effects; AIC, Akaike information criterion; BIC, Bayesian information criterion; DL, direct laryngoscopy; VL, video laryngoscopy.

Supplemental Figure 3. The causal diagram illustrates adjusted odds ratios for the associations between the independent variable and the dependent variable (a), the independent variable and the mediator (b), and the mediator and the dependent variable (c). The adjusted odds ratios between obesity / morbid obesity and poor glottic view and between poor glottic view and first-attempt success were significant, with confidence intervals that do not cross one.

Using these models (detailed outputs in Supplemental Table 3), we conducted the mediation analysis. The effect of obesity / morbid obesity on first-attempt success was partially mediated via poor glottic view. The indirect effect was aOR 0.990 (95% CI 0.983 to 0.996), and the direct effect was aOR 0.984 (95% CI 0.980 to 0.998). Since both were significant, we observed partial mediation.

Supplemental Figure 4. Density Plots of Bootstrapped Adjusted Regression Estimates for Sensitivity Analyses



DL, direct laryngoscopy; VL, video laryngoscopy

Supplemental Figure 4. Density plots of bootstrapped adjusted regression estimates for sensitivity analyses. For the first-attempt success after multiple imputation outcome, we used the same model as the main analysis for first-attempt success; however, the model was applied to the study dataset after random forest multiple imputation (see Supplemental Table 2 for details). For the first-attempt success with interaction outcome, the model included interaction terms between difficult airway type and laryngoscopy device type. For first-attempt success with only direct or video laryngoscopy, we exclude laryngoscopy device type from the model and subset the study dataset only to include cases using direct or video laryngoscopy, respectively. Each y axis presents probability densities for the x axis variable.

SUPPLEMENT TABLES

Supplemental Table 1. Coding for Difficult Airway Definitions and Model Variables

Variable	Collected	Analyzed
Age (years)	Continuous	Same
Difficult Airway Type	NA	Categorical, created from other variables as defined in Table 1.
Airway Obstruction	Categorical from the airway obstruction field (yes/no) and the medical indication field	Binary as a yes/no (component of the anatomically difficult airway definition)
Angioedema	Categorical from the medical indication field	Binary as a yes/no (component of the anatomically difficult airway definition)
Reduced Neck Mobility	Binary, yes/no	Binary as a yes/no (component of the anatomically difficult airway definition)
Mallampati >2	Categorical as classes 1-4 and not assessed	Binary as a >2 yes/no (component of the anatomically difficult airway definition)
Mouth Opening <3 Fingers	Categorical as 3+ fingers, 1-2 fingers, or not assessed	Binary as a <3 fingers yes/no (component of the anatomically difficult airway definition)
Thyromental Distance <3 Fingers	Categorical as 1-4+ fingers and not assessed	Binary as a <3 fingers yes/no (component of the anatomically difficult airway definition)
Facial Trauma	Categorical from the facial trauma field (yes/no) and the trauma indication field	Binary as a yes/no (component of the anatomically difficult airway definition)
Neck Trauma	Categorical from the trauma indication field	Binary as a yes/no (component of the anatomically difficult airway definition)
Blood in the Airway	Binary, yes/no	Binary as a yes/no (component of the anatomically difficult airway definition)
Obese or Morbidly Obese	Categorical as intubator assessment of body habitus including very thin, thin, normal, obese, or morbidly obese (body mass index >40)	Binary as obese / morbidly obese yes/no (component of both the anatomically and physiologically difficult airway definitions)*
Pre-intubation Hypoxemia <90% saturation	Continuous as oxygen saturation before the start of the first intubation attempt	Binary as <90% yes/no (component of the physiologically difficult airway definition)*
Pre-intubation Hypotension <100mmHg Systolic Blood Pressure	Categorical from field asking the description of the systolic blood pressure in the 10 minutes prior the intubation including	Binary as hypotension yes/no (component of the physiologically difficult airway definition)

