In February 2013, GlaxoSmithKline (GSK) announced a commitment to further clinical transparency through the public disclosure of GSK Clinical Study Reports (CSRs) on the GSK Clinical Study Register.

The following guiding principles have been applied to the disclosure:

- *Information will be excluded in order to protect the privacy of patients and all named persons associated with the study*
- *Patient data listings will be completely removed* to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the* ***GSK Clinical Study Register****.*
- *Aggregate data will be included; with any direct reference to individual patients excluded*

**Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered*

GlaxoSmithKline group of companies

Division	:	Worldwide Development
Information Type	:	Statistical Report

Title	:	MID207941 Meta Analysis Report
Compound Number	:	GW685698 + GW642444

Description: Meta-Analysis Plan for MID207941: A Study to Evaluate Risk Factors for Pneumonia and Chronic Obstructive Pulmonary Disease (COPD) Exacerbations in a COPD Population of Patients Treated with GW685698 + GW642444 (Fluticasone Furoate + Vilanterol); GW642444 (Vilanterol); CCI18781 (Fluticasone Propionate); GR33343 (Salmeterol); CCI18781+ GR33343 (Fluticasone Propionate + Salmeterol) and Placebo.

Compound Number: GW685698, GW642444, CCI18781, GR33343

Effective Date: 06-SEP-2018

Subject: COPD, pneumonia, COPD exacerbations, inhaled corticosteroids

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207941 META ANALYSIS REPORT

1. BACKGROUND AND AIMS

The effect of single factors on the risk of exacerbations and pneumonia in chronic obstructive pulmonary disease (COPD) has been explored previously. The risk of pneumonia has been found to be increased by inhaled corticosteroid (ICS) treatment, worse lung function, and low body mass index (BMI) [Crim, 2009; Mullerova, 2012].

Here, we examined how risk factors for exacerbations and pneumonia interact with each other, to give probability estimates for the occurrence of an exacerbation or pneumonia.

2. METHODS

In a pooled analysis (MID207941) of five studies of patients with COPD treated with ICS/long-acting β_2-agonist (LABA) combinations and comparator arms of ICS, LABA and/or placebo (NCT01009463 [Dransfield, 2013], NCT0101795, NCT00144911, NCT00115492 [Dransfield, 2013], and the Towards a Revolution in COPD Health [TORCH] study [Crim, 2009]), we used backwards elimination in a Cox's proportional hazards (PH) regression model to evaluate which combination of risk factors best predict:

1. time to first pneumonia

2. time to first moderate/severe COPD exacerbation.

We first examined a set of seven binary covariates: age (<65 years, ≥65 years), BMI (<25 kg/m^2, ≥25 kg/m^2), Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage (I & II: pre-bronchodilator forced expiratory volume in one second [FEV_1] ≥50%, III & IV: pre-bronchodilator FEV_1 <50%), history of exacerbations in the year prior to the study (<2, ≥2), history of smoking (former smoker, current smoker), sex (male, female), and study treatment (with ICS, without ICS).

We repeated the analyses with an expanded set of nine binary covariates, including race (Asian, non-Asian) and World Bank Country Income Group (high income, non-high income).

The backwards elimination process used to find the covariates that best explain the data worked as follows:

1. A Cox PH model containing all main and interaction effects was fitted (28 covariates in the smaller set or 45 covariates in the larger set);

2. The least statistically significant covariate was then removed until all remaining covariates were significant ($p<0.1$);

3. Main effects, however, were not removed from the model if they were present in an interaction effect that still remained in the model.

3. RESULTS

3.1. Pneumonia model

In the smaller covariate set, a low BMI, history of exacerbations, worse lung function (GOLD stage), and treatment with an ICS appeared to be important factors increasing the risk of pneumonia (Source: Figure 1.8; Table 1.3). Additionally, three interactions remained in the model (Source: Table 1.1).

1. The risk of pneumonia associated with age (≥65 vs <65 years) increased for men compared with women.

2. The risk of pneumonia associated with an exacerbation history (≥2 vs <2) was higher for younger subjects than for older subjects.

3. The risk of pneumonia associated with ICS treatment (vs non-ICS) was higher for subjects with lower BMI (<25 kg/m^2) than for those with higher BMI. No other risk factors were found to be modified by treatment with an ICS.

To investigate more fully how BMI modifies the risk of treatment with an ICS, we re-ran the analysis using a more detailed BMI covariate (Source: Table 1.5; Table 1.6; Figure 1.7).

The modeled probability of a pneumonia event varied between 3% and 12% during the first year in the identified subgroups. The most at-risk subgroups, were generally older, with a low BMI, a history of exacerbations, worse lung function (GOLD stage), and treated with an ICS. The inverse was true for the least at-risk subgroups (Source: Table 1.2; Figure 1.4).

The selected model from the larger covariate set qualitatively replicated the findings from this selected model and retained all the above terms (Source: Table 2.1). Income and race did not affect pneumonias in a qualitatively consistent manner across the different interaction levels (Source: Table 2.2; Table 2.3; Table 2.5; Figure 2.4; Figure 2.6).

3.2. Exacerbation model

In the smaller covariate set, history of exacerbations, worse lung function (GOLD stage), female gender, and non-ICS treatment appeared to be important factors increasing the risk of exacerbation. Four interactions remained in the model: age by smoking status, BMI by exacerbation history, sex by treatment, and sex by smoking status (Source: Table 1.10; Table 1.30; Figure 1.50).

The modeled probability of an exacerbation varied between 31% and 82% during the first year in the identified subgroups. The most at-risk subgroups were generally female, with a low BMI, a history of exacerbations, and worse lung function (as measured by GOLD stage), reflecting the inclusion criteria for the studies included in this analysis. The inverse was true for the least at-risk subgroups (Source: Table 1.20; Figure 1.40).

The selected model from the larger covariate set differed somewhat from the model selected from the smaller covariate set; of the interactions found above, only sex by smoking status and BMI by exacerbation history were replicated (Source: Table 2.10; Table 2.20; Table 2.30; Figure 2.40; Figure 2.50).

3.3. Exacerbation model using pneumonia subgroups

Of particular interest from a risk–benefit point of view, is how the subgroups selected in the pneumonia model behave in terms of exacerbations. We refitted the model selected by pneumonia data to the exacerbation data, to investigate how the subgroups selected to explain the risk of pneumonia would predict exacerbation.

Of note, subjects <25 kg/m^2 treated with ICS vs non-ICS had a hazard ratio of 0.87 (95% CI: 0.81, 0.93) for exacerbations and 1.83 (95% CI: 1.54, 2.17) for pneumonia. Subjects ≥25 kg/m^2 treated with ICS vs non-ICS had a hazard ratio of 0.85 (95% CI: 0.79, 0.91) for exacerbations and 1.32 (1.09, 1.59) for pneumonia (Source: Figure 9.3; Table 9.2).

Probabilities from survival curves for pneumonia and exacerbations were presented for the subgroups defined by the pneumonia model (Source: Table 9.1; Figure 9.4).

4. CONCLUSIONS

The modeled probabilities of an exacerbation (31% to 82%) were considerably higher than those for pneumonia (3% and 12%).

Age may interact with sex and exacerbation history to predict pneumonia. Sex may interact with smoking status, and BMI may interact with exacerbation history to predict exacerbations.

The only risk factor for pneumonia modified by ICS treatment was BMI. When exacerbations were modeled using the same subgroups as found in the pneumonia model (i.e. those which best explain the risk of pneumonia) it did not appear that BMI significantly modified the treatment effect on exacerbations.

This analysis suggests that in patients with lower BMI, ICS treatment increases the risk of pneumonia but without increasing benefit in terms of exacerbation reduction; as a consequence, the risk–benefit ratio will be worse in such patients.

It is possible to develop a personal risk predictor for pneumonia and exacerbations in COPD patients from the model estimates found.

The nature of repeated testing in the backwards elimination procedure did not conserve the type I error, and the results are hypothesis generating.

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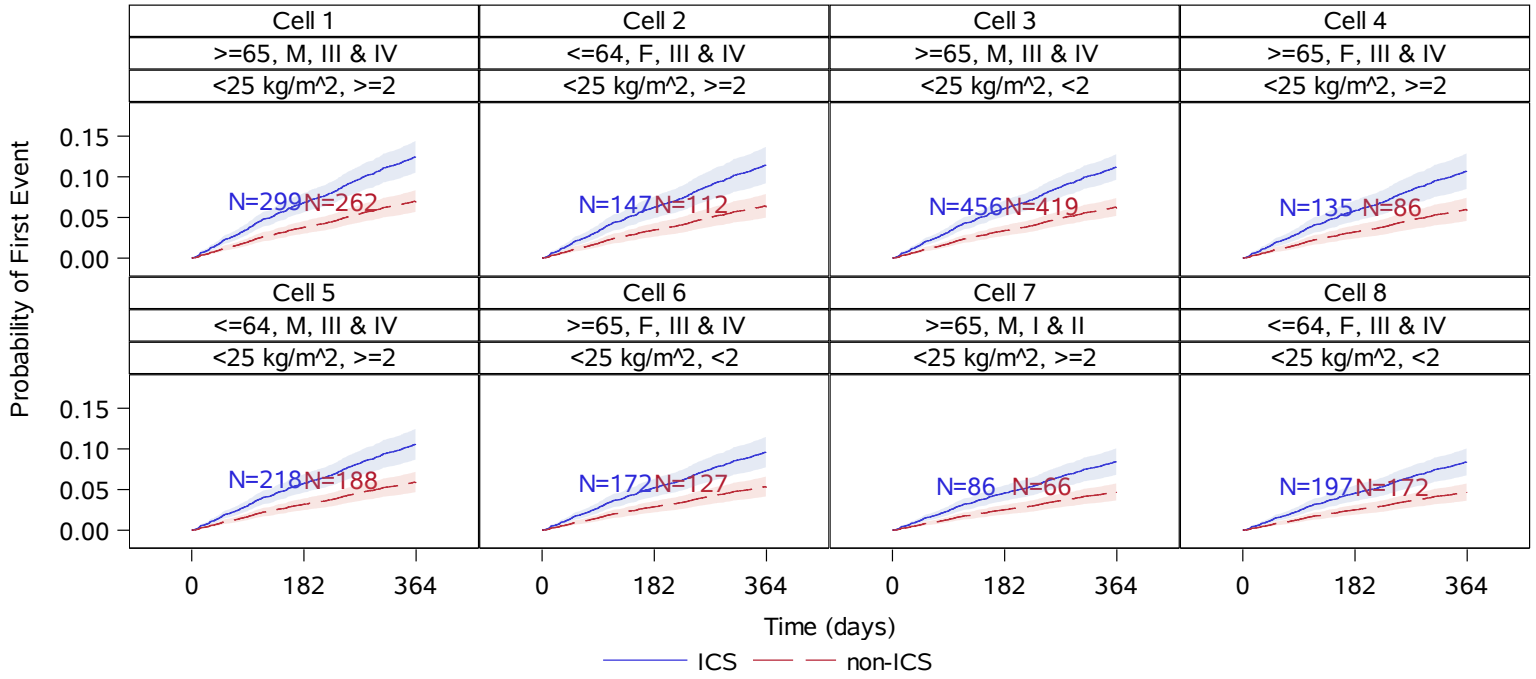
Crim C, Calverley PMA, Anderson JA, Celli B, Ferguson GT, et al. Pneumonia risk in COPD patients receiving inhaled corticosteroids alone or in combination: TORCH study results. Eur Respir J 2009;34:641–647.

Mullerova H, Chigbo C, Hagan GW, Woodhead MA, Miravitlles M, et al. The natural history of community-acquired pneumonia in COPD patients: a population database analysis. Respir Med 2012;106:1124–1133.

Dransfield MT, et al. Once-daily inhaled fluticasone furoate and vilanterol versus vilanterol only for prevention of exacerbations of COPD: two replicate double-blind, parallel-group, randomised controlled trials Lancet Respir Med 2013;1:210–23.

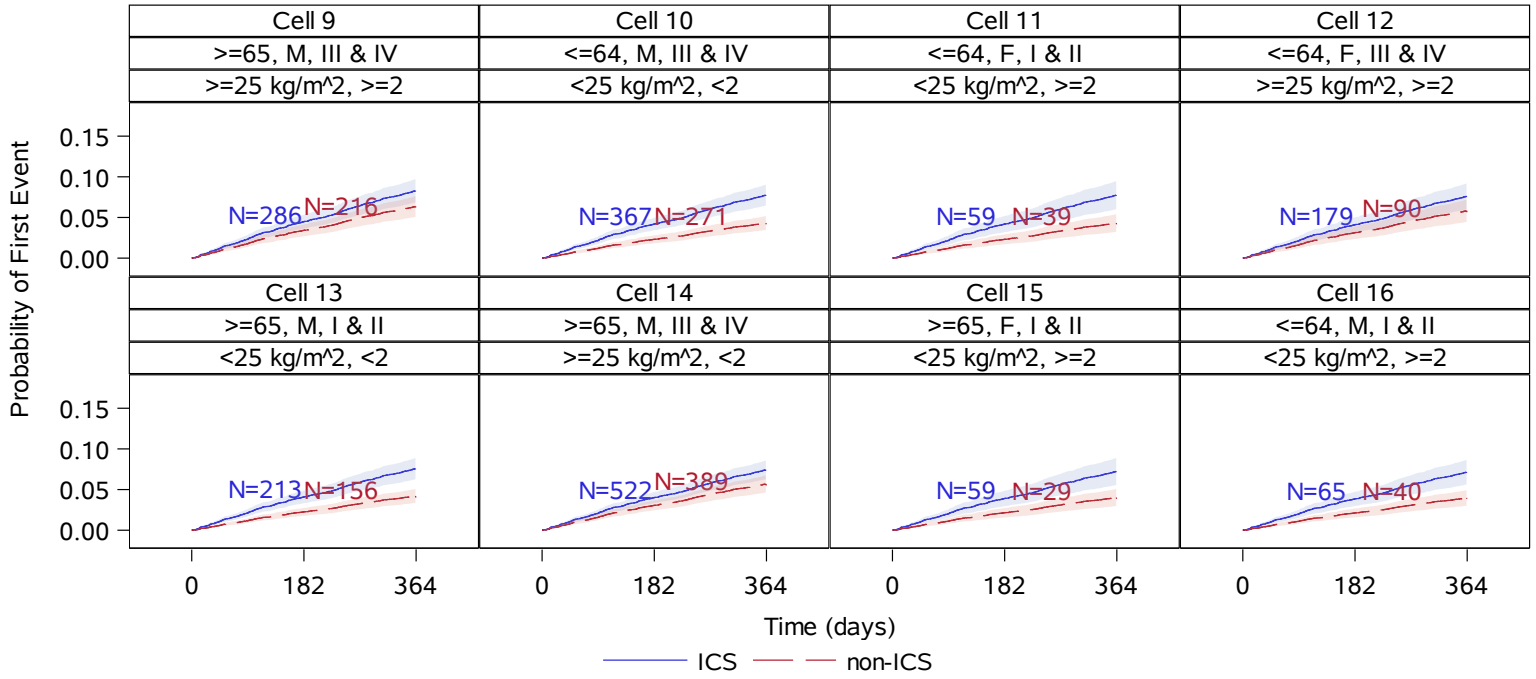
Figure 1.4
Probability of First Pneumonia During Year on Study Treatment Survival Curves
(Based on Seven Covariates)



Cell Header Line 1: Age, Sex, GOLD
Cell Header Line 2: BMI, Exac.
Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

PPD

Figure 1.4
Probability of First Pneumonia During Year on Study Treatment Survival Curves
(Based on Seven Covariates)



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Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

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Figure 1.4
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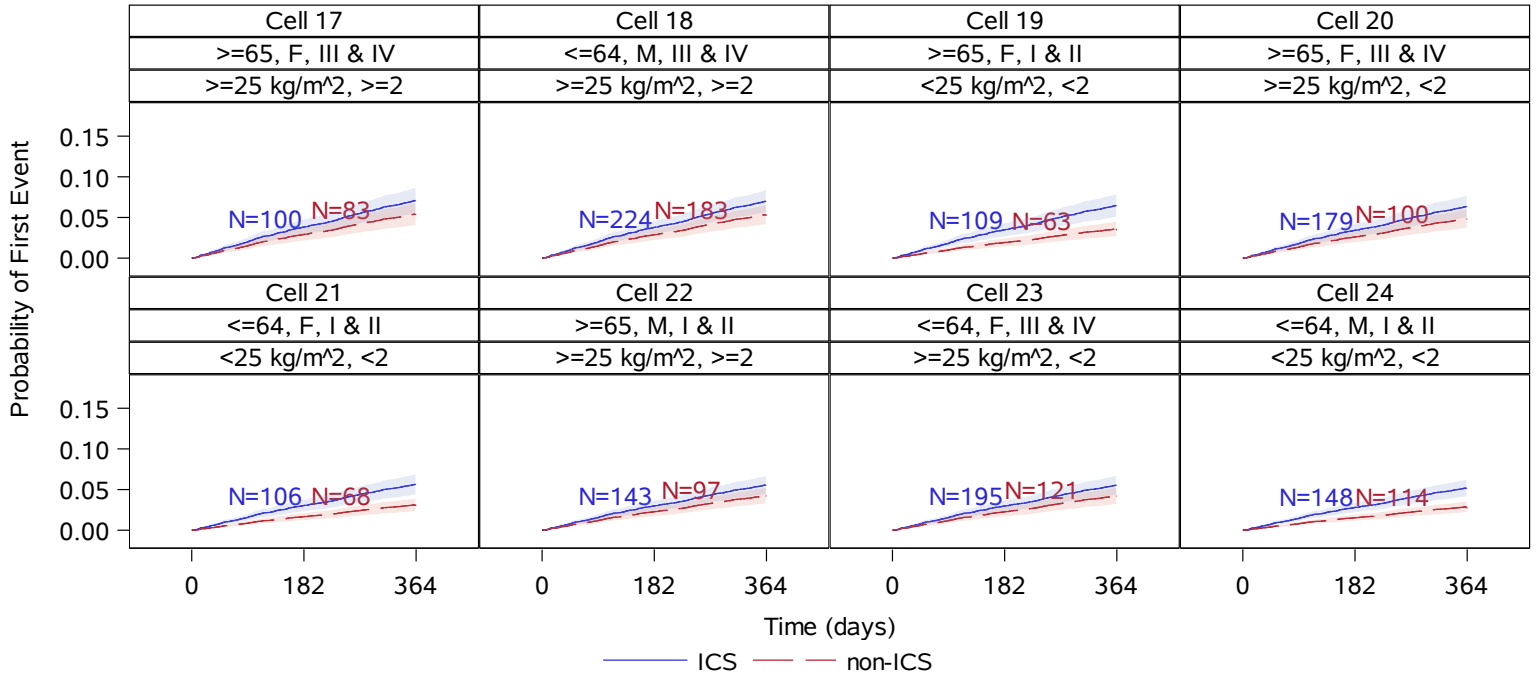

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Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

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Figure 1.4
Probability of First Pneumonia During Year on Study Treatment Survival Curves
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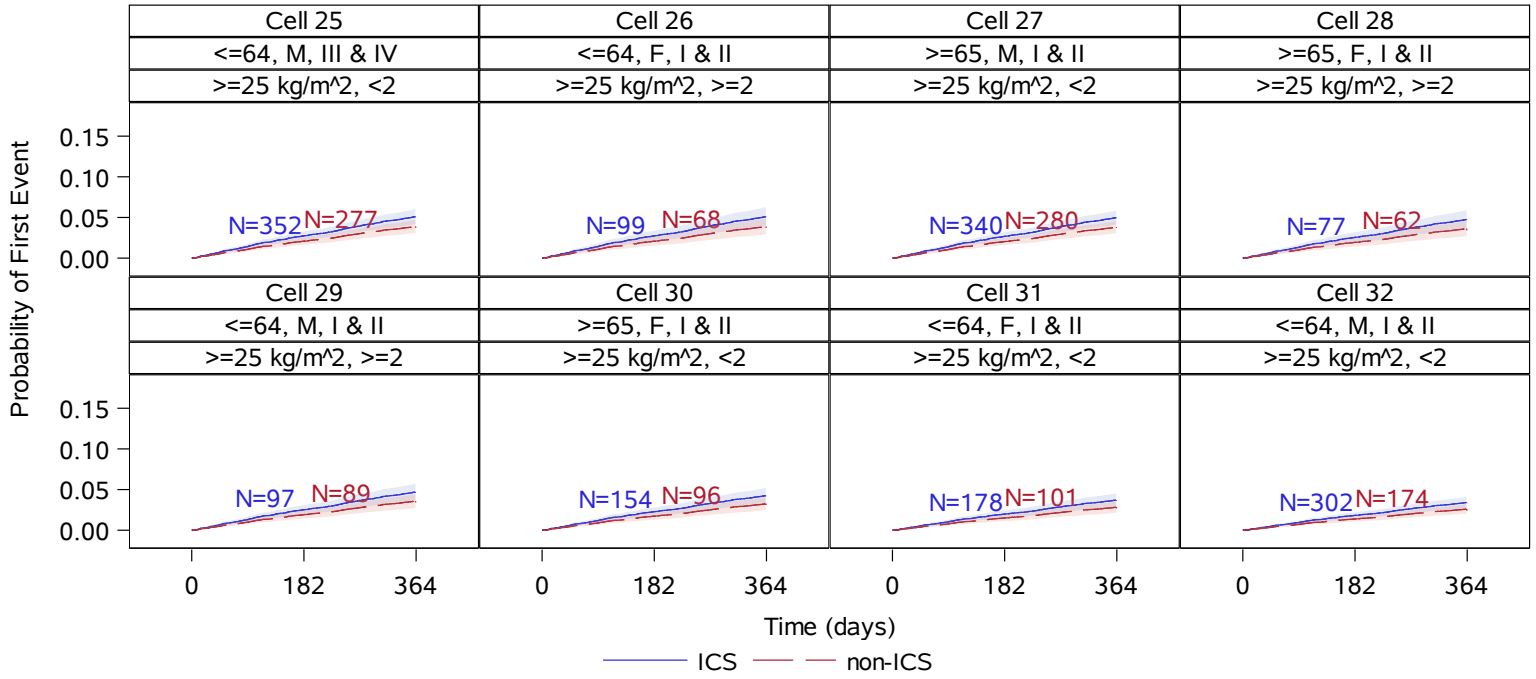