<table>
<tr><td></td><td>hypertensive (>140 mmHg), normal (100-139 mmHg), hypotensive (<100 mmHg with no treatment vs. intravenous fluids or blood vs. intravenous fluids or blood and vasopressors)</td><td></td></tr>
<tr><td>Peri-Intubation vasopressor use</td><td>Categorical from individual first-attempt vasopressor fields (i.e., epinephrine, norepinephrine, and phenylephrine)</td><td>Binary as vasopressor administration yes/no (component of the physiologically difficult airway definition)</td></tr>
<tr><td>Shock</td><td>Categorical from medical indication field including cardiogenic, sepsis, distributive not sepsis, pulmonary embolism, or tamponade</td><td>Binary as shock yes/no (component of the physiologically difficult airway definition)</td></tr>
<tr><td>Device Type</td><td>Categorical, collected as laryngoscopy device</td><td>Categorical, coded as:<table><tr><td>Devices Used**</td><td>Type</td></tr><tr><td>Airtraq</td><td>VL</td></tr><tr><td>C-MAC D-Blade</td><td>VL</td></tr><tr><td>C-MAC Standard Blade</td><td>VL</td></tr><tr><td>C-MAC Straight blade</td><td>VL</td></tr><tr><td>Clarus video system</td><td>VL</td></tr><tr><td>Direct laryngoscope (MacIntosh)</td><td>DL</td></tr><tr><td>Direct laryngoscope (Miller)</td><td>DL</td></tr><tr><td>GlideScope</td><td>VL</td></tr><tr><td>GlideScope cobalt</td><td>VL</td></tr><tr><td>GlideScope teaching blade</td><td>VL</td></tr><tr><td>GlideScope titanium Mac blade</td><td>VL</td></tr><tr><td>McGrath video laryngoscope</td><td>VL</td></tr><tr><td>Other video laryngoscope</td><td>VL</td></tr></table></td></tr>
<tr><td>First-Attempt Success</td><td>Categorical, yes/no</td><td>Same</td></tr>
<tr><td>Adverse Events</td><td>Categorical yes/no from first-attempt adverse event variables, specifically peri-intubation vomiting, esophageal intubation (immediately recognized and delayed recognition), bradydysrhythmia, cardiac arrest, hypoxemia (<90% or drop of 10% of oxygen saturation), hypotension (systolic blood pressure <100 mmHg), and tachydysrhythmia.</td><td>Same</td></tr>
</table>

First-Attempt Success without Adverse Events	Categorical from first-attempt success and first-attempt adverse event variables specifically peri-intubation vomiting, esophageal intubation (immediately recognized and delayed recognition), bradydysrhythmia, cardiac arrest, hypoxemia (<90% or drop of 10% of oxygen saturation), hypotension (systolic blood pressure <100 mmHg), and tachydysrhythmia.	Binary, yes/no
Level of Training	Categorical, PGY 1,2,3,4, PGY≥5 or Fellow, Attending	Same
Peri-Intubation Cardiac Arrest on Any Attempt	Categorical, collected by attempt	Binary yes/no, combined from attempt-specific fields
Poor Glottic View (Cormack-Lehane Grade 3 or 4)	Categorical, collected as Cormack-Lehane Grades 1-4 by attempt	Binary, Grade 3 or 4 (yes/no)
Post-Induction Hypoxemia	Categorical, <90% or 10% drop in SpO2 yes/no by attempt	Same
Rescue Surgical Airway	Categorical, from laryngoscopy device field by attempt	Binary, combined from attempt-specific fields
Site Code	Categorical	Same
Total Attempts	Categorical, collected by attempt	Continuous, combined from attempt-specific fields
Trauma	Categorical, collected as trauma indications	Binary, trauma indication (yes/no)

NA, not applicable; DL, direct laryngoscopy; VL, video laryngoscopy; PGY, post-graduate year

*These variables were dichotomized to obesity / morbid obesity and pre-intubation hypoxemia due to association with peri-intubation cardiac arrest (1-2).
**Devices used after exclusions.

1. April MD, Arana A, Reynolds JC, et al. Peri-intubation cardiac arrest in the Emergency Department: A National Emergency Airway Registry (NEAR) study. Resuscitation. May 2021;162:403-411. doi:10.1016/j.resuscitation.2021.02.039
2. De Jong A, Rolle A, Molinari N, et al. Cardiac Arrest and Mortality Related to Intubation Procedure in Critically Ill Adult Patients: A Multicenter Cohort Study. Crit Care Med. Apr 2018;46(4):532-539. doi:10.1097/ccm.0000000000002925.