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Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

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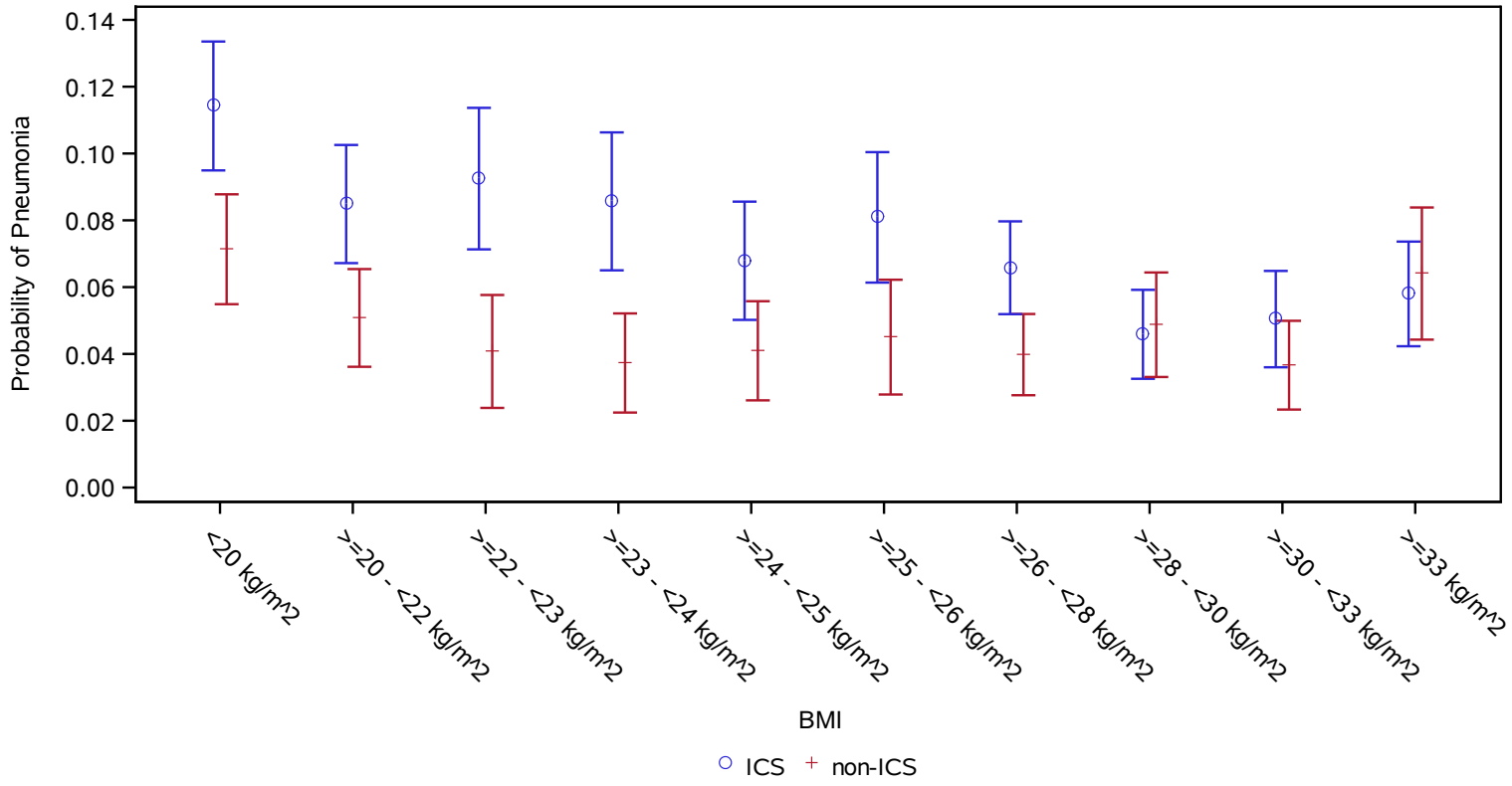
Figure 1.7
Pneumonia Probabilities by BMI Decile (Direct Adjusted Probabilities)
Based on Seven Covariate Selected Model with Expanded BMI Category



Average probability estimates based on direct adjusted survival curves of the ITT sample.

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Figure 1.8
Hazard Ratios from Selected Pneumonia Cox Model (Based on Seven Covariates)

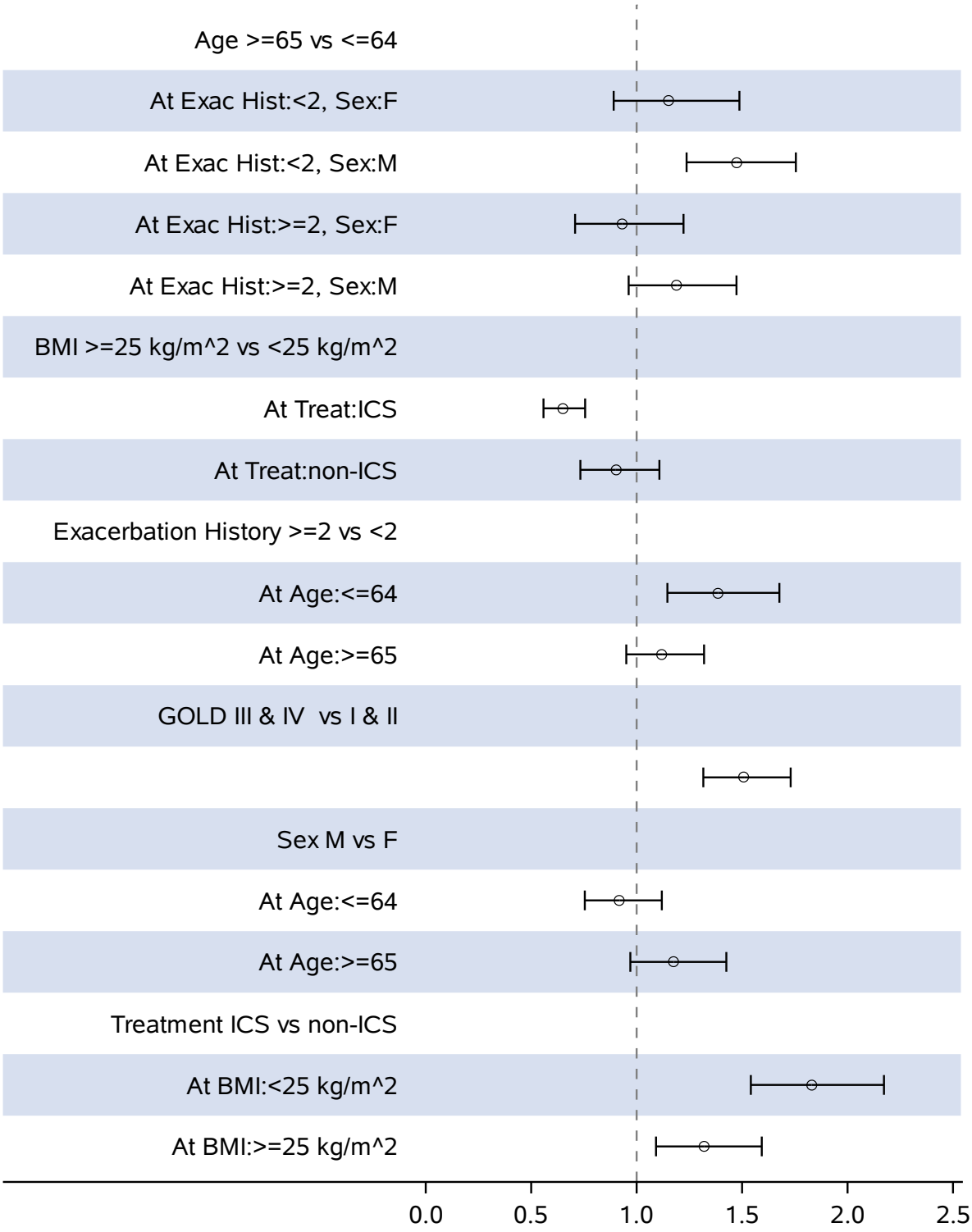
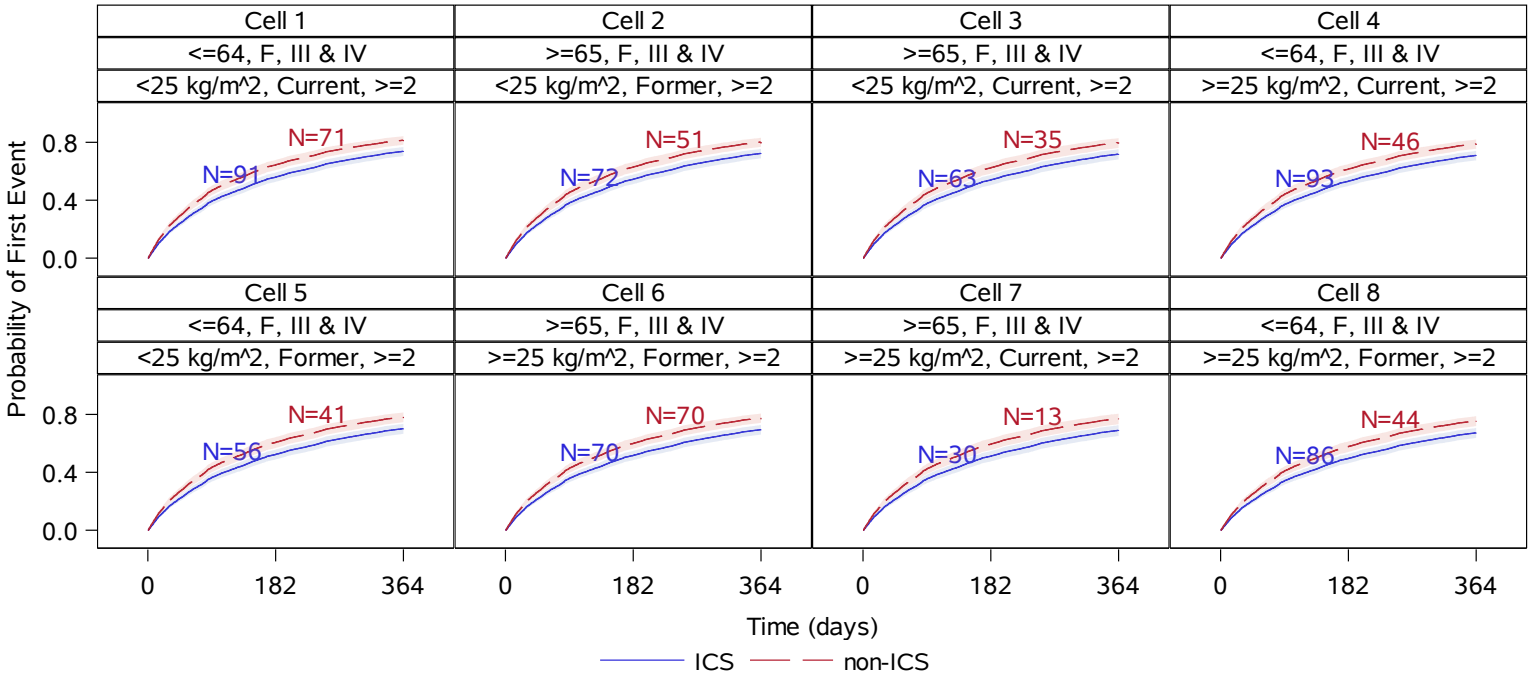


Figure 1.40
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Seven Covariates)



Cell Header Line 1: Age, Sex, GOLD
Cell Header Line 2: BMI, Smoking., Exac.
Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

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Figure 1.40
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Seven Covariates)

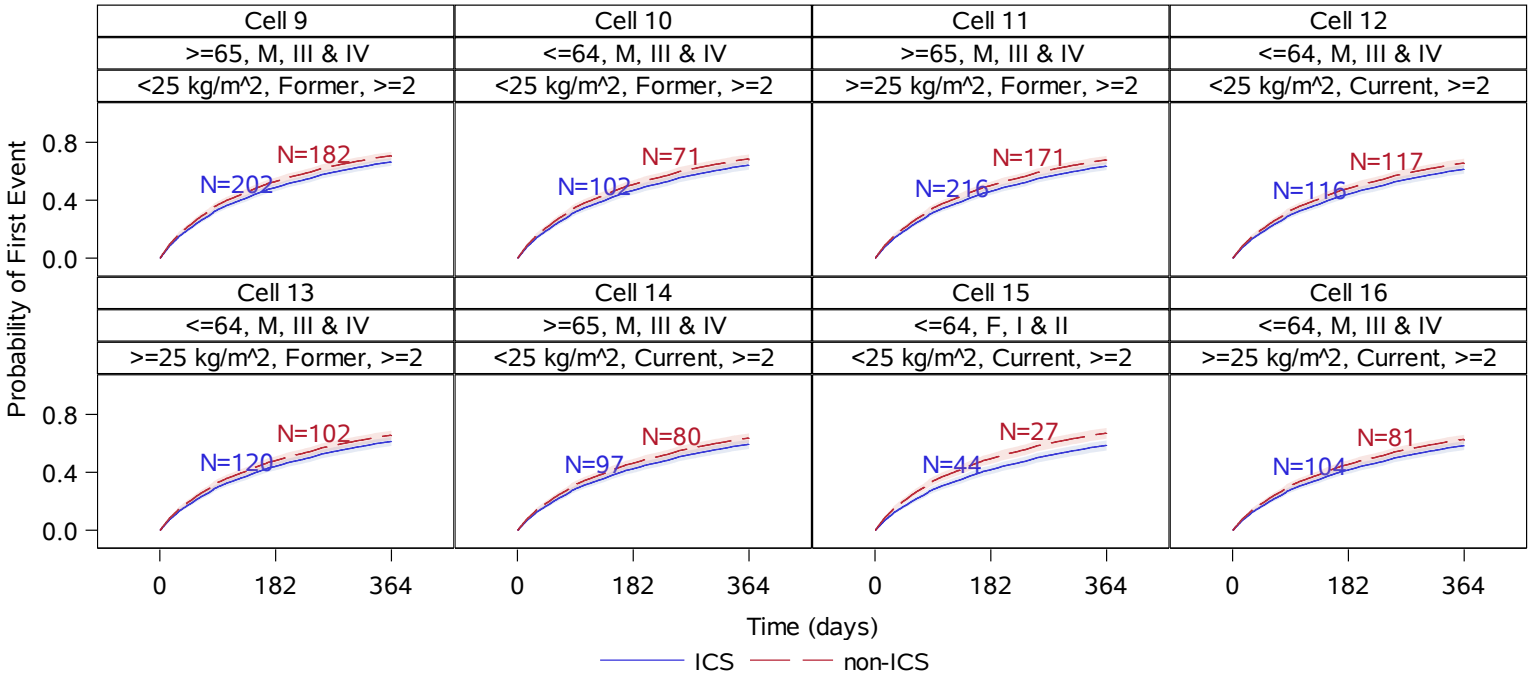

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Figure 1.40
Probability of First Exacerbation During Year on Study Treatment Survival Curves
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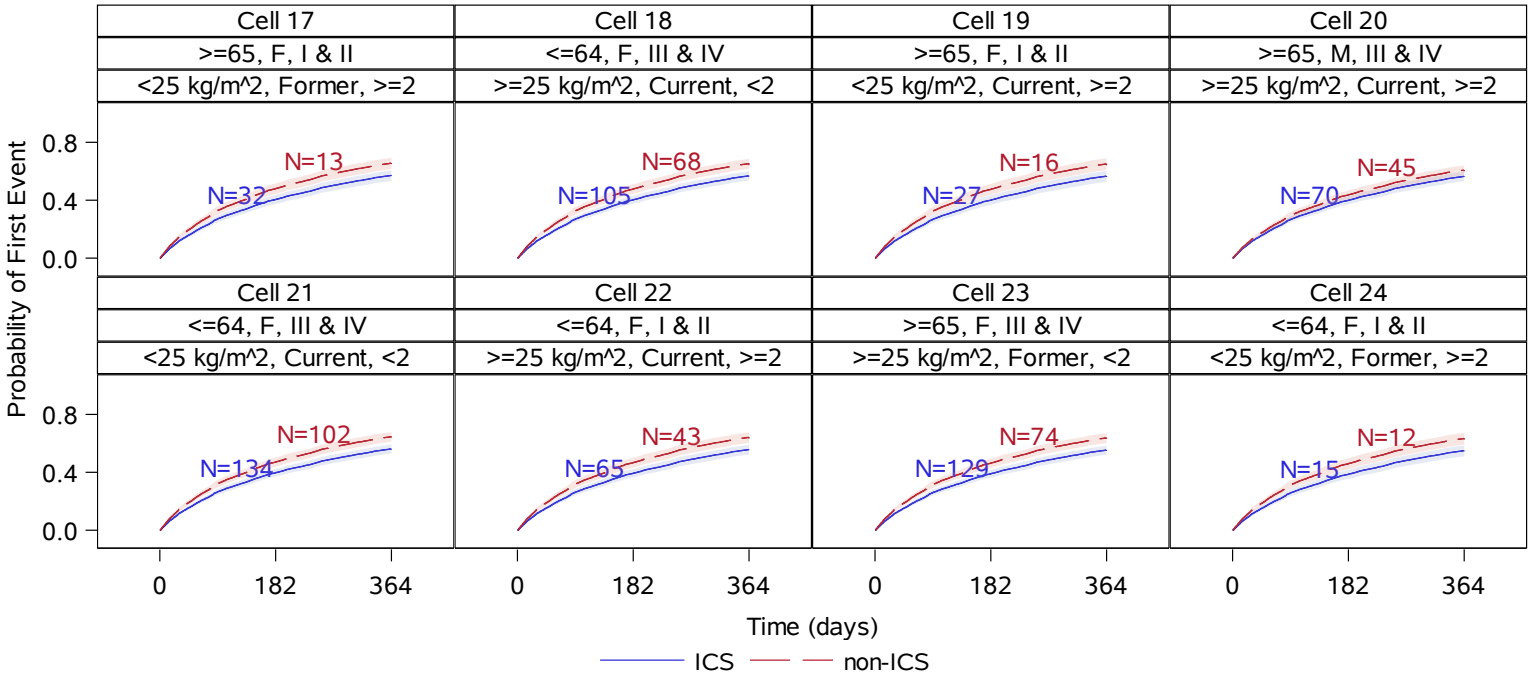

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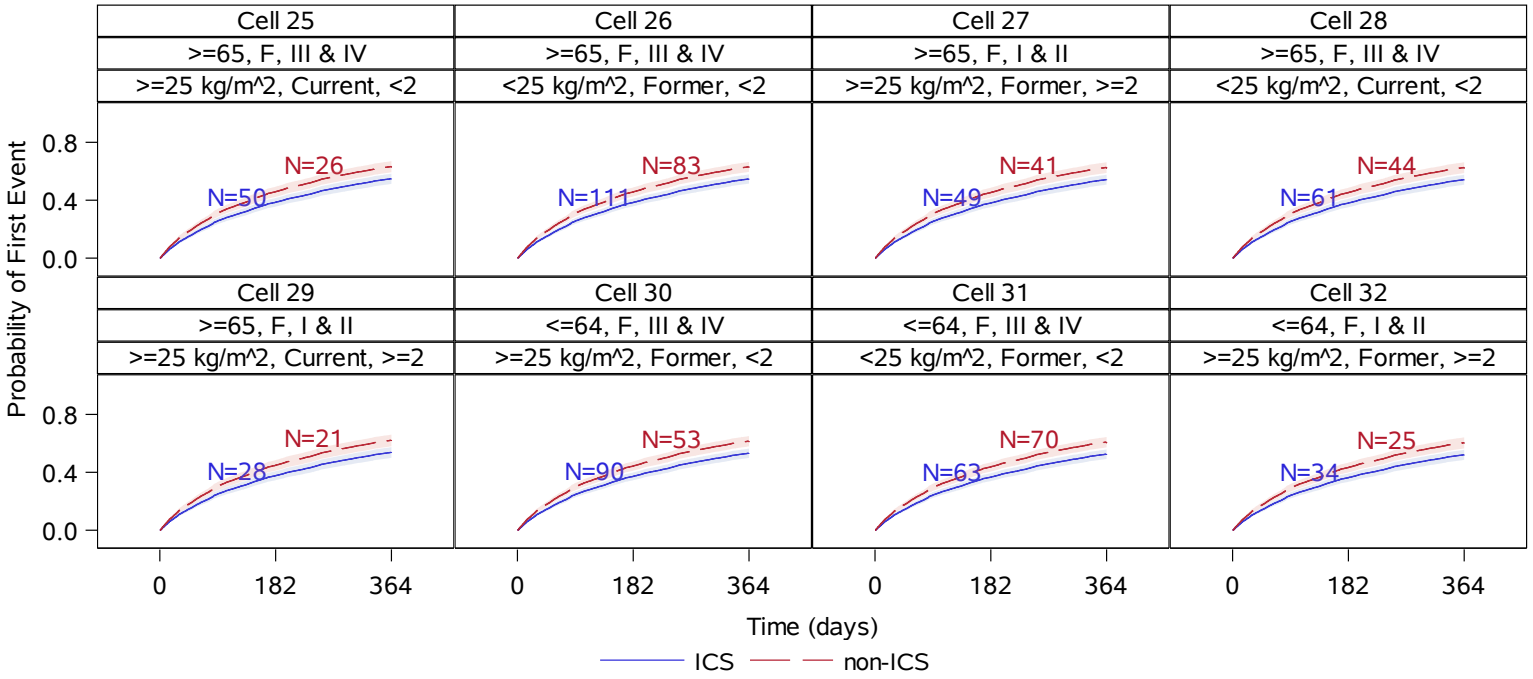