Supplemental Table 2. Missingness Before and After Multiple Imputation

Variable*	Missingness Before, n (%)	Missingness After, n (%)**
Age	0 (0)	0 (0)
Laryngoscope Type (direct, video)	0 (0)	0 (0)
Difficult Airway Type (i.e., neither, ADA, PDA, both)	0 (0)	0 (0)
First-Attempt Success	19 (0.1)	0 (0)
Grade 3 or 4 Glottic View	345 (2.5)	0 (0)
Intubator Training Level	306 (2.2)	0 (0)
Obesity / Morbid Obesity	40 (0.3)	0 (0)
Post-Induction Hypoxemia	0 (0)	0 (0)
Site	0 (0)	0 (0)
Trauma	0 (0)	0 (0)

ADA, anatomically difficult airway; PDA, physiologically difficult airway

*These variables were used for the multiple imputation. Multiple imputation of these variables assumes that the missing data are missing at random. Missing at random assumes that the tendency for a data point to be missing is not related to the missing data, and therefore can be imputed using related, observed data.

**Nonparametric missing value imputation was performed using random forest with 10 iterations and 100 trees per forest. The normalized root mean squared error (NRMSE) was 0.0000000, and the proportion of falsely classified (PFC) was 0.1186926.

Supplemental Table 3. Regression Estimates for the Causal Diagram Models Used in the Mediation Analysis

	Post-Induction Hypoxemia Mediator			Grade 3 or 4 Glottic View Mediator		
Outcome	**First-Attempt Success** a*	**Post-Induction Hypoxemia** b*	**First-Attempt Success** c*	**First-Attempt Success** a**	**Grade 3 or 4 Glottic View** b**	**First-Attempt Success** c**
Variable	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)	aOR (95% CI)
Obesity / Morbid Obesity	0.69 (0.61 to 0.78)	2.62 (2.23 to 3.08)	0.82 (0.72 to 0.93)	0.69 (0.61 to 0.78)	1.43 (1.25 to 1.63)	0.75 (0.65 to 0.87)
Laryngoscopy Device: VL vs DL	1.85 (1.63 to 2.1)	1.2 (1.03 to 1.4)	1.97 (1.73 to 2.25)	1.85 (1.63 to 2.1)	0.35 (0.31 to 0.4)	1.25 (1.07 to 1.44)
Intubator Training Level						
PGY-1	1.6 (1.35 to 1.89)	0.81 (0.66 to 1)	1.58 (1.33 to 1.88)	1.6 (1.35 to 1.89)	1.02 (0.83 to 1.25)	1.87 (1.54 to 2.26)
PGY-2	1.87 (1.57 to 2.23)	0.88 (0.71 to 1.08)	1.88 (1.57 to 2.25)	1.87 (1.57 to 2.23)	0.95 (0.77 to 1.16)	2.2 (1.8 to 2.69)
PGY-3	2.23 (1.73 to 2.87)	0.76 (0.56 to 1.03)	2.19 (1.69 to 2.84)	2.23 (1.73 to 2.87)	1.06 (0.81 to 1.38)	2.91 (2.18 to 3.9)
PGY-4	1.93 (1.27 to 2.92)	1.02 (0.68 to 1.54)	2.04 (1.33 to 3.13)	1.93 (1.27 to 2.92)	1.09 (0.72 to 1.63)	2.52 (1.55 to 4.1)
PGY≥5 or Fellow	1.98 (1.4 to 2.78)	0.92 (0.63 to 1.35)	2.01 (1.42 to 2.85)	1.98 (1.4 to 2.78)	0.97 (0.67 to 1.4)	2.44 (1.65 to 3.62)
Trauma	0.8 (0.7 to 0.92)	1.01 (0.86 to 1.18)	0.81 (0.7 to 0.93)	0.8 (0.7 to 0.92)	1.24 (1.07 to 1.44)	0.84 (0.72 to 0.99)
Patient Age	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)
Post-Induction Hypoxemia	NA	NA	0.19 (0.16 to 0.22)	NA	NA	NA
Grade 3 or 4 Glottic View	NA	NA	NA	NA	NA	0.04 (0.04 to 0.05)

aOR, adjusted odds ratio; CI, confidence interval; VL, video laryngoscopy; DL, direct laryngoscopy; PGY, post-graduate year

*Letters correspond to models graphically displayed in Supplemental Figure 2.
**Letters correspond to models graphically displayed in Supplemental Figure 3.
Note: NA (not applicable) means there is no estimate because the variable was not included in the model. Adjusted odds ratios were considered significant if the confidence interval did not cross one.