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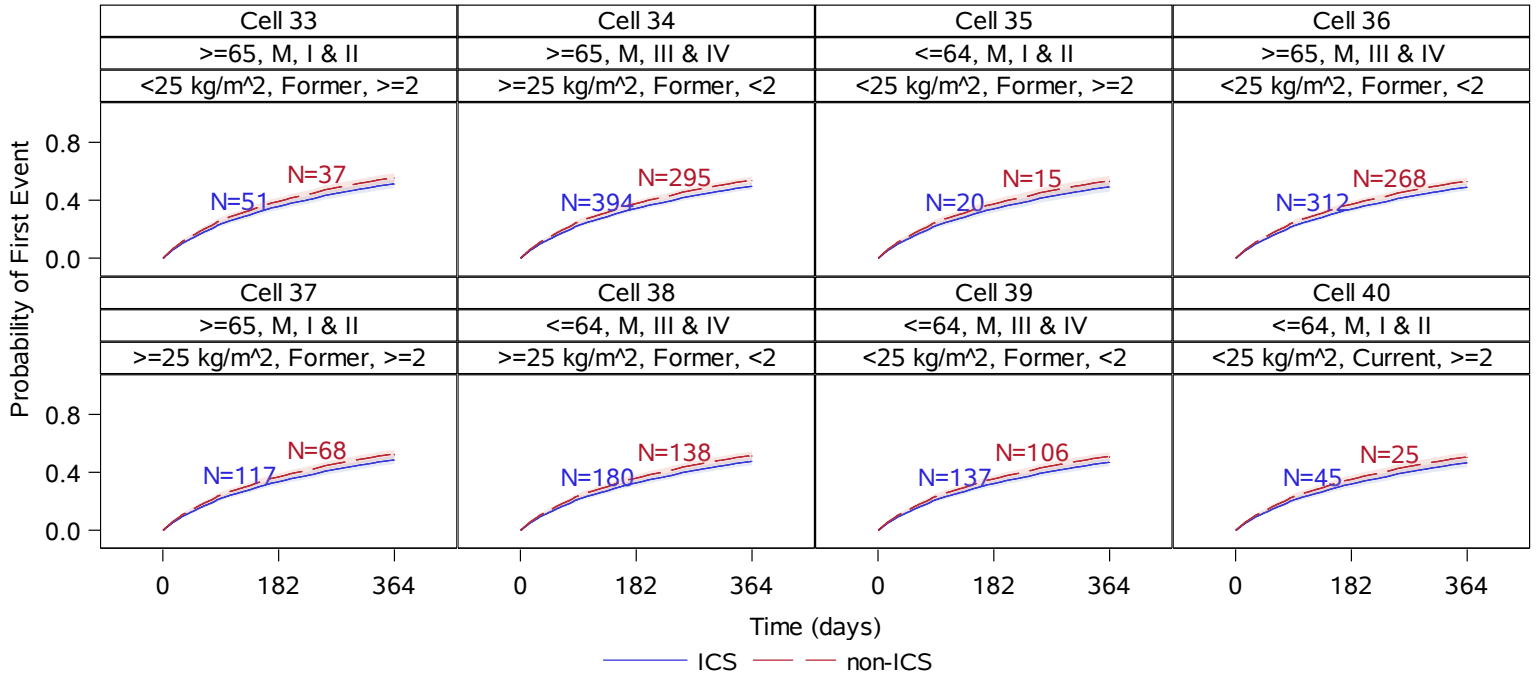

Cell Header Line 1: Age, Sex, GOLD
Cell Header Line 2: BMI, Smoking., Exac.
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(Based on Seven Covariates)

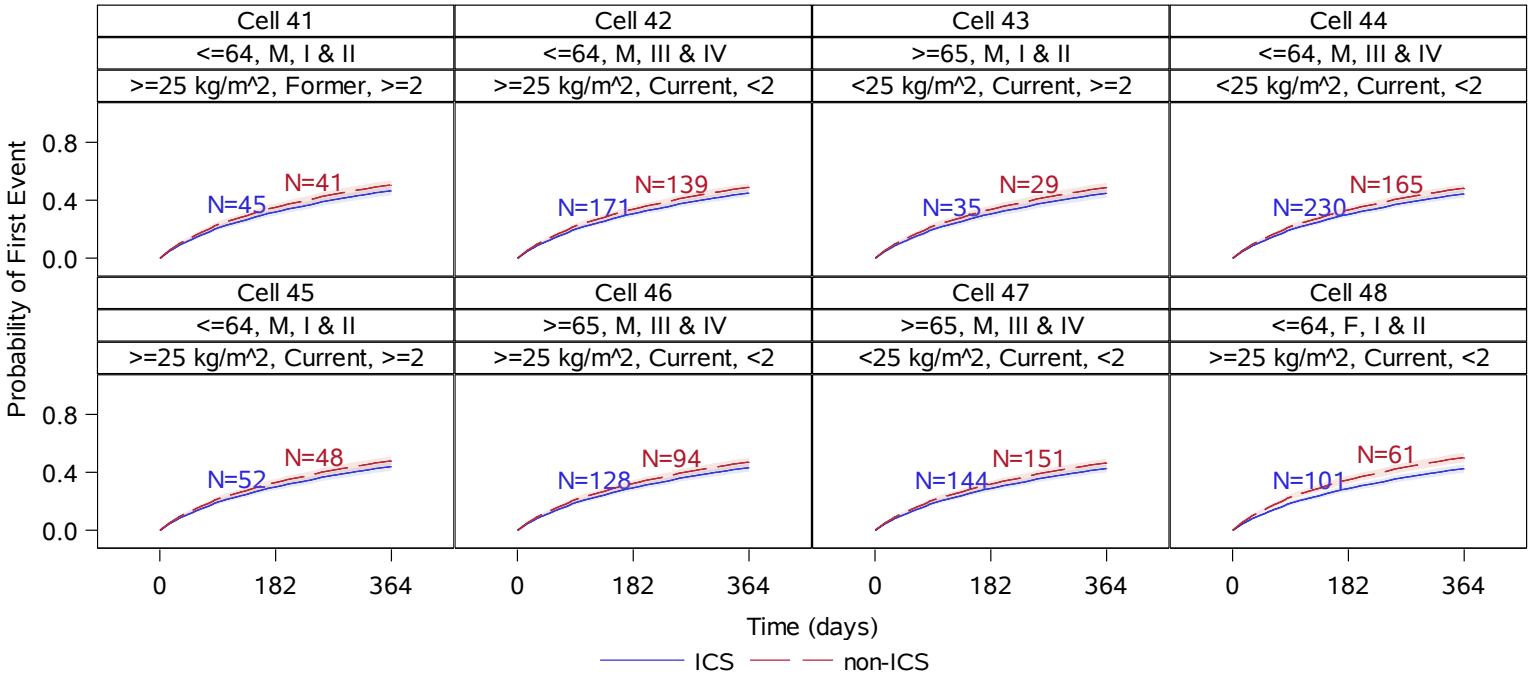

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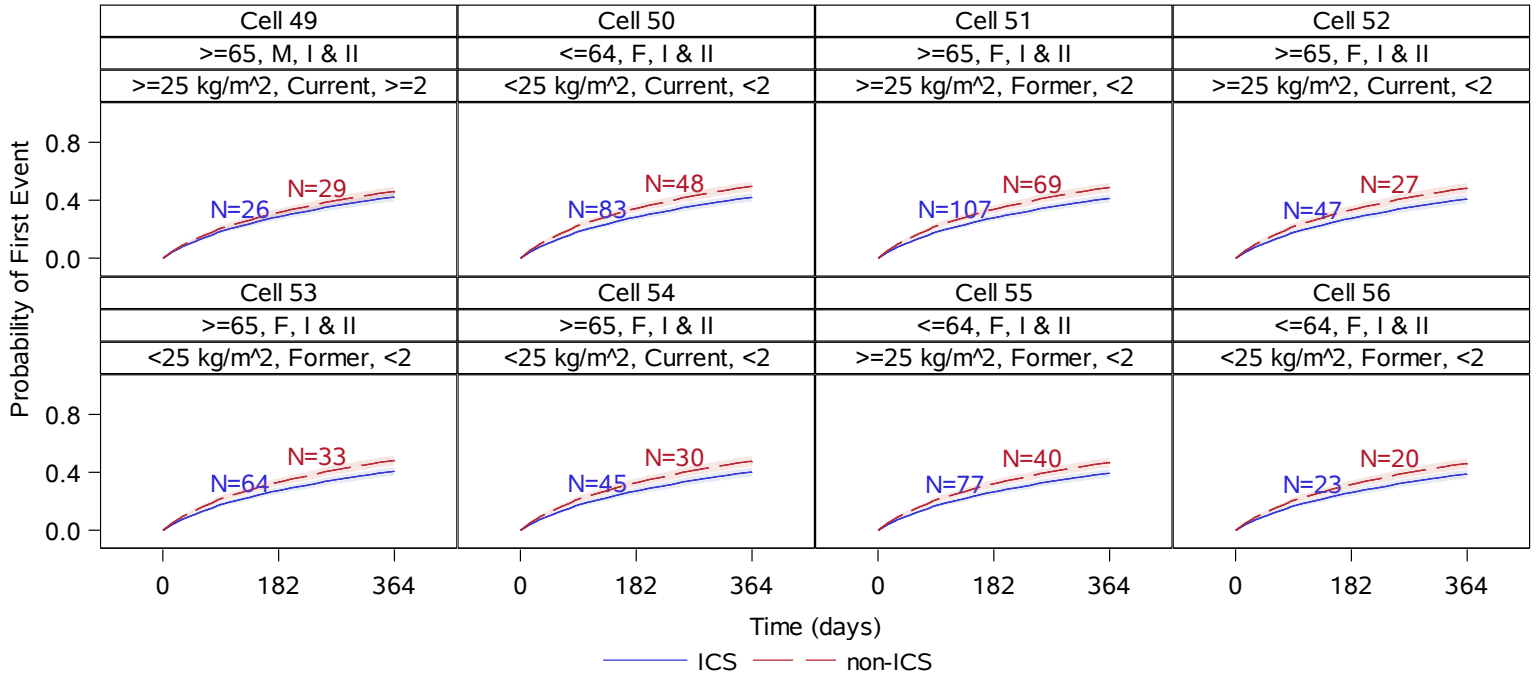
Figure 1.40
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Seven Covariates)



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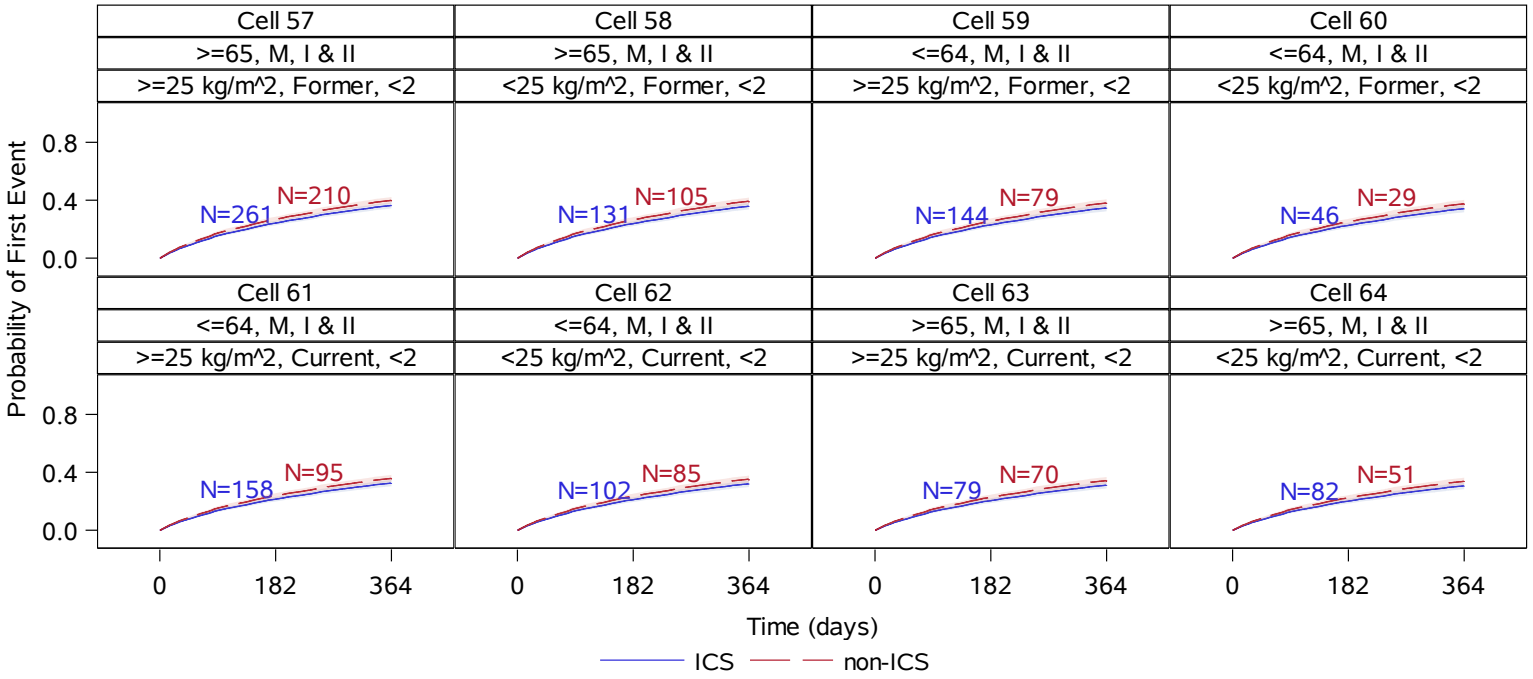
(Based on Seven Covariates)



Cell Header Line 1: Age, Sex, GOLD
Cell Header Line 2: BMI, Smoking., Exac.
Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

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Figure 1.50
Hazard Ratios from Selected Exacerbation Cox Model (Based on Seven Covariates)

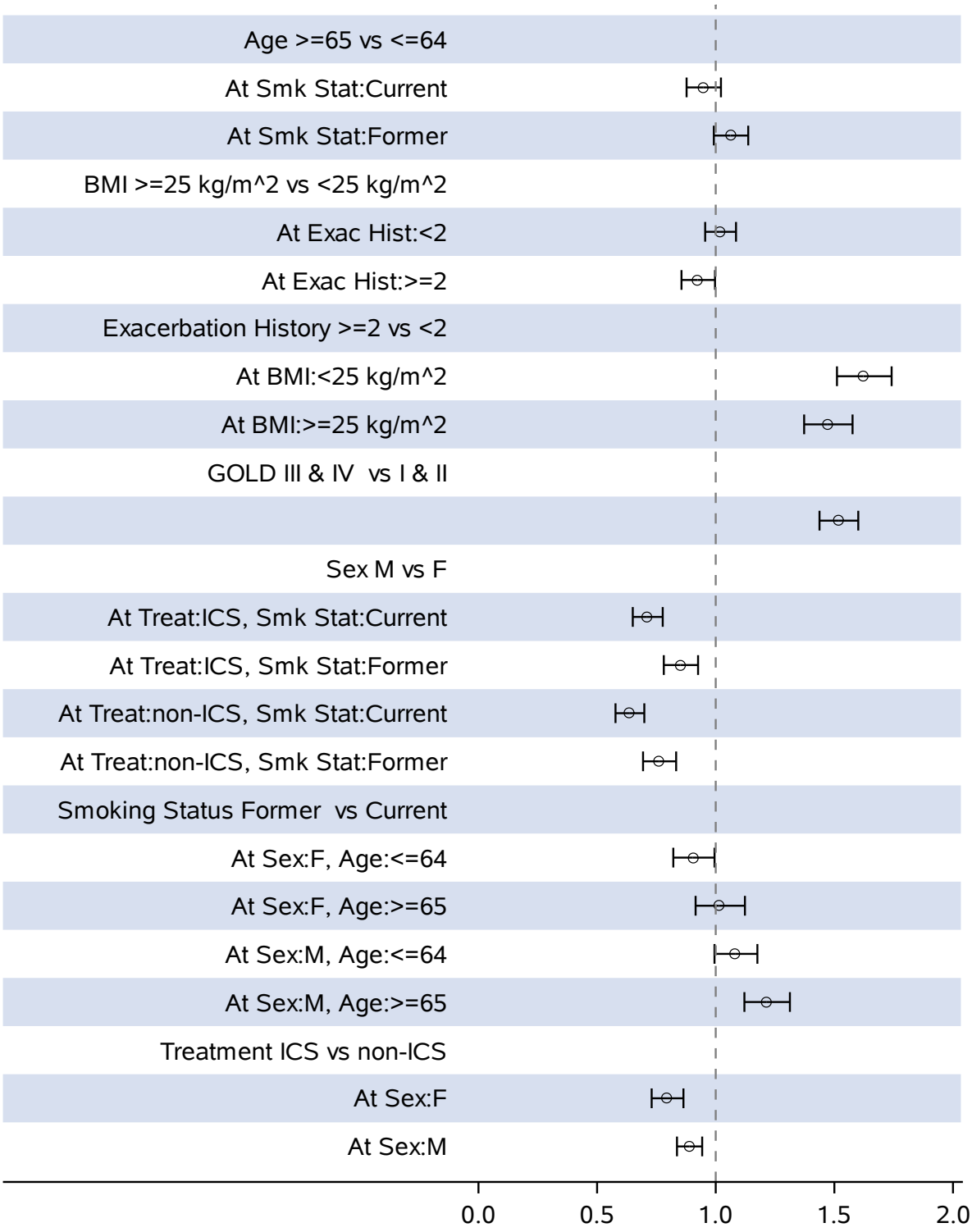
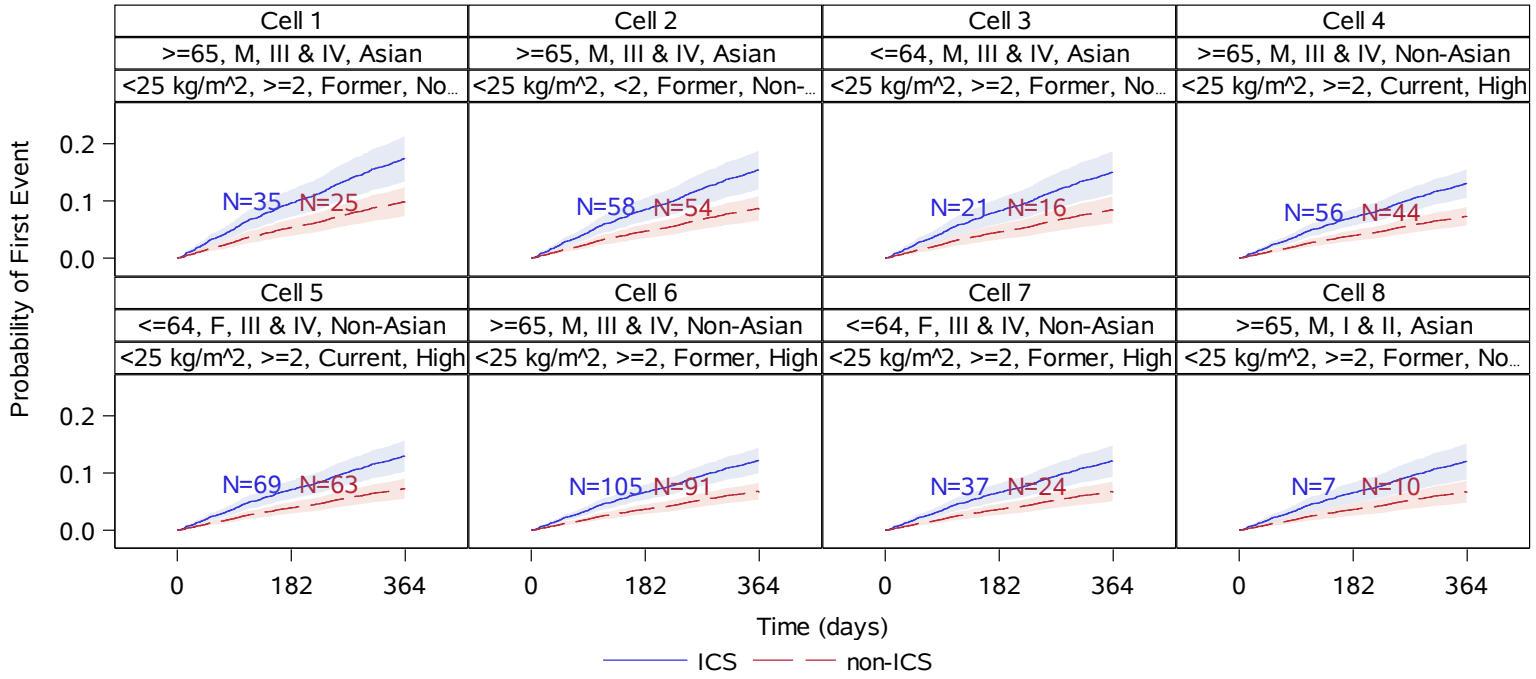