Supplemental Table 4. Regression Estimates for Primary Outcomes, Secondary Outcomes, and Sensitivity Analyses

	Primary Outcome		Secondary Outcomes and Sensitivity Analyses						
	FAS	FAS	FAS without AE+	Total Attempts	Peri-Intubation Cardiac Arrest*	FAS with Interaction	FAS Imputed***	FAS (DL only)	FAS (VL only)
Variable	Univariate OR (95%CI)	aOR (95%CI)	aOR (95%CI)	Adjusted Estimate (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)
Difficult Airway Type									
Neither	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
ADA	0.55 (0.45 to 0.69)	0.53 (0.4 to 0.68)	0.72 (0.59 to 0.89)	0.06 (0.04 to 0.08)	1.35 (0.3 to 23.7)	0.53 (0.35 to 0.76)	0.54 (0.41 to 0.68)	0.52 (0.32 to 0.78)	0.47 (0.3 to 0.68)
PDA	0.88 (0.66 to 1.17)	0.96 (0.68 to 1.36)	0.79 (0.62 to 1.01)	0.01 (-0.02 to 0.03)	7.71 (2.39 to 130.94)	1.04 (0.65 to 1.78)	0.95 (0.67 to 1.32)	1.09 (0.58 to 2.02)	0.89 (0.5 to 1.61)
Both	0.46 (0.37 to 0.56)	0.44 (0.34 to 0.56)	0.44 (0.37 to 0.54)	0.08 (0.06 to 0.1)	8.75 (3.66 to 152.72)	0.49 (0.33 to 0.69)	0.45 (0.35 to 0.56)	0.47 (0.3 to 0.67)	0.37 (0.24 to 0.54)
Patient Age	1 (1 to 1)	1 (1 to 1)	1 (0.99 to 1)	0 (0 to 0)	1.02 (1.01 to 1.03)	1 (1 to 1)	1 (1 to 1)	1 (0.99 to 1)	1 (1 to 1)
Laryngoscopy Device: VL vs DL	2.23 (1.99 to 2.48)	1.91 (1.69 to 2.18)	1.35 (1.21 to 1.51)	-0.08 (-0.1 to -0.07)	0.88 (0.6 to 1.37)	2.16 (1.34 to 4.03)	1.89 (1.67 to 2.16)	NA	NA
Intubator Training Level									
PGY-1	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
PGY-2	1.25 (1.05 to 1.47)	1.46 (1.21 to 1.75)	1.27 (1.11 to 1.48)	-0.04 (-0.06 to -0.01)	0.59 (0.37 to 1)	1.46 (1.22 to 1.75)	1.61 (1.36 to 1.91)	1.47 (1.11 to 1.97)	1.45 (1.14 to 1.84)
PGY-3	1.75 (1.48 to 2.07)	1.72 (1.45 to 2.09)	1.33 (1.14 to 1.56)	-0.06 (-0.08 to -0.04)	0.68 (0.44 to 1.13)	1.72 (1.45 to 2.09)	1.87 (1.59 to 2.26)	1.76 (1.32 to 2.3)	1.7 (1.32 to 2.17)
PGY_4	1.47 (1.16 to 1.86)	2.01 (1.58 to 2.68)	1.51 (1.23 to 1.89)	-0.06 (-0.09 to -0.03)	0.76 (0.31 to 1.52)	2.02 (1.58 to 2.67)	2.25 (1.74 to 2.95)	1.82 (1.24 to 2.67)	2.3 (1.53 to 3.46)
PGY>=5 or Fellow	1.68 (1.18 to 2.45)	1.73 (1.16 to 2.7)	1.33 (0.98 to 1.85)	-0.05 (-0.09 to -0.01)	0.73 (0.12 to 1.94)	1.74 (1.16 to 2.71)	2.01 (1.33 to 3.06)	1.71 (0.79 to 4.78)	1.75 (1.11 to 2.9)
Attending	1.42 (1.02 to 2.01)	1.83 (1.22 to 2.52)	1.35 (1.03 to 1.82)	-0.06 (-0.1 to -0.01)	0.37 (0 to 1.03)	1.83 (1.23 to 2.52)	2.06 (1.39 to 2.84)	2.69 (1.6 to 4.93)	1.25 (0.81 to 2.05)
Trauma	0.88 (0.78 to 0.99)	0.9 (0.78 to 1.04)	1.01 (0.91 to 1.13)	0.01 (0 to 0.03)	1.25 (0.82 to 1.92)	0.9 (0.78 to 1.03)	0.91 (0.79 to 1.05)	0.86 (0.7 to 1.09)	0.88 (0.72 to 1.06)
Difficult Airway Type and Device Interaction**									