Figure 2.4
Probability of First Pneumonia During Year on Study Treatment Survival Curves
(Based on Nine Covariates)



Cell Header Line 1: Age, Sex, GOLD, Race
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Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

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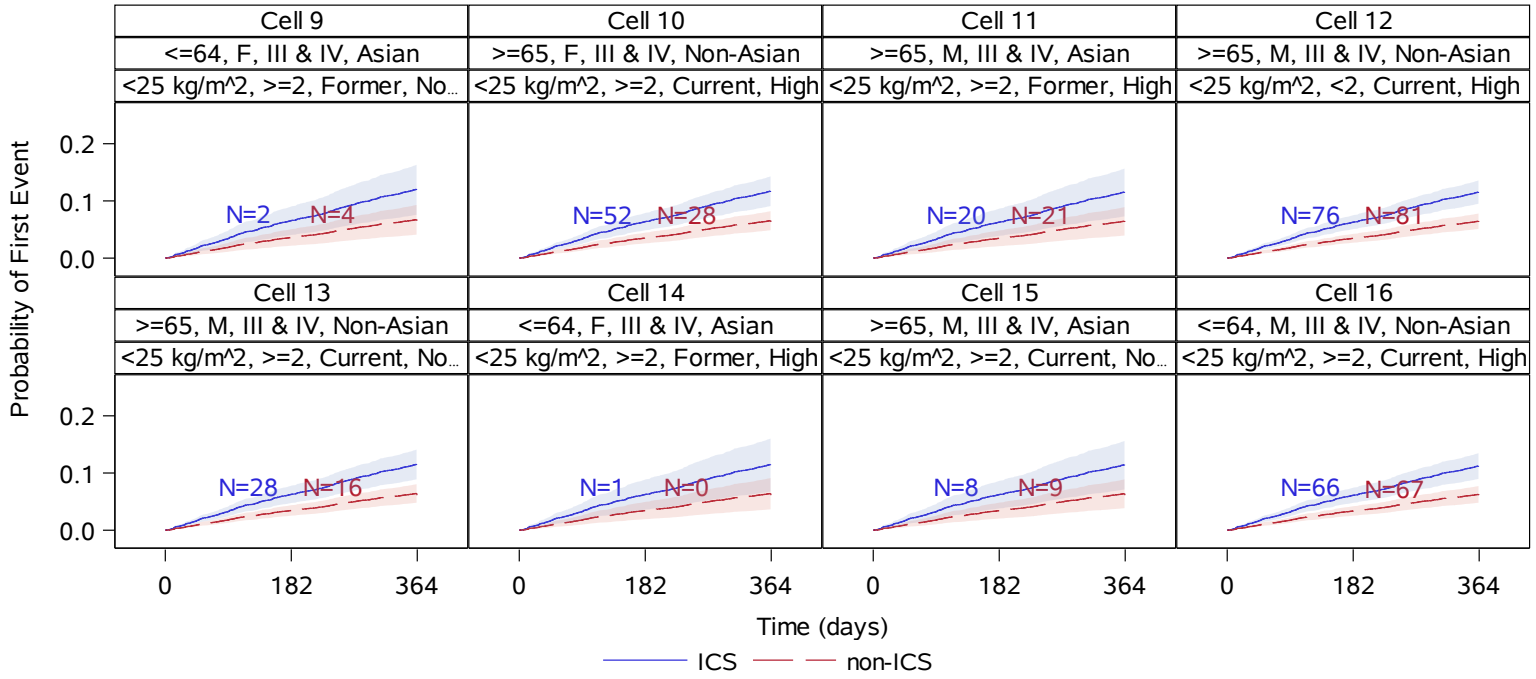
Probability of First Pneumonia During Year on Study Treatment Survival Curves
(Based on Nine Covariates)



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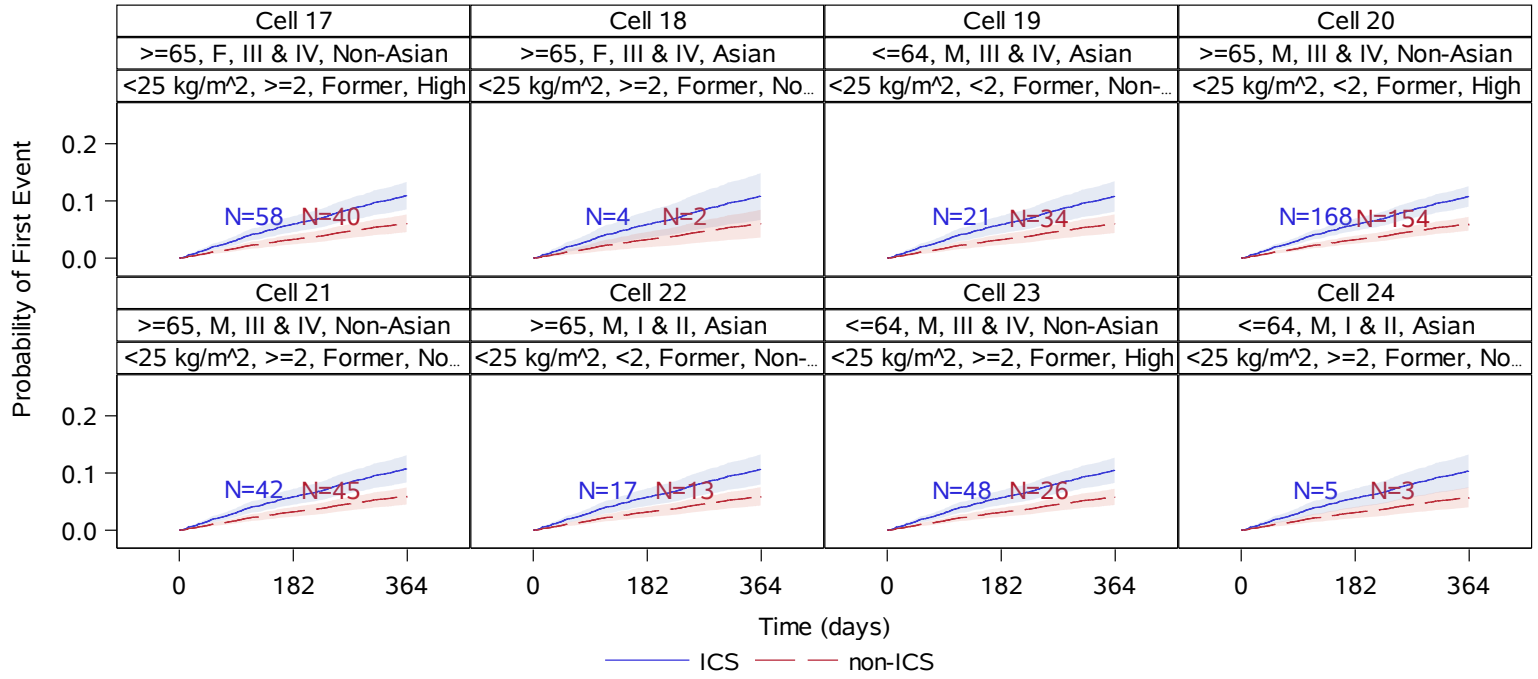

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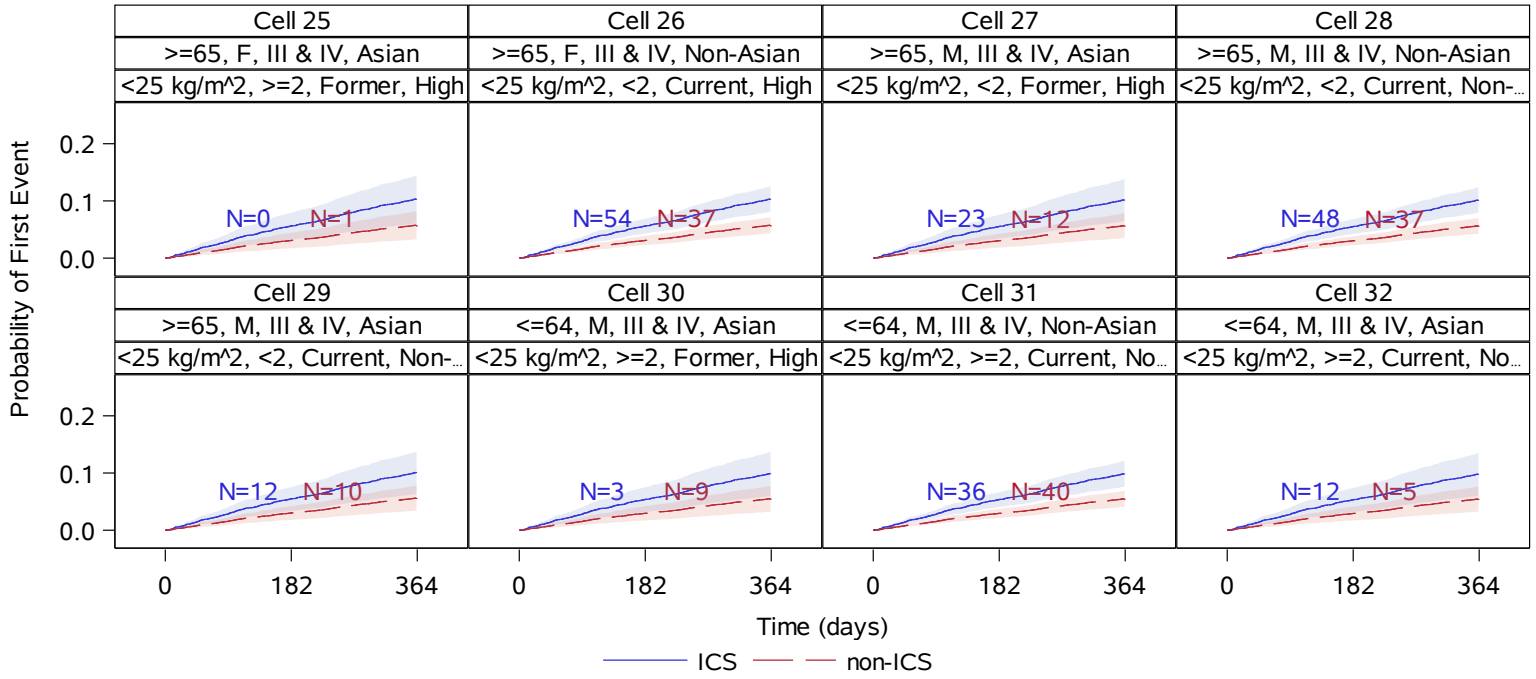

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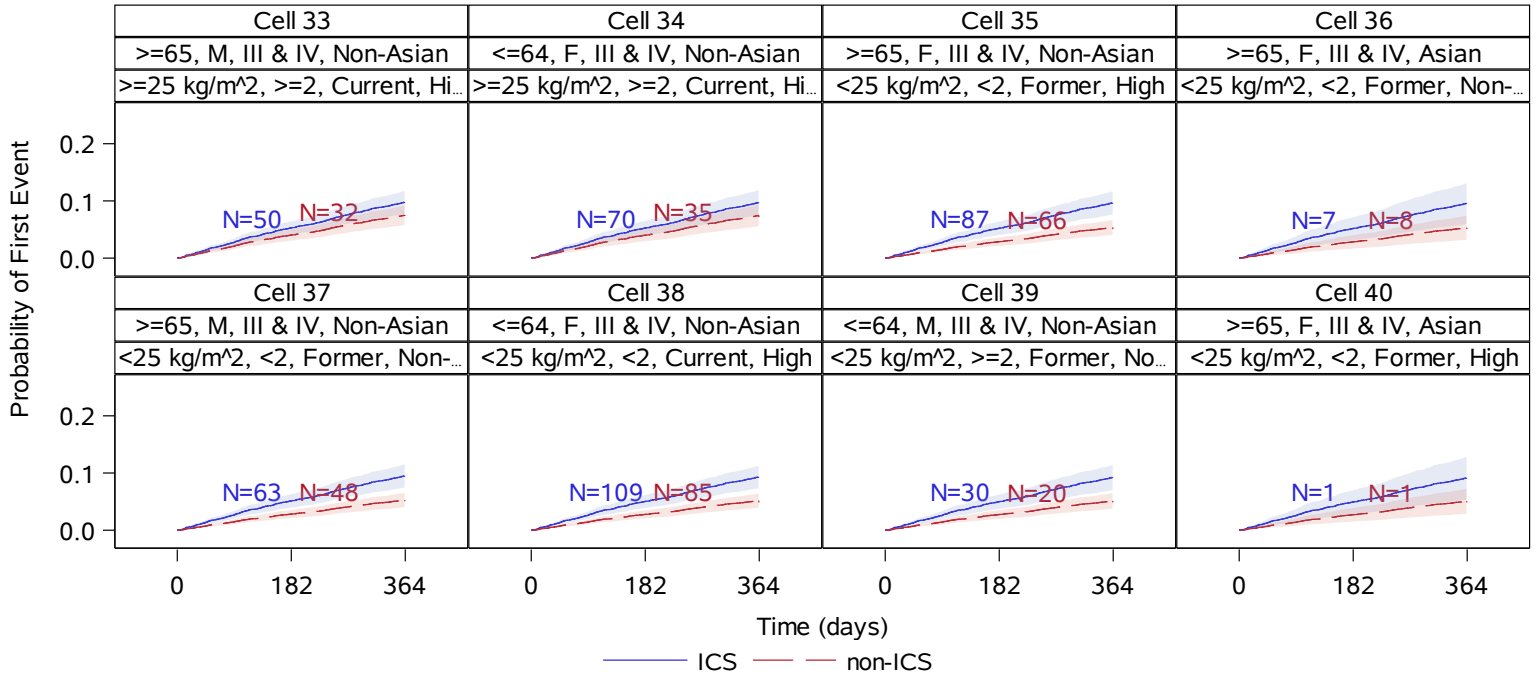

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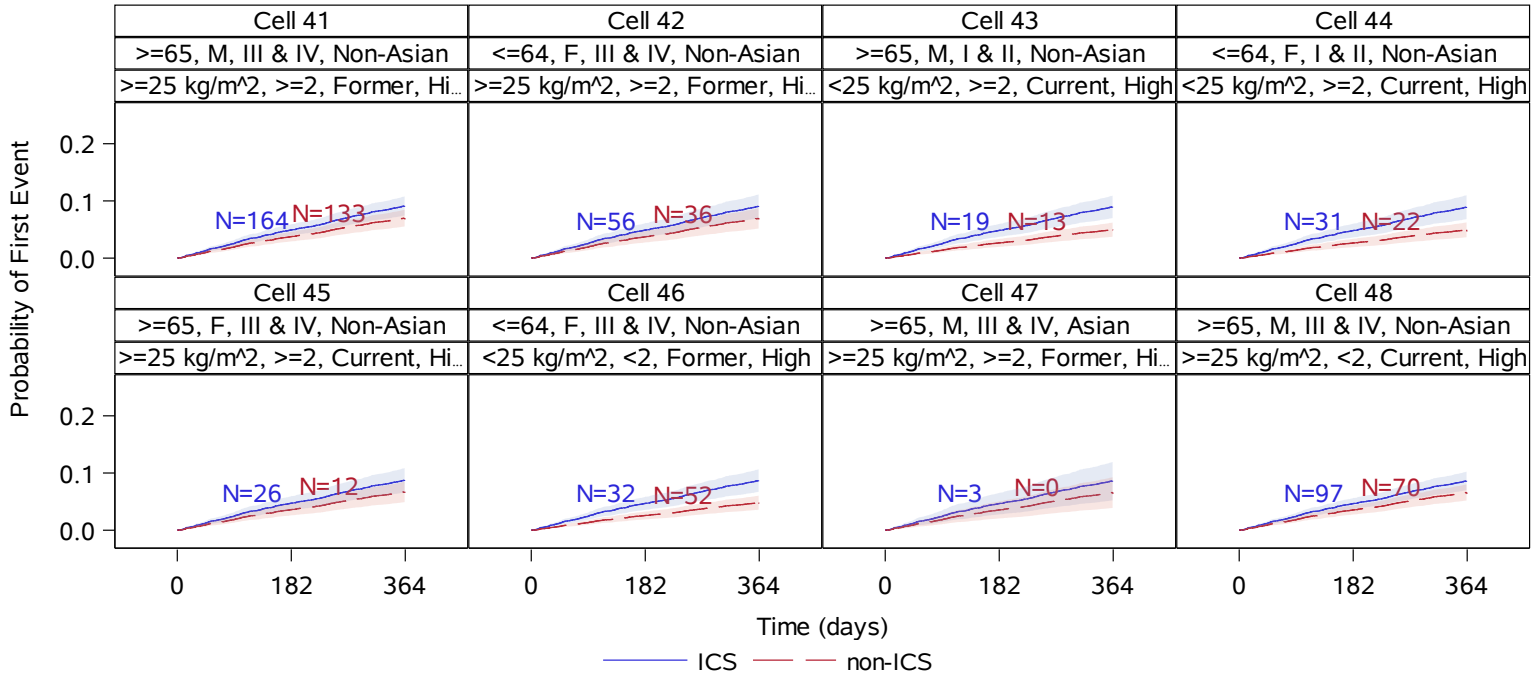

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PPD

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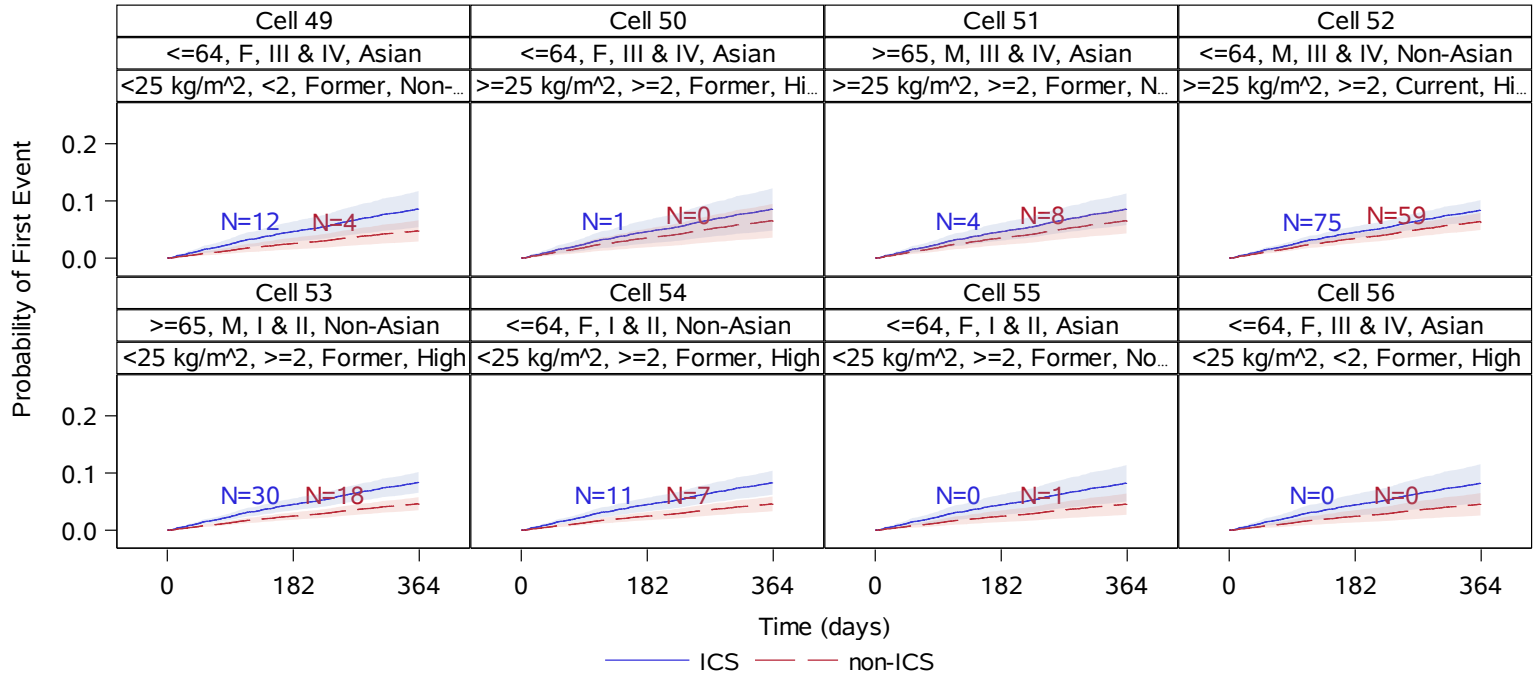

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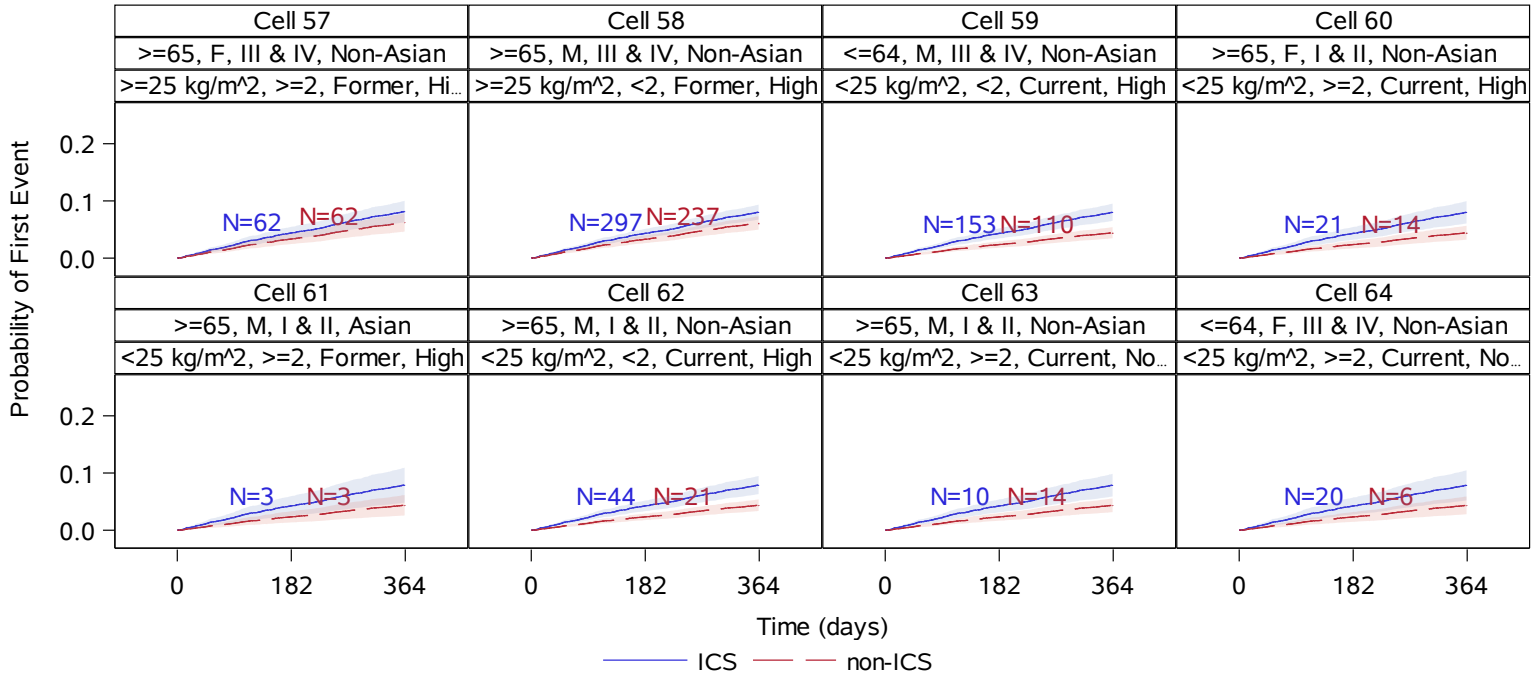

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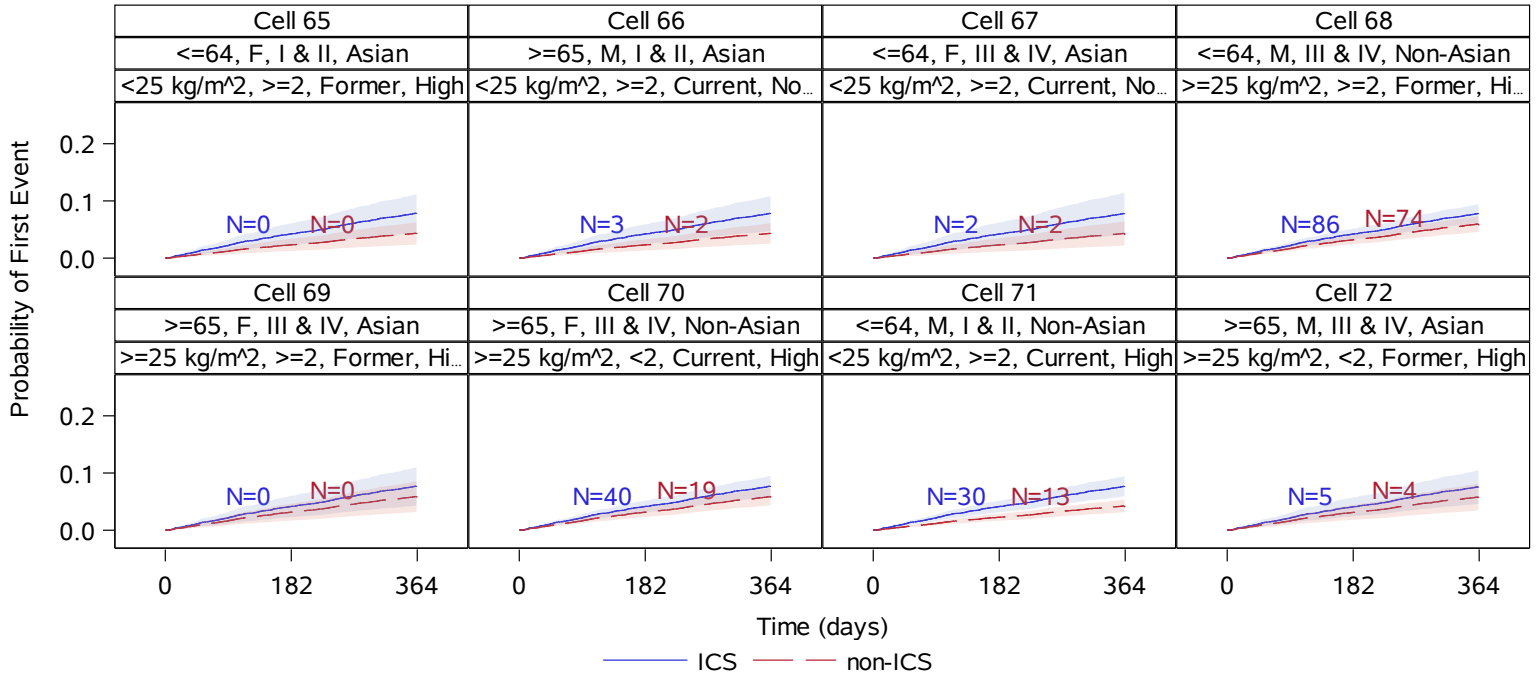

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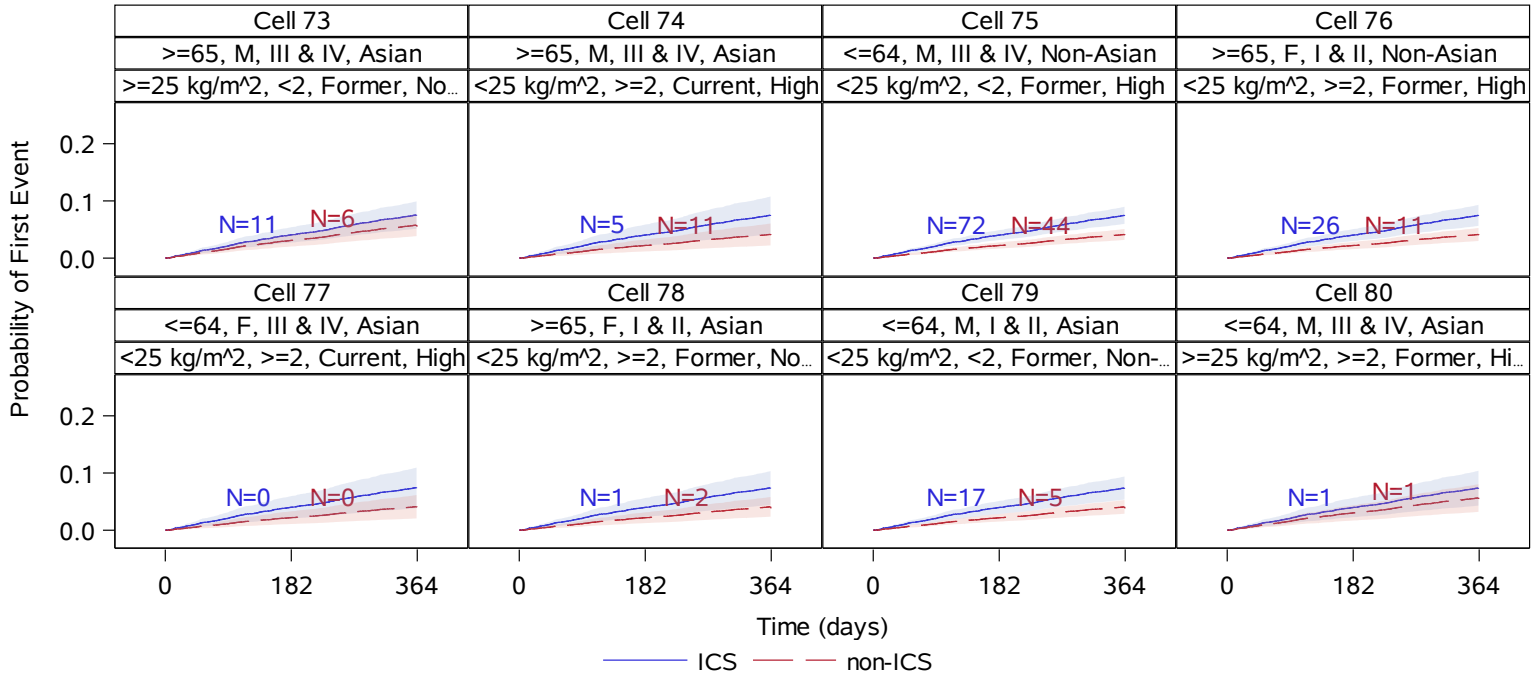

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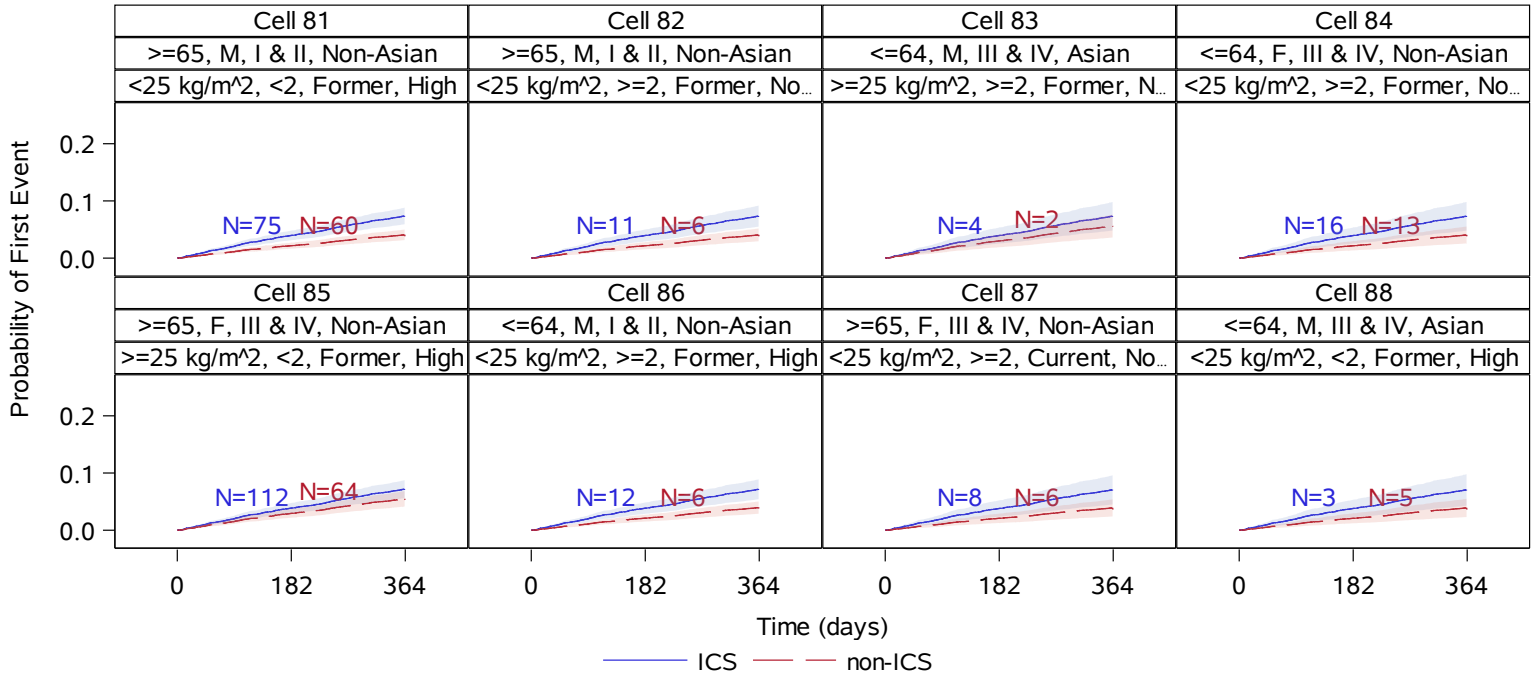

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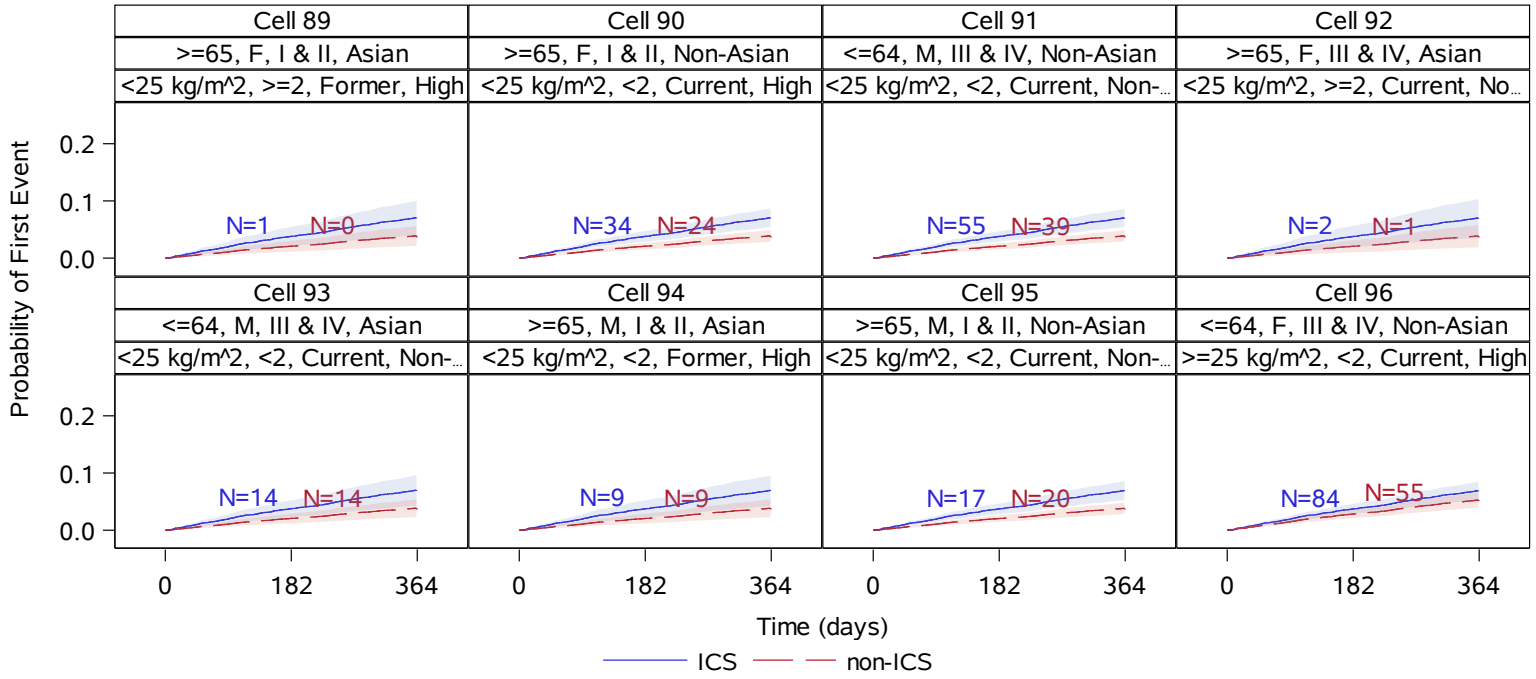

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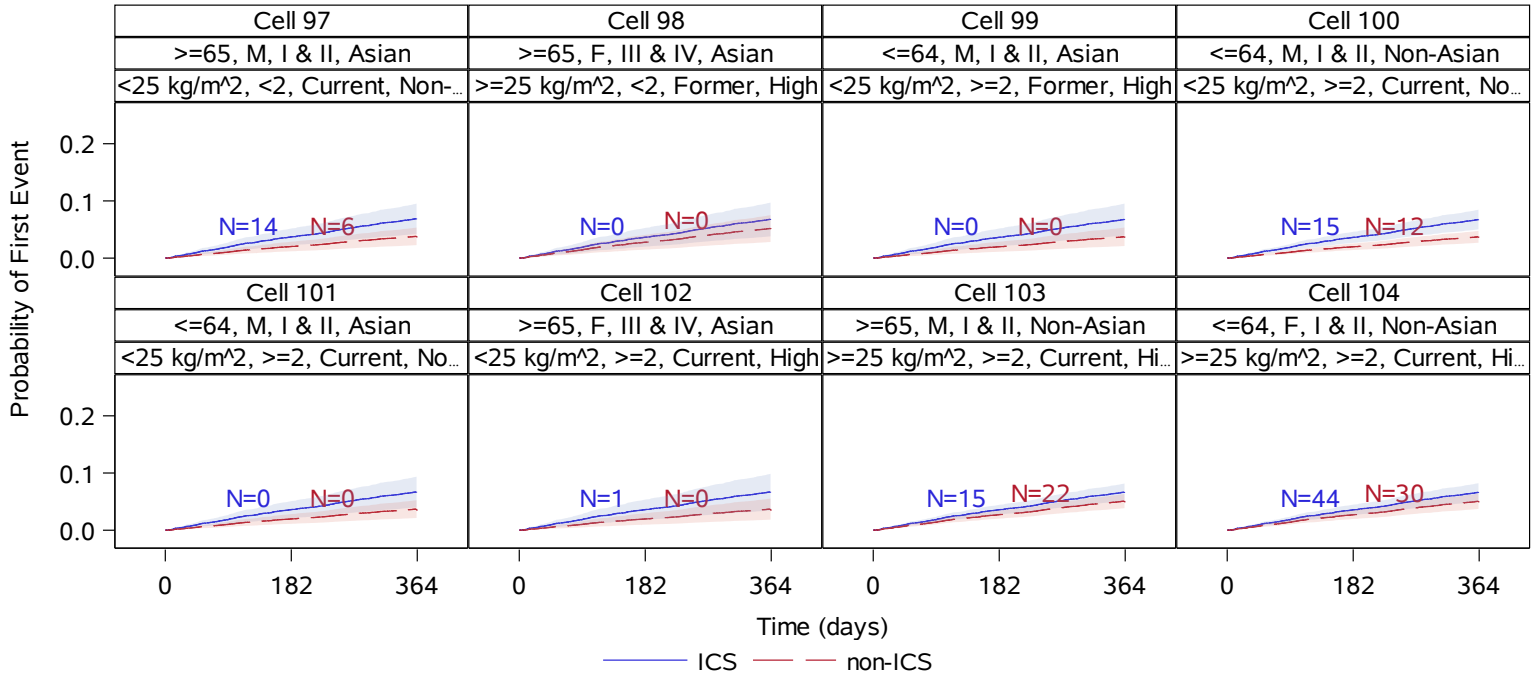

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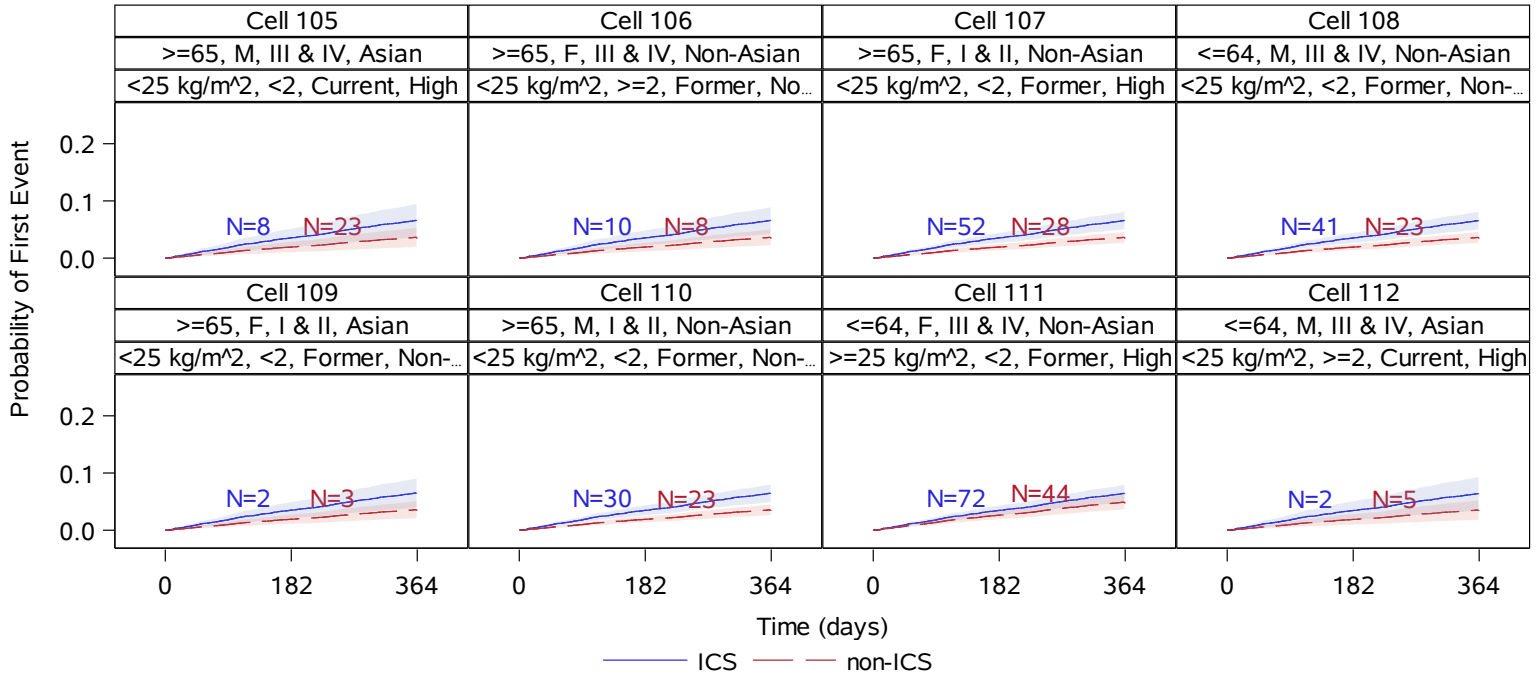