Neither:VL	NA	NA	NA	NA	NA	Reference	NA	NA	NA
ADA:VL	NA	NA	NA	NA	NA	1 (0.51 to 1.69)	NA	NA	NA
PDA:VL	NA	NA	NA	NA	NA	0.83 (0.38 to 1.66)	NA	NA	NA
Both:VL	NA	NA	NA	NA	NA	0.83 (0.43 to 1.39)	NA	NA	NA
AIC[++]	*NA*	*8626*	*13088*	*29878*	*1488*	*8628*	*8925*	*3599*	*5032*
BIC[++]	*NA*	*8791*	*13253*	*30043*	*1654*	*8816*	*9091*	*3732*	*5182*
Observations	*13938*	*13938*	*13938*	*13938*	*13938*	*13938*	*13938*	*4190*	*9748*

FAS, first-attempt success; wo, without; AE, adverse events; DL, direct laryngoscopy; VL, video laryngoscopy; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; ADA, anatomically difficult airway; PDA, physiologically difficult airway; AIC, Akaike information criterion; BIC, Bayesian information criterion

*Peri-intubation cardiac arrest occurring during or after any attempt.
**Interaction between difficult airway type (neither, anatomically difficult, physiologically difficult, and both) and laryngoscope device type (video vs. direct laryngoscopy).
***After nonparametric missing value imputation performed using random forest (see Supplemental Table 2 for details).
[+]First-attempt success without any of the following adverse events during or immediately after the first attempt: vomiting, esophageal intubation (immediately recognized and delayed recognition), bradydysrhythmia, cardiac arrest, hypoxemia (<90% or drop of 10% of oxygen saturation), and tachydysrhythmia
[++]Regression Diagnostics
Note: NA (not applicable) means there is no estimate because the variable was not included in the model. Adjusted odds ratios were considered significant if the confidence interval did not cross one. Similarly, adjusted estimates were considered significant if the confidence interval did not cross zero.

Supplemental Table 5. Regression Estimates for the Full and Reduced Models Used in the Interaction Analyses

	First-Attempt Success		First-Attempt Success without Adverse Events[+]	
Variable	Full Model aOR (95% CI)	Reduced Model aOR (95% CI)	Full Model aOR (95% CI)	Reduced Model aOR (95% CI)
ADA	0.58 (0.46 to 0.72)	0.53 (0.45 to 0.62)	0.78 (0.66 to 0.92)	0.66 (0.58 to 0.74)
PDA	1.00 (0.76 to 1.38)	0.86 (0.77 to 0.98)	0.84 (0.68 to 1.02)	0.64 (0.58 to 0.71)
Patient Age	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.00)	1.00 (0.99 to 1.00)	1.00 (0.99 to 1.00)
Laryngoscopy Device: VL vs DL	1.89 (1.67 to 2.15)	1.90 (1.67 to 2.15)	1.33 (1.20 to 1.47)	1.33 (1.20 to 1.47)
Intubator Training Level				
PGY-1	Reference	Reference	Reference	Reference
PGY-2	1.45 (1.21 to 1.74)	1.45 (1.21 to 1.74)	1.26 (1.11 to 1.47)	1.27 (1.11 to 1.47)
PGY-3	1.71 (1.43 to 2.07)	1.72 (1.43 to 2.07)	1.31 (1.13 to 1.53)	1.31 (1.14 to 1.53)
PGY_4	2.00 (1.57 to 2.66)	2.01 (1.58 to 2.67)	1.50 (1.22 to 1.89)	1.51 (1.22 to 1.89)
PGY>=5 or Fellow	1.71 (1.14 to 2.61)	1.71 (1.14 to 2.6)	1.33 (0.98 to 1.86)	1.33 (0.98 to 1.86)
Attending	1.81 (1.23 to 2.51)	1.81 (1.23 to 2.51)	1.35 (1.02 to 1.81)	1.35 (1.02 to 1.81)
Trauma	0.91 (0.79 to 1.04)	0.91 (0.79 to 1.05)	1.02 (0.92 to 1.14)	1.03 (0.92 to 1.14)
ADA and PDA Interaction	0.84 (0.60 to 1.14)	NA	0.72 (0.58 to 0.91)	NA
AIC[++]	*8669*	*8632*	*13128*	*13104*
BIC[++]	*8767*	*8722*	*1322*	*13194*
Observations	*13616*	*13938*	*13616*	*13938*

DL, direct laryngoscopy; VL, video laryngoscopy; aOR, adjusted odds ratio; CI, confidence interval; ADA, anatomically difficult airway; PDA, physiologically difficult airway; AIC, Akaike information criterion; BIC, Bayesian information criterion

[+]First-attempt success without any of the following adverse events during or immediately after the first attempt: vomiting, esophageal intubation (immediately recognized and delayed recognition), bradydysrhythmia, cardiac arrest, hypoxemia (<90% or drop of 10% of oxygen saturation), and tachydysrhythmia

[++]Regression Diagnostics

Note: The full models contain the interaction term between ADAs and PDAs, while the reduced models exclude the interaction term. NA (not applicable) means there is no estimate because the variable was not included in the model. Adjusted odds ratios were considered significant if the confidence interval did not cross one.

Supplemental Table 6. Measures of Interaction Between Anatomically and Physiologically Difficulty Airways

	Outcomes	
Measures of Interaction	FAS	FAS wo AE
Additive Interaction Tests, estimate (95% CI)*		
Relative Excess Risk due to Interaction (RERI)	-0.10 (-0.48 to 0.17)	-0.15 (-0.38 to 0.05)
Attributable Proportion (AP)	-0.19 (-0.92 to 0.40)	-0.32 (-0.74 to 0.12)
Multiplicative Interaction Test, p-value		
Likelihood Ratio Test**	0.275	0.005

FAS, first-attempt success; wo, without; AE, adverse events; CI, confidence interval

*The 95% CI for each measure of additive interaction were calculated from the 1,000 bootstrapped regression estimates from the full interaction models presented in Supplemental Table 5. If the 95% CI crosses zero for the RERI or AP, an additive interaction is unlikely. If the 95% CI is below or above zero, there is evidence of antagonism or synergy, respectively.

**The p-value for interaction was calculated by performing the likelihood ratio test on the full and reduced models (with and without interaction terms) for each outcome. The full and reduced models are presented in Supplemental Table 5. A p-value <0.05 was considered significant and evidence of a multiplicative interaction.

Additional Analysis Details

1. Details for Multiple Imputation

Nonparametric missing value imputation was performed using random forest with 10 iterations and 100 trees per forest. The variables used for multiple imputation included patient age, laryngoscopy device type (i.e., direct vs. video), difficult airway type (i.e., neither, ADA, PDA, both), first-attempt success, poor glottic view (Cormack-Lehane grades 3 or 4), intubator training level (e.g., PGY level), obesity / morbid obesity, post-induction hypoxemia, site, and trauma indication. Missingness before and after multiple imputation is reported in Supplemental Table 2. The normalized root mean squared error (NRMSE) was 0.0000000, and the proportion of falsely classified (PFC) was 0.1186926. The multiple imputation procedure assumes that the missing data are missing at random. Missing at random assumes that the tendency for a data point to be missing is not related to the missing data, and therefore can be imputed using related, observed data.