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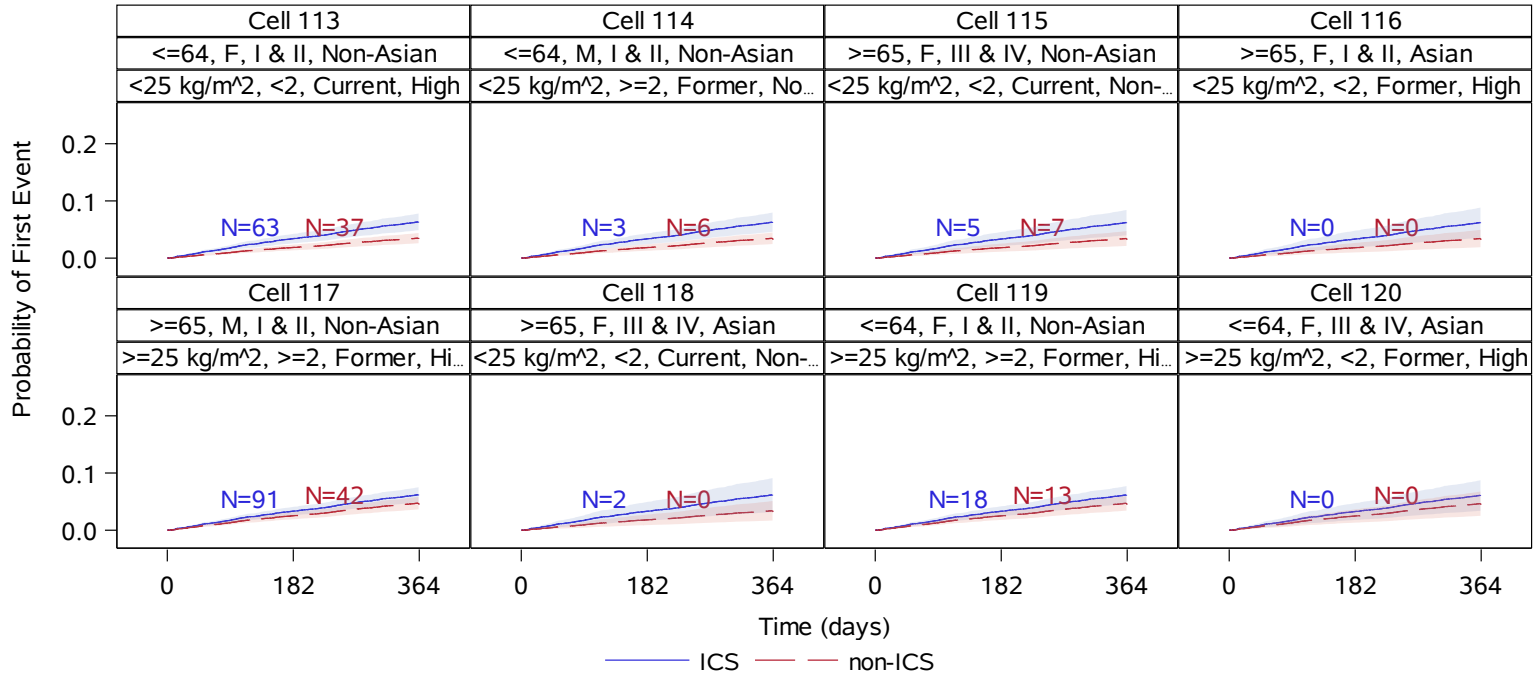

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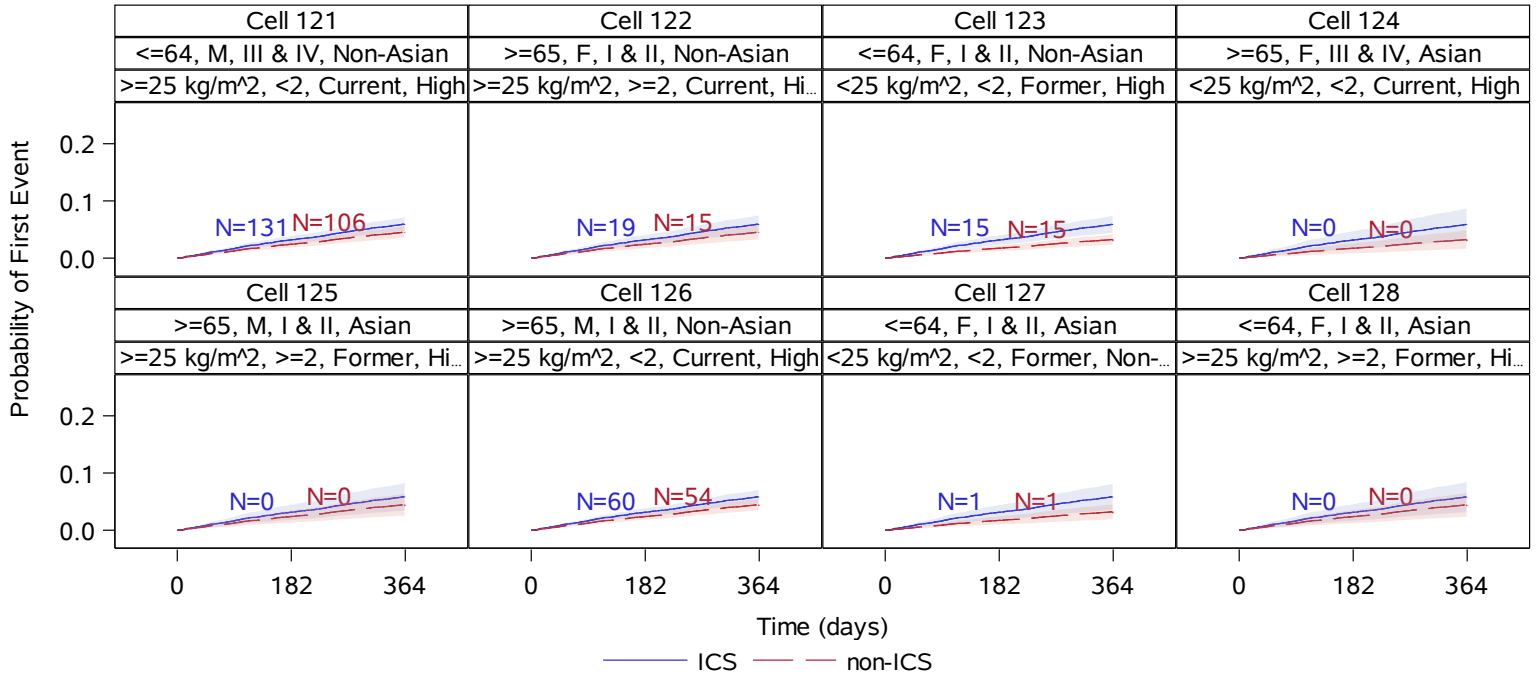

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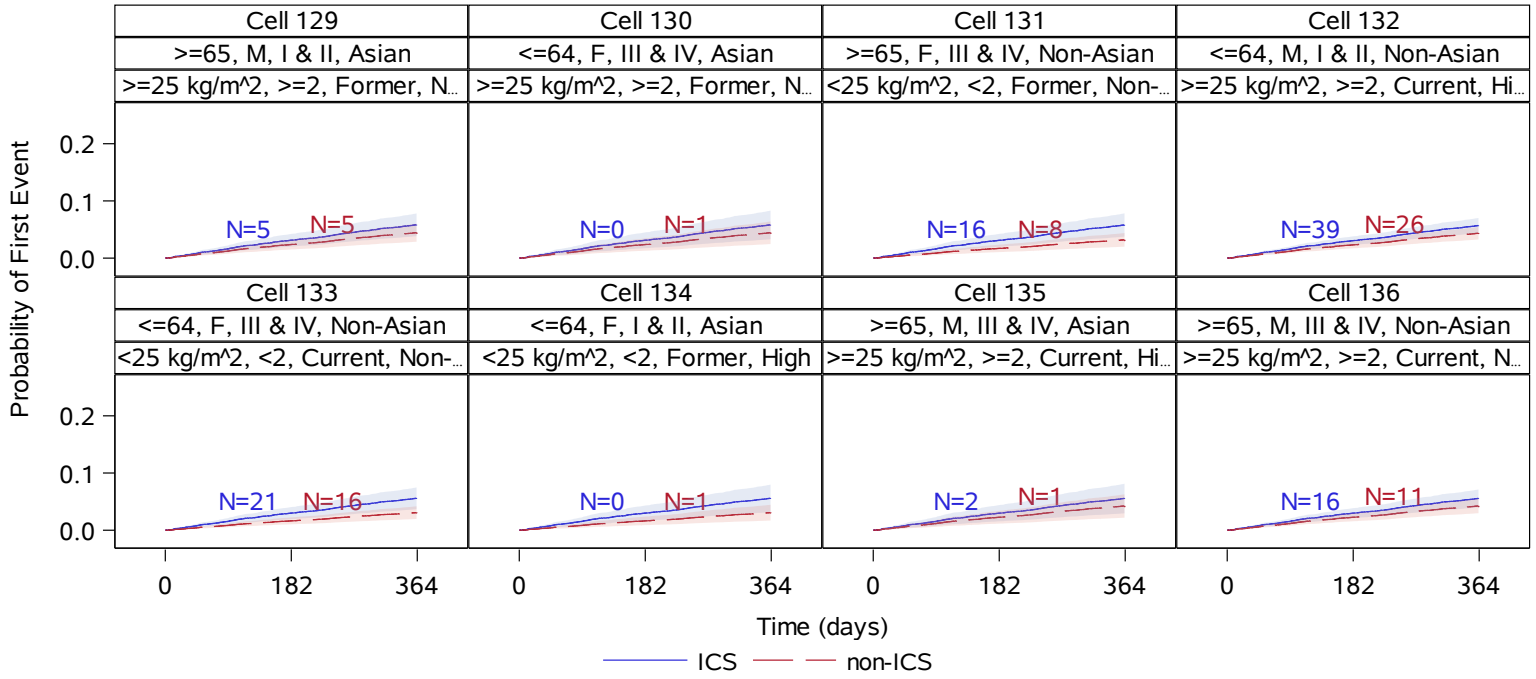

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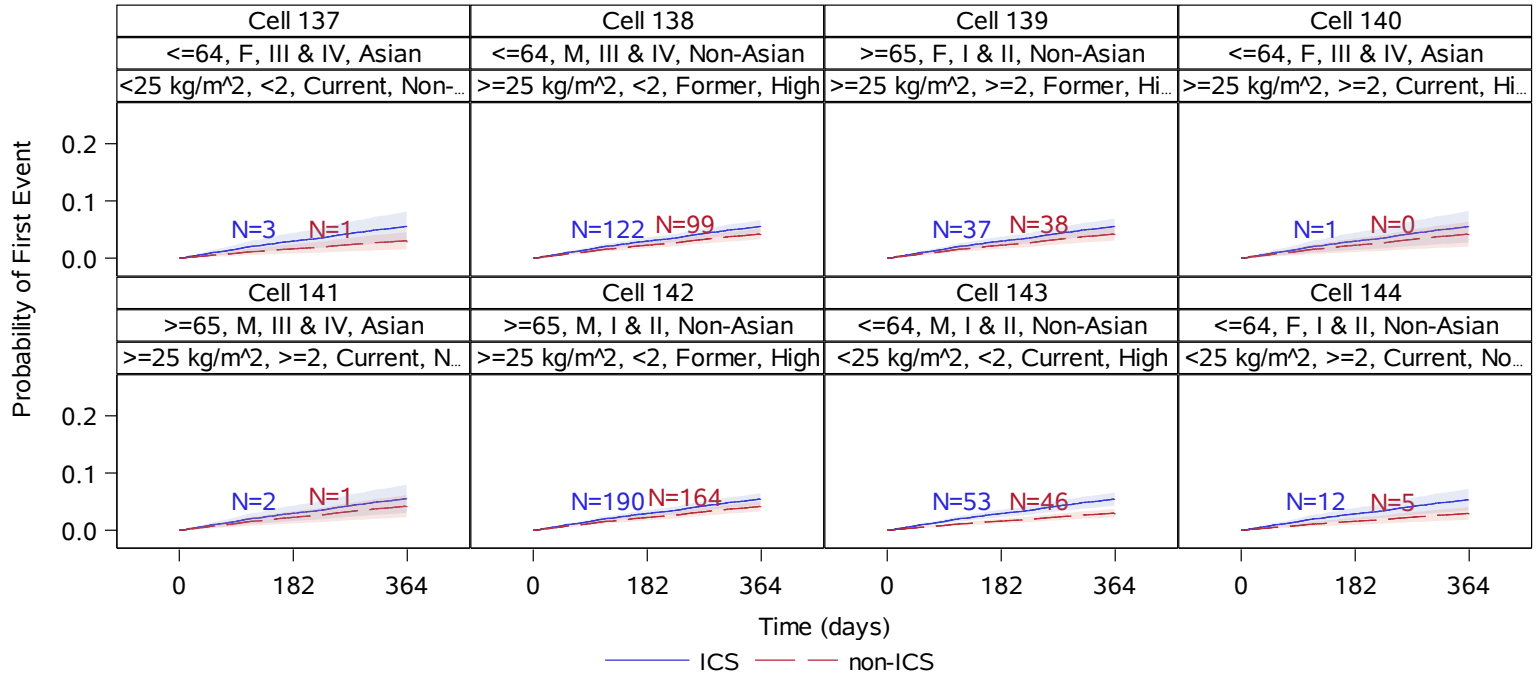

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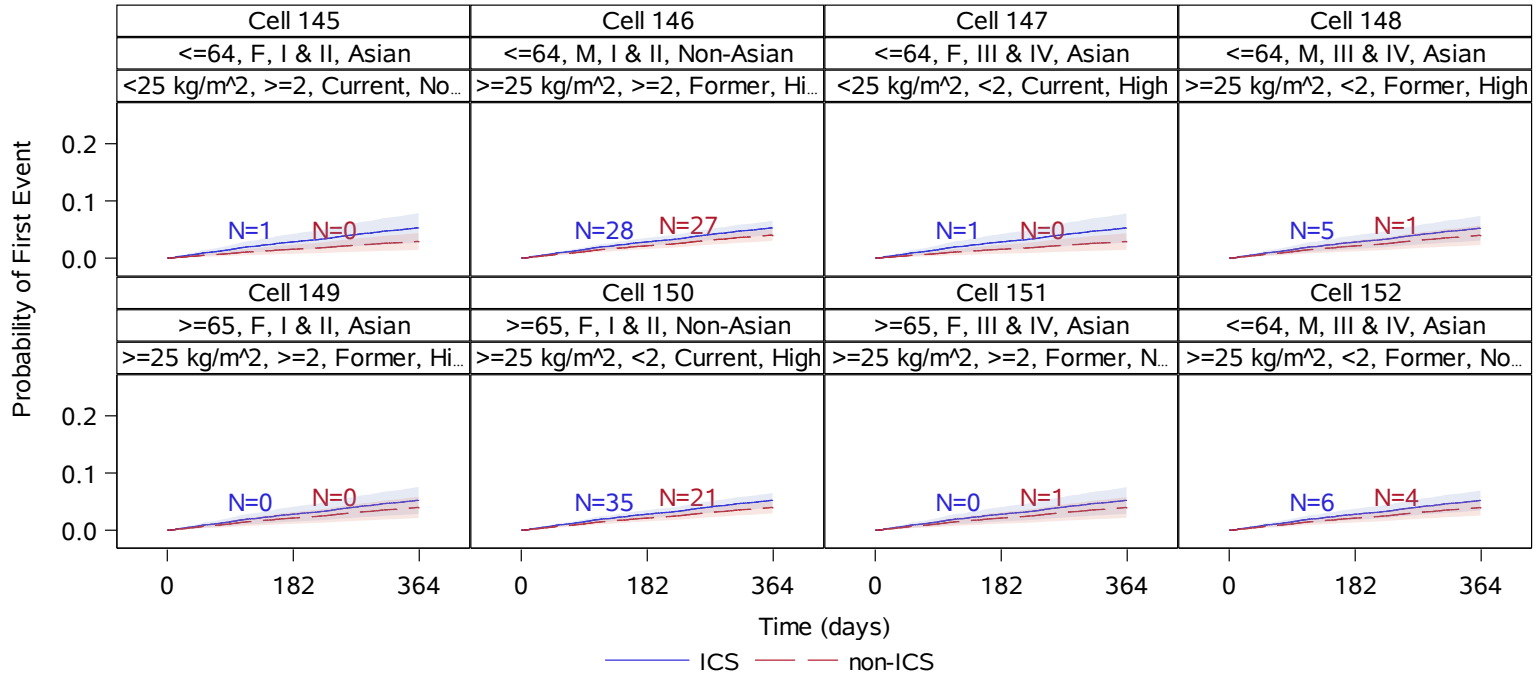

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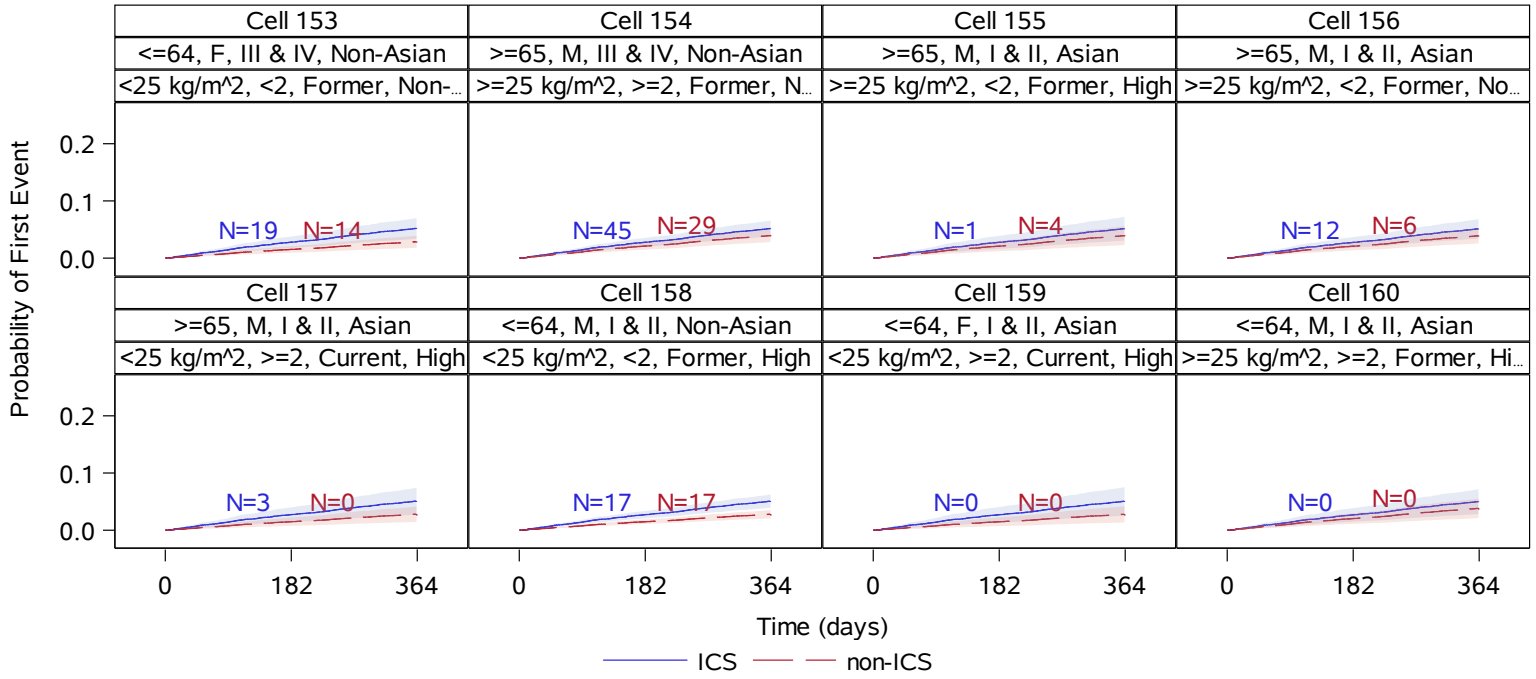

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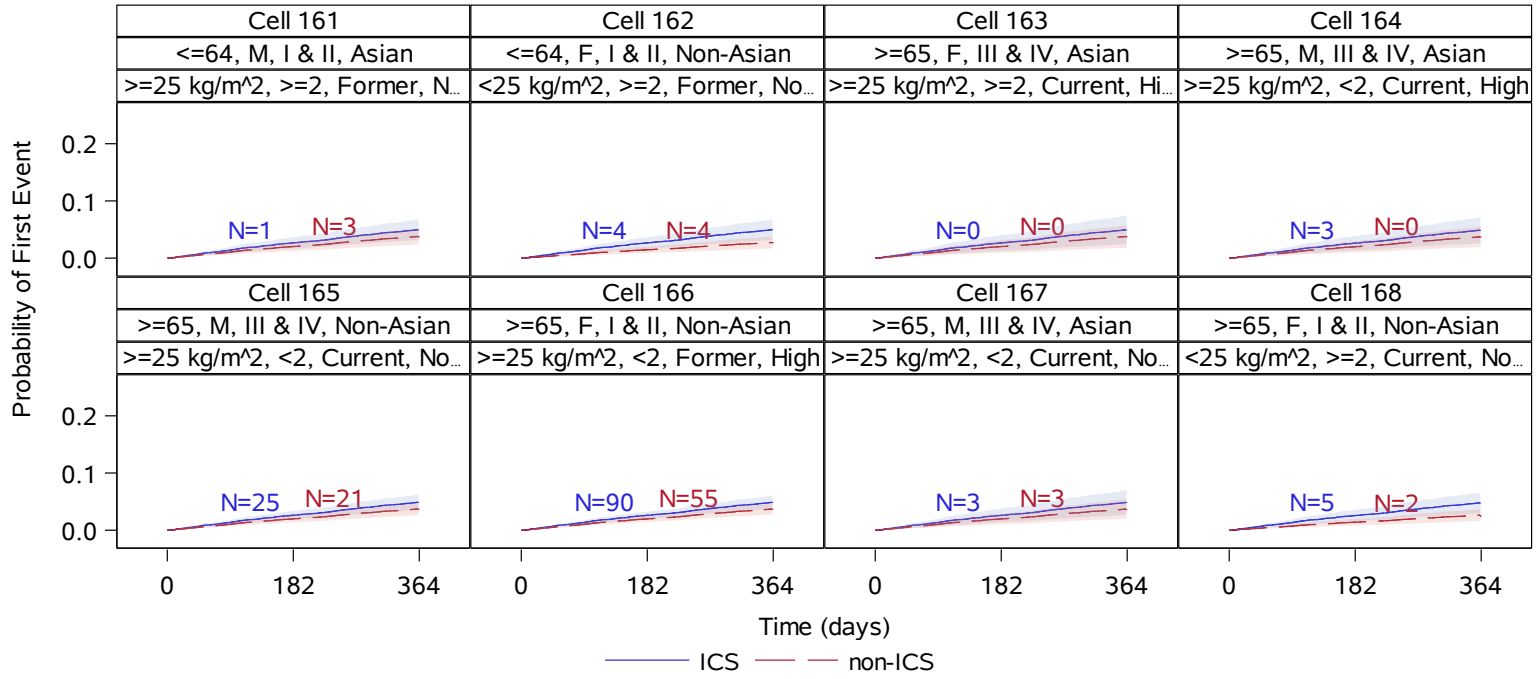

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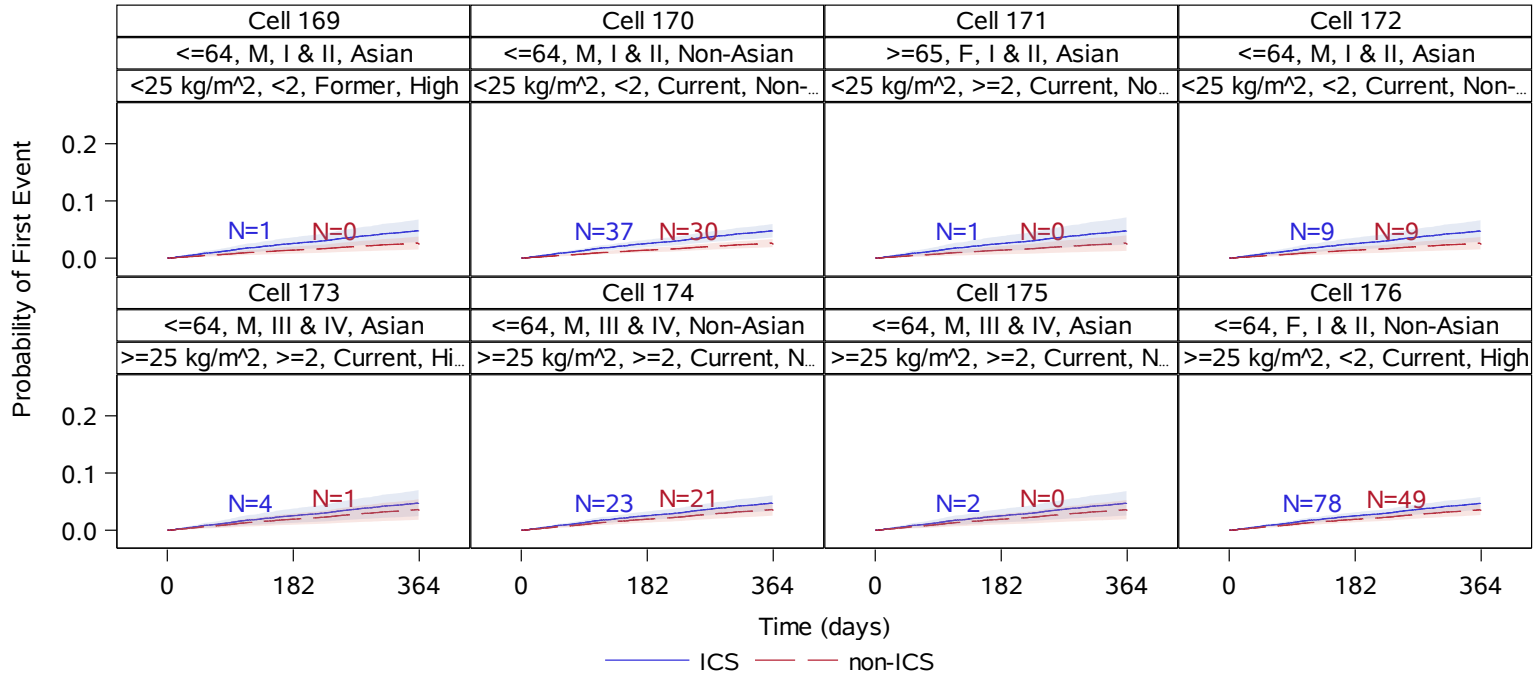

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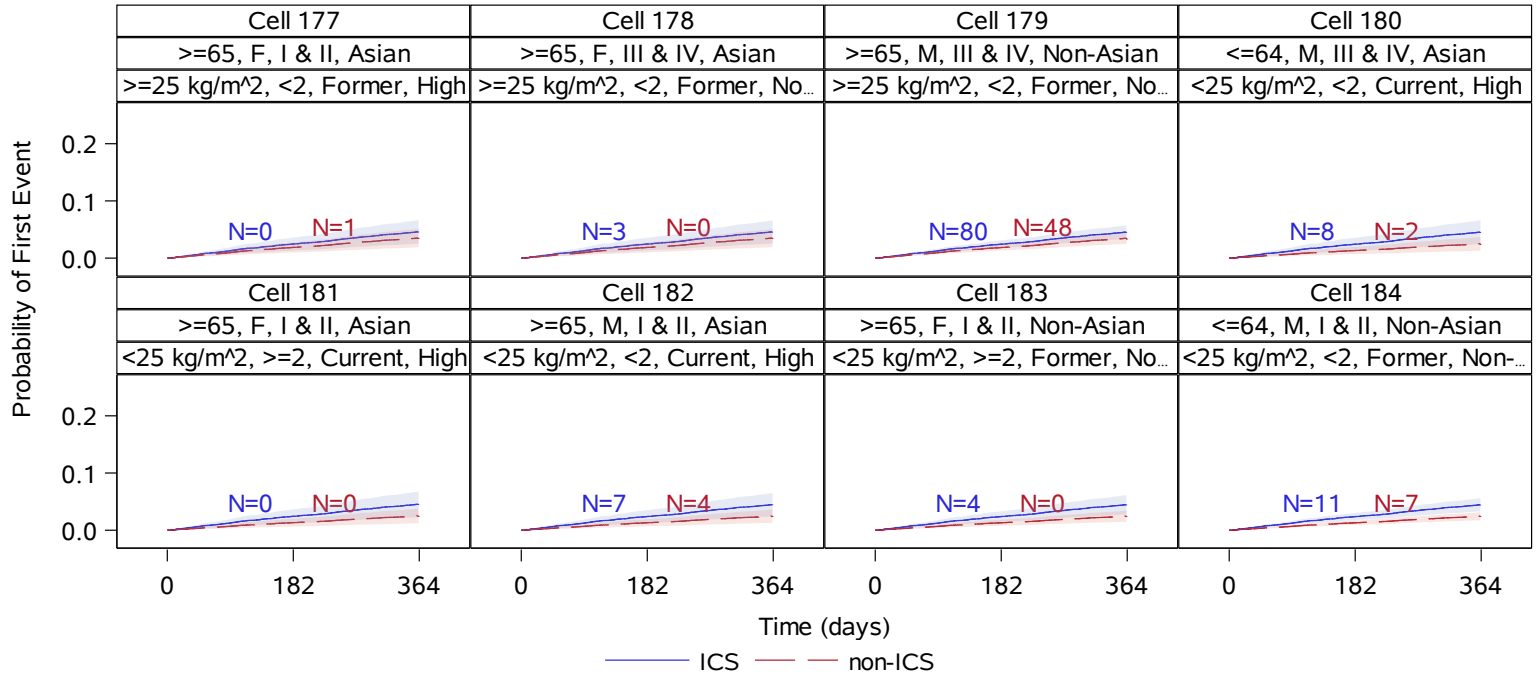

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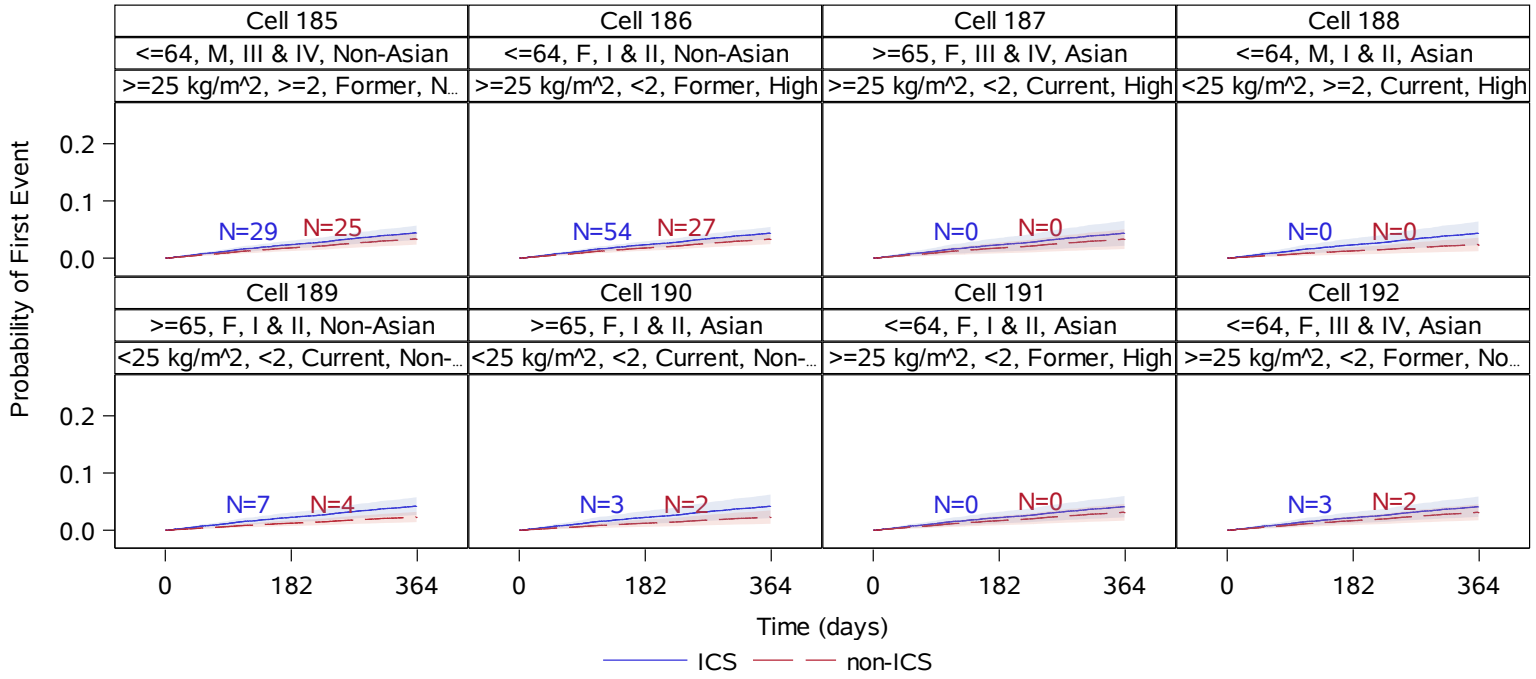

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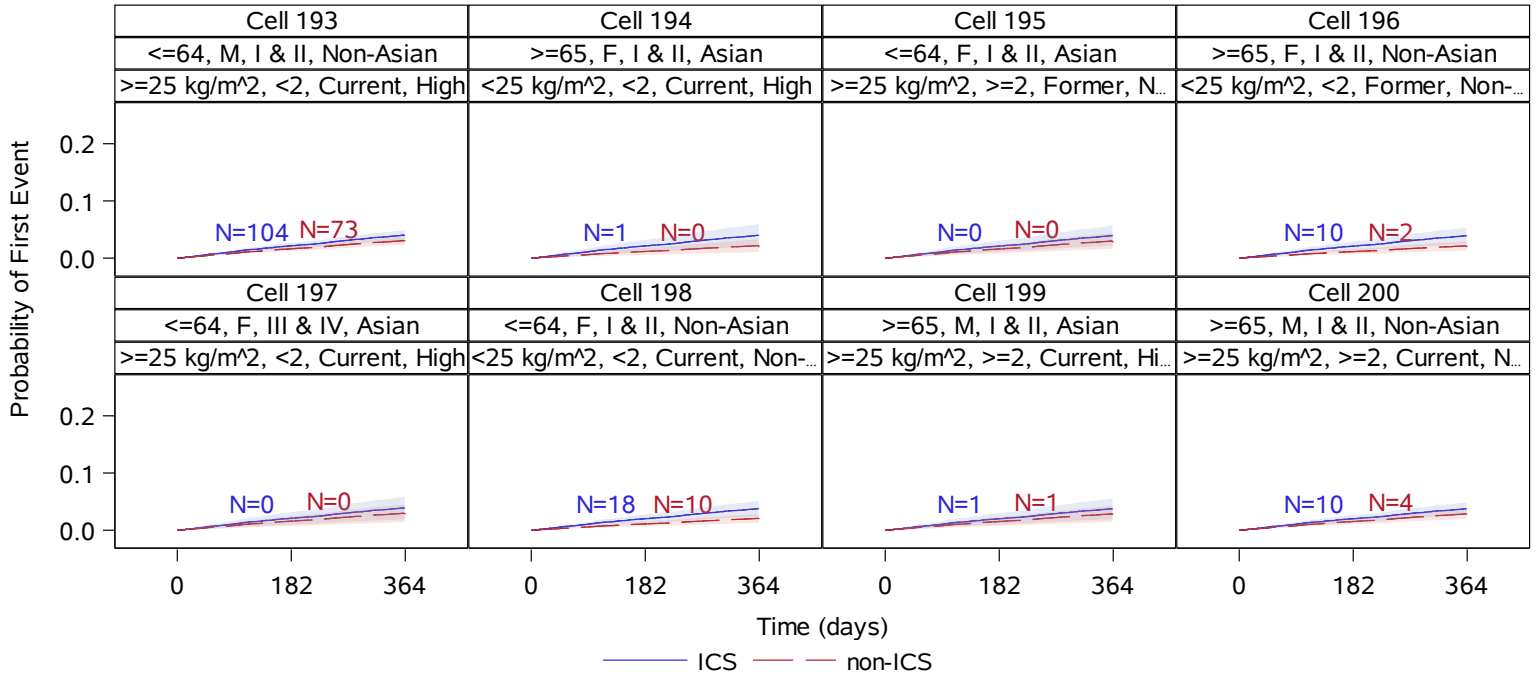

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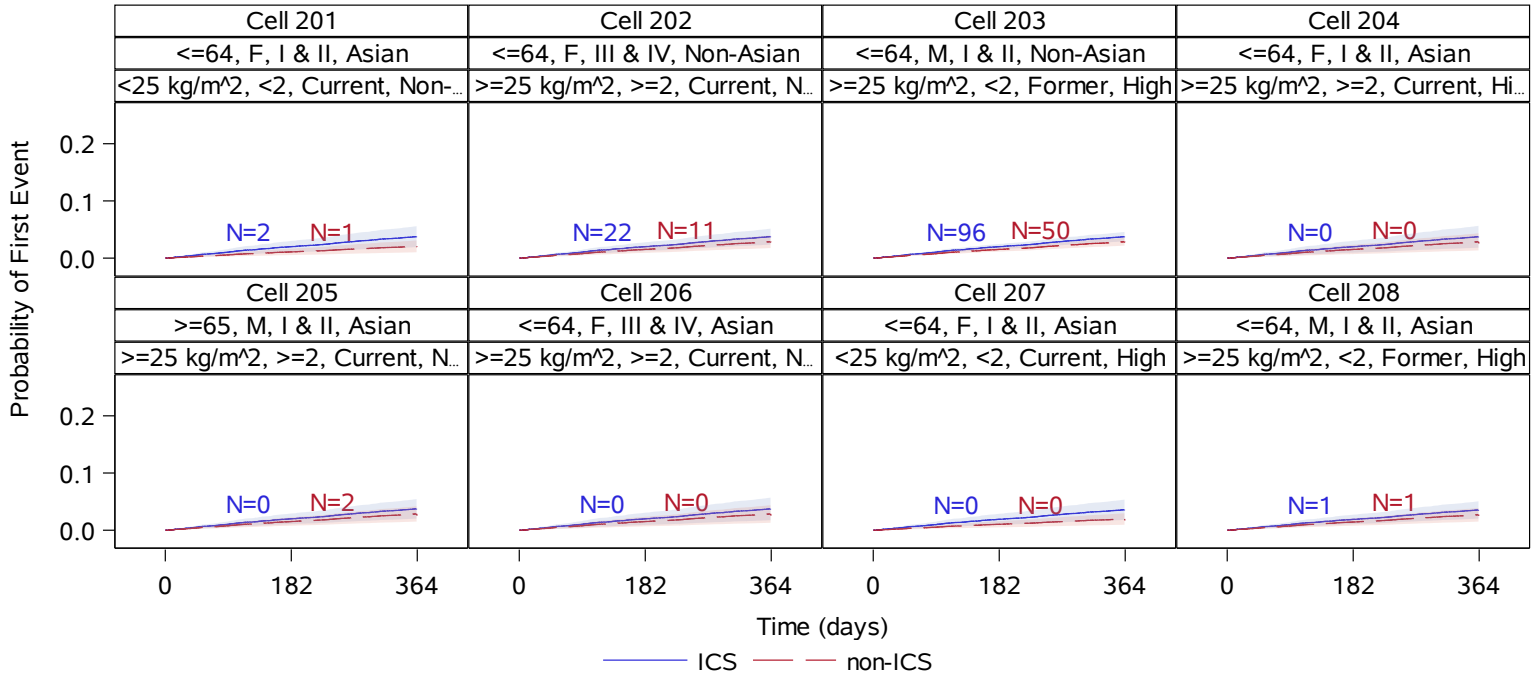

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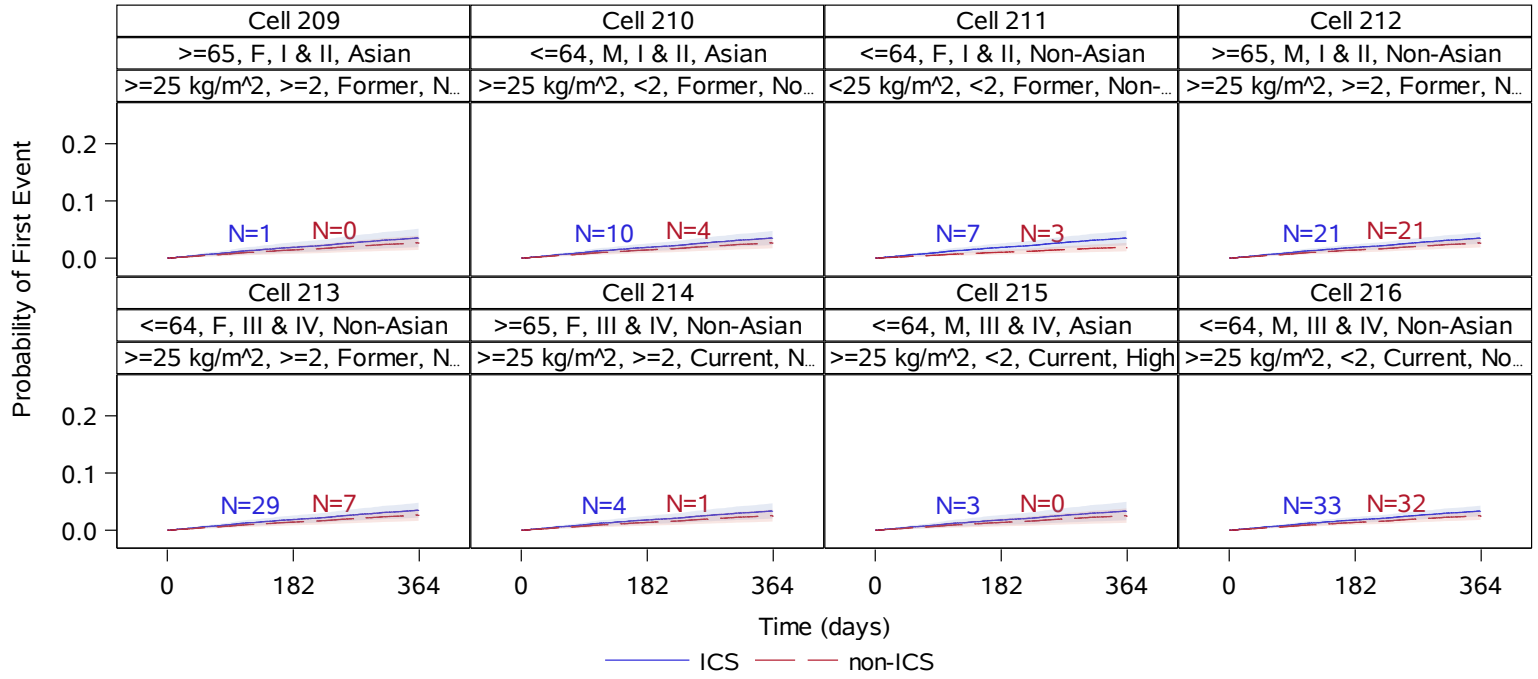