2. Details for Causal Diagram Models and Mediation Analysis (Supplemental Figure 2, Supplemental Figure 3, Supplemental Table 3)

Causal diagrams are used to graphically display relationships between independent, confounding, mediator, and dependent variables. We constructed causal diagrams to investigate the potential for mediation of the association between obesity / morbid obesity (independent variable) and first-attempt success (dependent variable) by post-induction hypoxemia and poor glottic view (mediators) (Supplemental Figures 2 and 3). These causal diagrams are used to build regression models, including the relevant variables for each vector displayed in the diagrams (Supplemental Figures 2 and 3, Supplemental Table 3). These model estimates are then used to perform a mediation analysis, which quantifies the effects between the independent and dependent variables through the direct (a) and indirect (b+c) pathways (Supplemental Figures 2&3). The significance of each pathway is determined by confidence intervals and/or p-values of the average direct effects or ADE (direct pathway) and average causal mediation effects or ACME (indirect pathway). The ADE coefficient represents the effect of the independent variable on the dependent variable adjusting for the mediator, while the ACME coefficient represents the effect of the independent variable on the dependent variable that is mediated through the mediator variable. If the ADE is significant and the ACME is not, there is no mediation, if the ADE is not significant and the ACME is, there is full mediation, and if they are both significant, then there is partial mediation.

Using the imputed dataset (described in Supplemental Table 2), multiple logistic regression mixed effects models were used to determine adjusted odds ratios (aOR) with 95% confidence intervals for each association (i.e., each vector) in the causal diagrams accounting for fixed effects, including device type (i.e., direct and video laryngoscopy), intubator training level (i.e., post-graduate training level), trauma, and age as well as the site as a random effect. 95% confidence intervals were determined using conventional standard errors (Supplemental Figures 2&3), since these are less computationally demanding. Generalized variance inflation factors were assessed for all models and were <2 for all model variables. Models were assessed using the Akaike and Bayesian information criteria.

For the mediation analysis, we tested the significance of direct and indirect effects using 95% quasi-Bayesian confidence intervals from 1,000 Monte Carlo simulations (1-3). This is the default method for the mediation package (2). Significance was determined by an aOR 95% confidence interval excluding one or p-value <0.05.

1. Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. Psychol Methods. Dec 2010;15(4):309-34. doi:10.1037/a0020761
2. Tingley D, Yamamoto T, Hirose K, Keele L, Imai K. mediation: R Package for Causal Mediation Analysis. J Stat Softw. 09/02 2014;59(5):1 - 38. doi:10.18637/jss.v059.i05
3. King G, Tomz M, Wittenberg J. Making the Most of Statistical Analyses: Improving Interpretation and Presentation. AJPS. April 2000;44:341–355.

3. Details for Unadjusted, Adjusted, and Sensitivity Analyses (Figure 2, Supplemental Figure 4, Supplemental Table 4)

Unadjusted Analysis Details

Univariate odds ratios were determined by logistic regression for each variable predicting first-attempt success (Supplemental Table 4). For these univariate odds ratios, 95% confidence intervals were determined using conventional standard errors, since these are less computationally demanding.

Adjusted and Sensitivity Analysis Details

For the primary (first-attempt success) and select secondary (first-attempt success without adverse events, total number of airway attempts, peri-intubation cardiac arrest) outcomes, adjusted estimates were determined by multiple variable mixed-effects models applied to 1,000 bootstrapped samples. Poisson regression was used for the total number of airway attempts, while logistic regression was used for the remaining binary outcomes. Fixed effects included the presence of a difficult airway type (independent variable) and covariates including device type (i.e., direct and video laryngoscopy), intubator training level (i.e., post-graduate training level), trauma, and age as well as the site as a random effect.

Sensitivity analyses examined first-attempt success with the same model but with the following alterations: after multiple imputation of the study dataset (Supplemental Table 2), after excluding laryngoscopy device type from the model and selecting only direct or video laryngoscopy cases, and after including interaction terms between difficult airway type and laryngoscopy device type. Repeating the analysis after random forest multiple imputation provided insight into the impact missingness might have on the results (Supplemental Table 2). Similarly, repeating the analysis on the direct and video laryngoscopy subsets provided insight into the possibility of conditional effects by laryngoscopy device type. Furthermore, repeating the analysis with difficult airway type and laryngoscopy device type interaction terms accounted for possible modification of the association between difficult airway type and first-attempt success by laryngoscopy device type.

Adjusted estimates and 95% confidence intervals are the 50^{th}, 2.5^{th}, and 97.5^{th} percentiles of the bootstrapped estimates (percentile method) reported in Supplemental Table 4, while Figure 2 and Supplemental Figure 4 graphically display the bootstrapped estimates as probability densities determined by the kernel density estimate (1-2). Generalized variance inflation factors were calculated to assess for multicollinearity and were <2 for all variables in all models. Akaike and Bayesian information criteria were calculated for each model. Significance was determined by 95% confidence intervals excluding one for aORs and zero for coefficients.

We examined several secondary outcomes in the unadjusted analyses displayed in Table 3; however, we limited the adjusted analyses to the primary outcome and secondary outcomes that were most clinically relevant, given that bootstrapping methods with mixed effects models are computationally demanding.

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2. Jung K, Lee J, Gupta V, Cho G. Comparison of Bootstrap Confidence Interval Methods for GSCA Using a Monte Carlo Simulation. Front Psychol. 2019;10:2215. doi:10.3389/fpsyg.2019.02215

4. Details for Interaction Analysis (Supplemental Tables 5&6)

In addition to examining the difficult airway types (anatomically difficult (ADA), physiologically difficult (PDA), and combined) compared to neither ADA nor PDA, we examined the interaction between ADAs and PDAs and their association with first-attempt success and first-attempt success without adverse events. We felt these select outcomes would be most relevant since the presence or absence of interaction would address our hypothesis that both difficult airway types would be associated with first-attempt success.

Using tests that address both multiplicative and additive scales (1-2), we investigated the hypotheses that the interaction between ADAs and PDAs was associated with first-attempt success and first-attempt success without adverse events. We first created an interaction model (full model) using mixed-effects logistic regression, where fixed effects included the presence of an ADA characteristic (defined in Table 1), the presence of a PDA characteristic (defined in Table 1), an ADA and PDA interaction term, device type (i.e., direct and video laryngoscopy), intubator training level (i.e., post-graduate training level), trauma, and age as well as the site as a random effect. Then, we removed the interaction term to create a new model (reduced model).

Assessment for Multiplicative Interaction

First, for each outcome, the full model was applied to 1,000 bootstrapped samples of the data. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated from the bootstrapped estimates using the percentile method. We initially tested the hypothesis that a multiplicative interaction between ADAs and PDAs existed by examining the 95% CI for the ADA and PDA interaction term. If the 95% CI crossed one, we considered no multiplicative interaction to be present (i.e., the interaction effect is not significantly different from the product of the individual effects) (Supplemental Table 5) (1). If the 95% CI was less than 1, we considered a negative multiplicative interaction to be present (the interaction effects being less than the product of the individual effects) (1,4). If the 95% CI was greater than 1, we considered a positive multiplicative interaction to be present (the interaction effects being greater than the product of the individual effects) (1,4). We also performed a likelihood ratio test on the full and reduced models (with and without the ADA and PDA interaction term) for each outcome; a p-value <0.05 was considered significant for the presence of a multiplicative interaction (Supplemental Table 6).

Assessment for Additive Interaction

We tested the hypothesis that an additive interaction between ADAs and PDAs existed by calculating measures of additive interaction, including relative excess risk due to interaction (RERI) and attributable proportion (AP) (1-2). The 95% CI for each measure of additive interaction was calculated from the 1,000 bootstrapped regression estimates using the full model, since this method may be superior to the delta method (2-3). If the 95% CI crossed zero for the RERI or AP, the interaction was considered zero additive (i.e., the interaction effects being not significantly different than the sum of the individual effects) (4). If the 95% CIs were below or above zero, this suggested evidence of antagonism or synergism, respectively (i.e., the interaction effects being significantly less or more than the sum of the individual effects) (1-4) (Supplemental Table 6).

1. VanderWeele TJ, Knol MJ. A Tutorial on Interaction. Epidemiologic Methods. 2014;3(1):33-72. doi:doi:10.1515/em-2013-0005

2. Goldstein ND. Epi Vignettes: Interaction and effect modification. Updated 2016-05-09. Accessed 2023-07-11, 2023. https://www.goldsteinepi.com/blog/epivignettesinteractionandeffectmodification/
3. Assmann SF, Hosmer DW, Lemeshow S, Mundt KA. Confidence intervals for measures of interaction. Epidemiology. May 1996;7(3):286-90. doi:10.1097/00001648-199605000-00012
4. VanderWeele TJ. The Interaction Continuum. Epidemiology. Sep 2019;30(5):648-658. doi:10.1097/ede.0000000000001054