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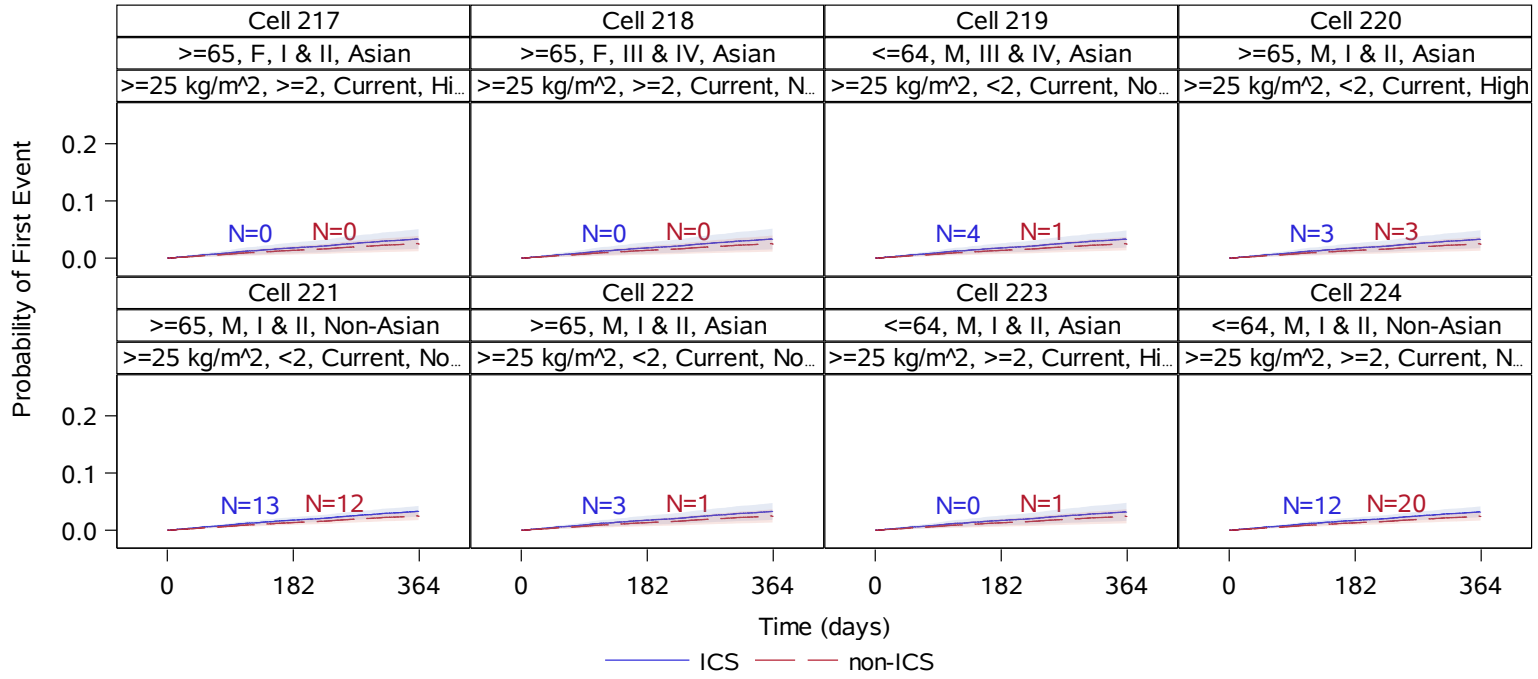

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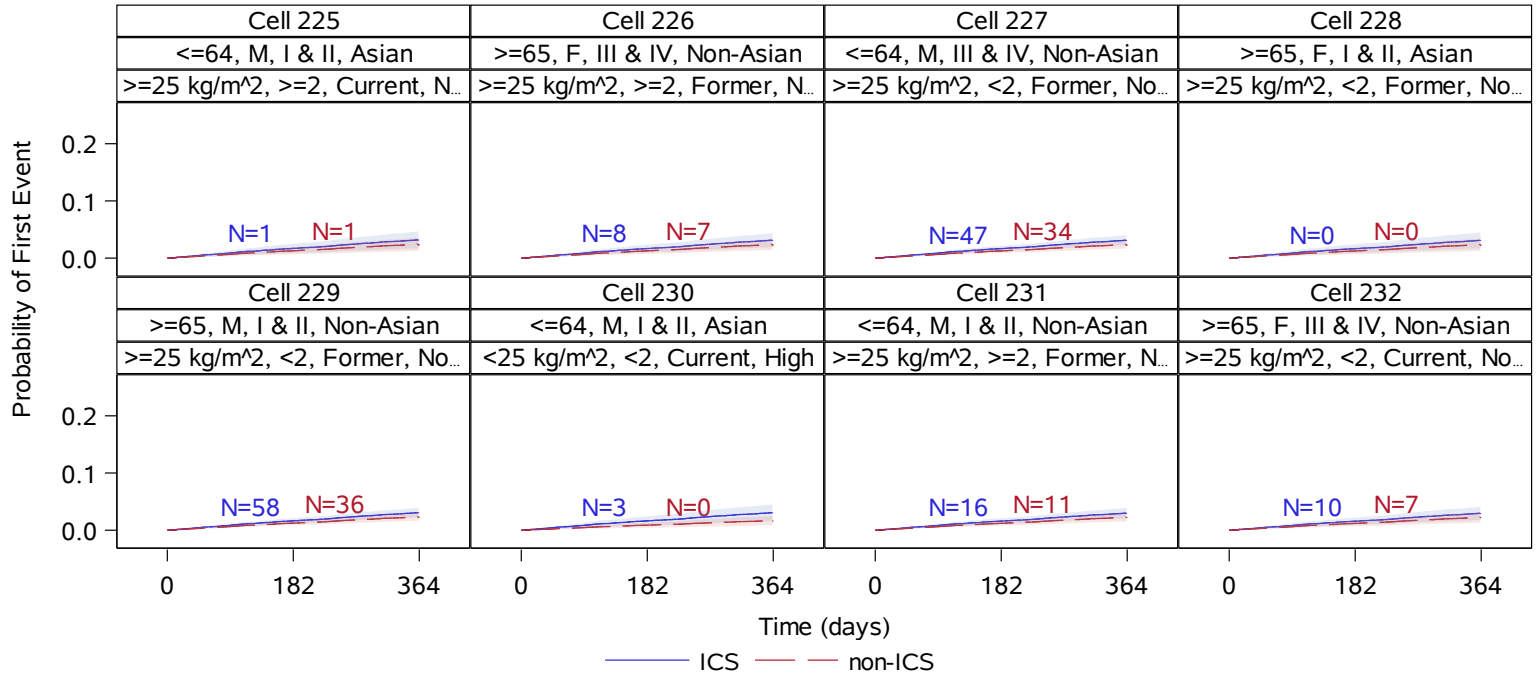

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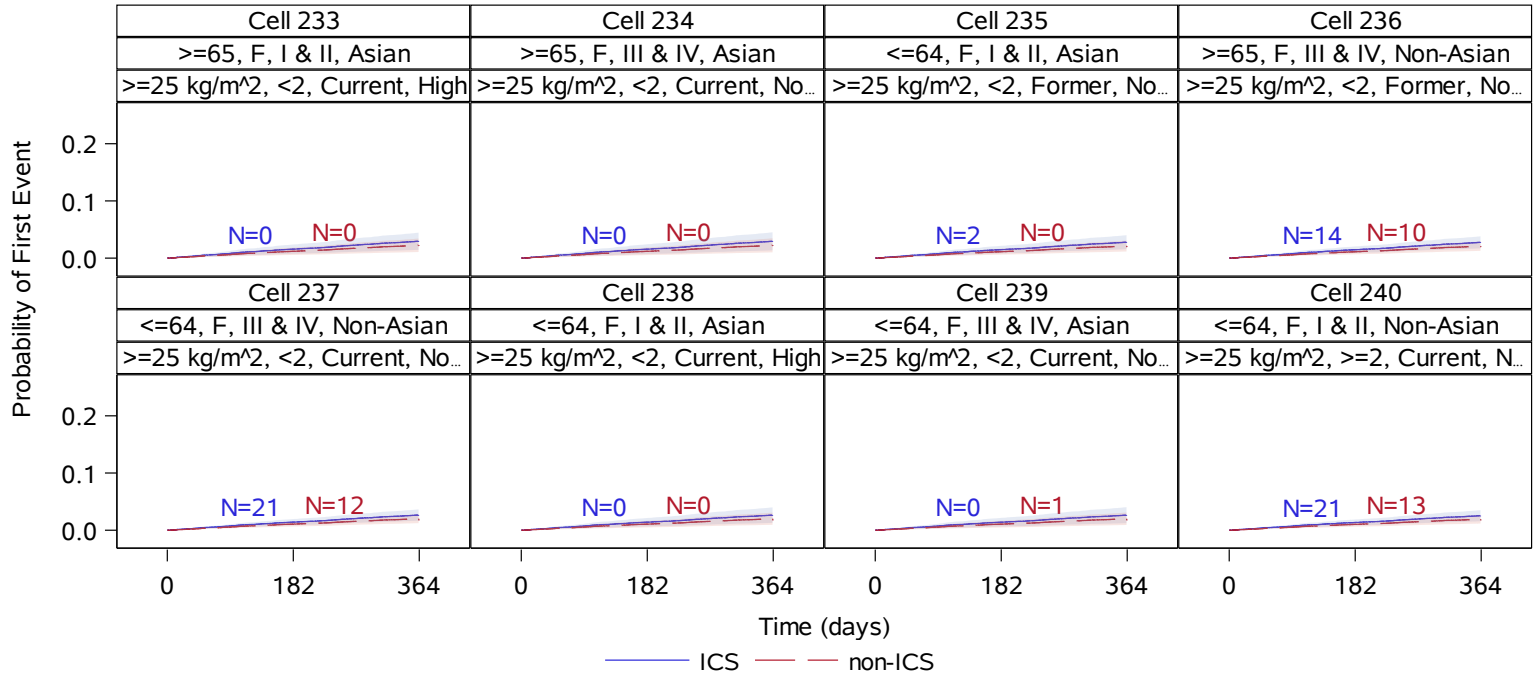

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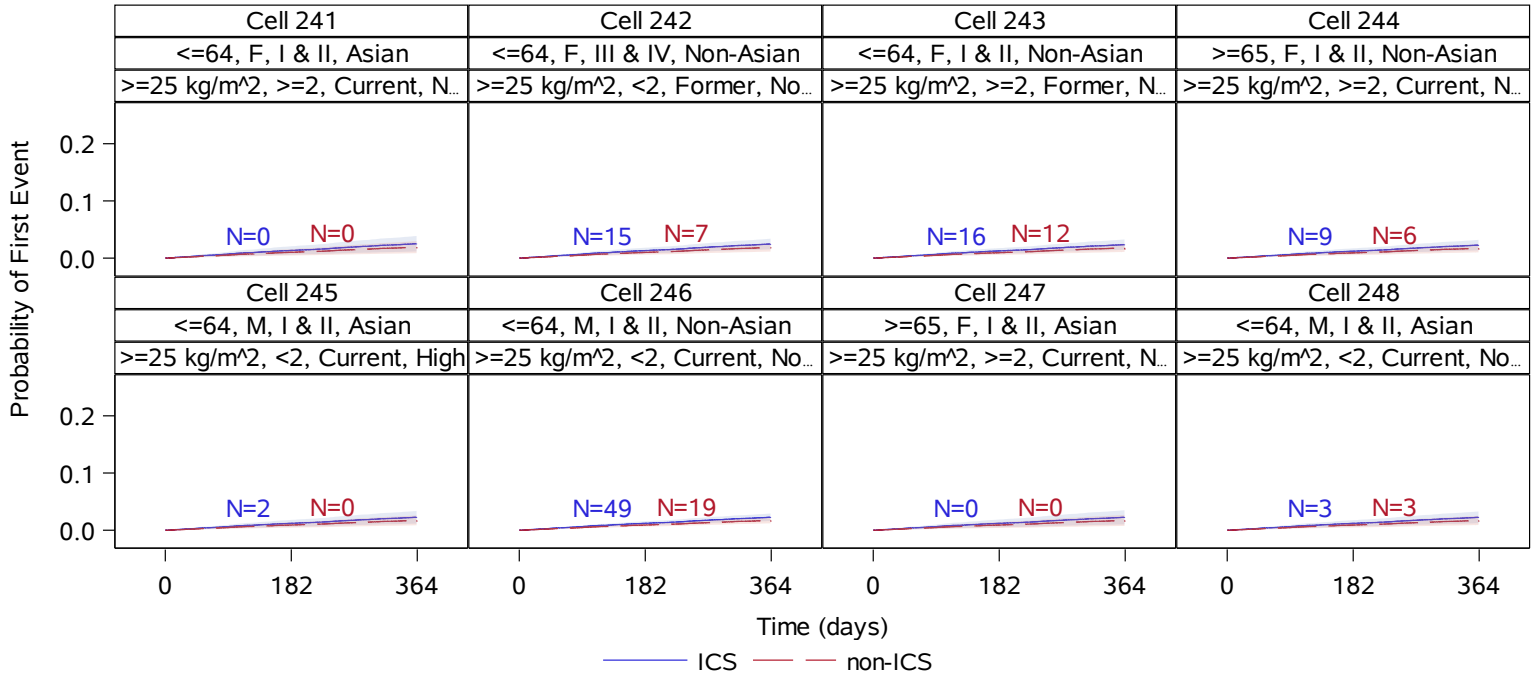

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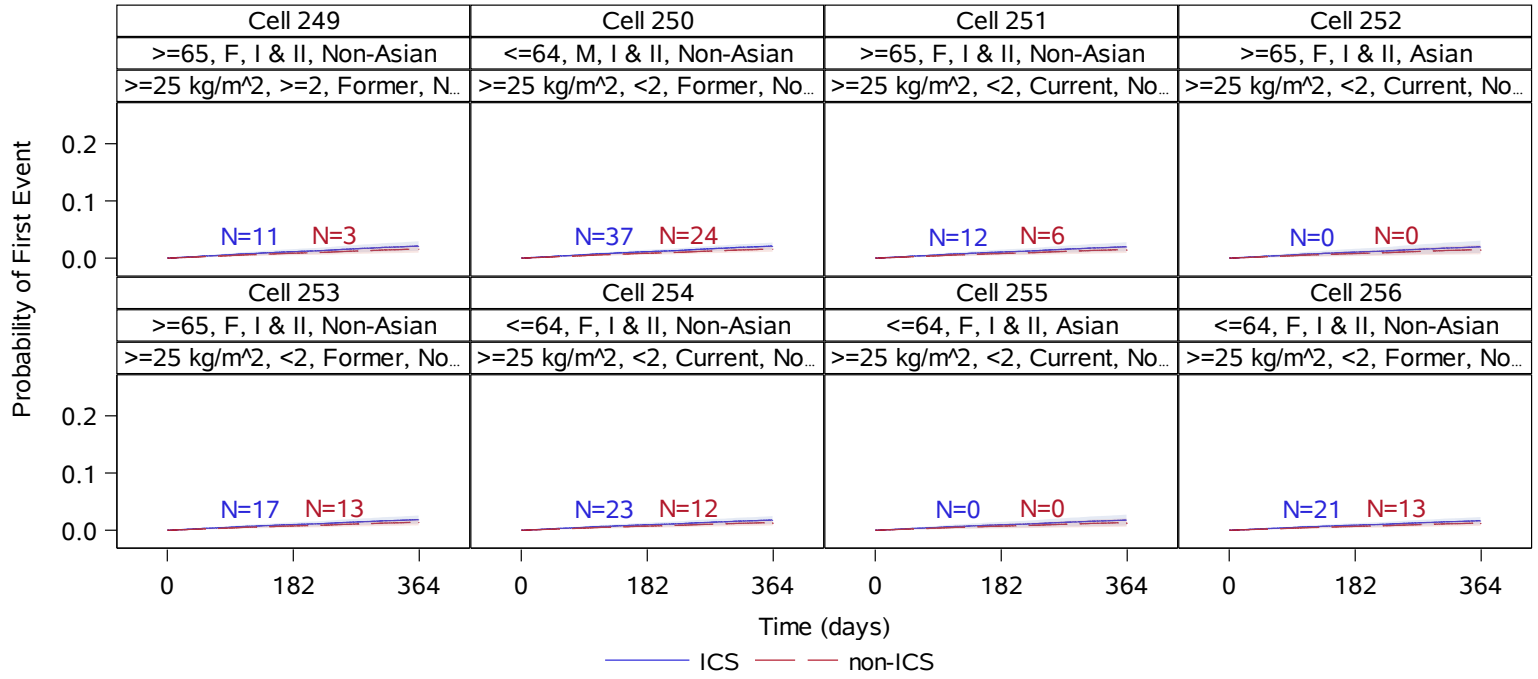

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Figure 2.6
Hazard Ratios from Selected Pneumonia Cox Model (Based on Nine Covariates)

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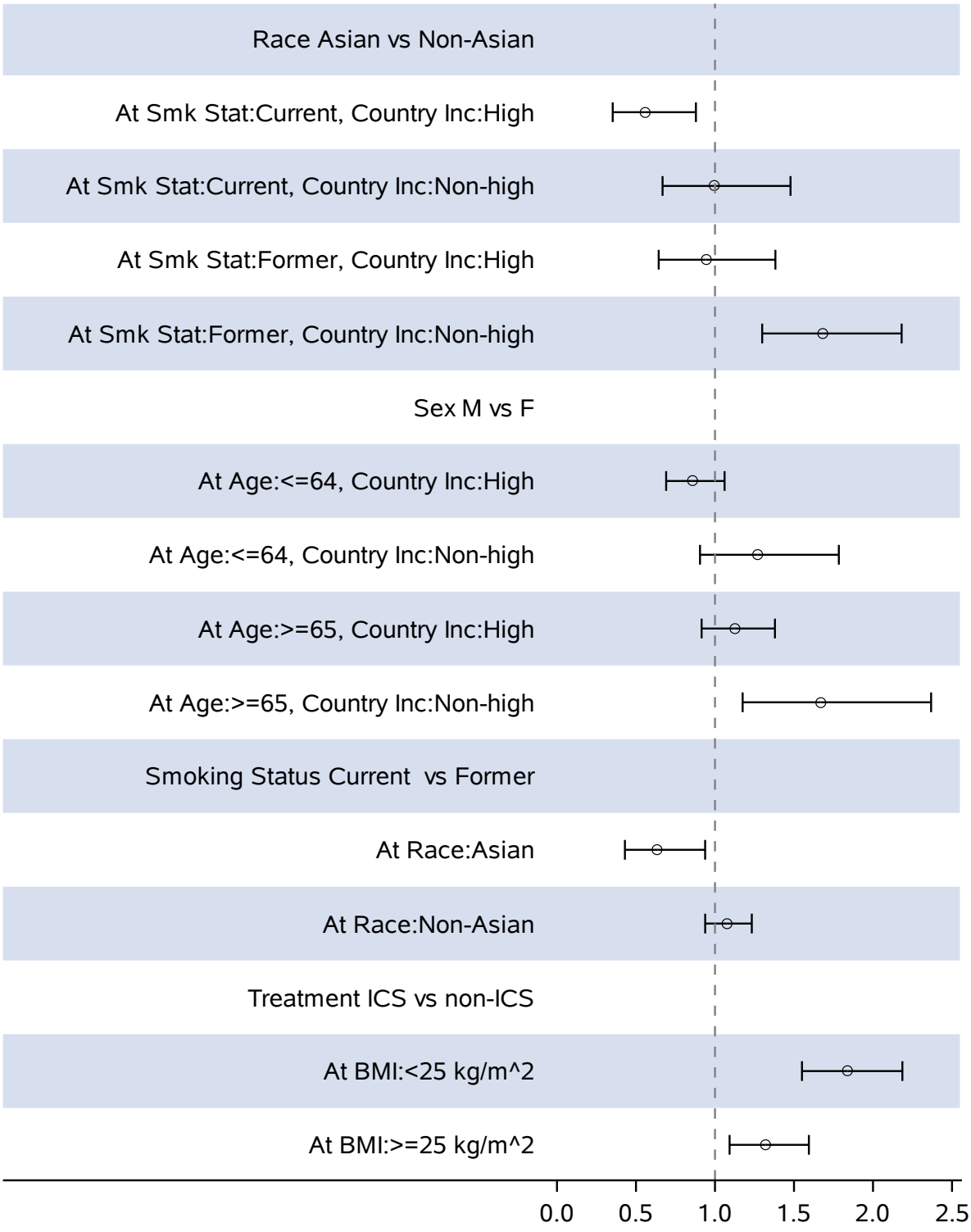
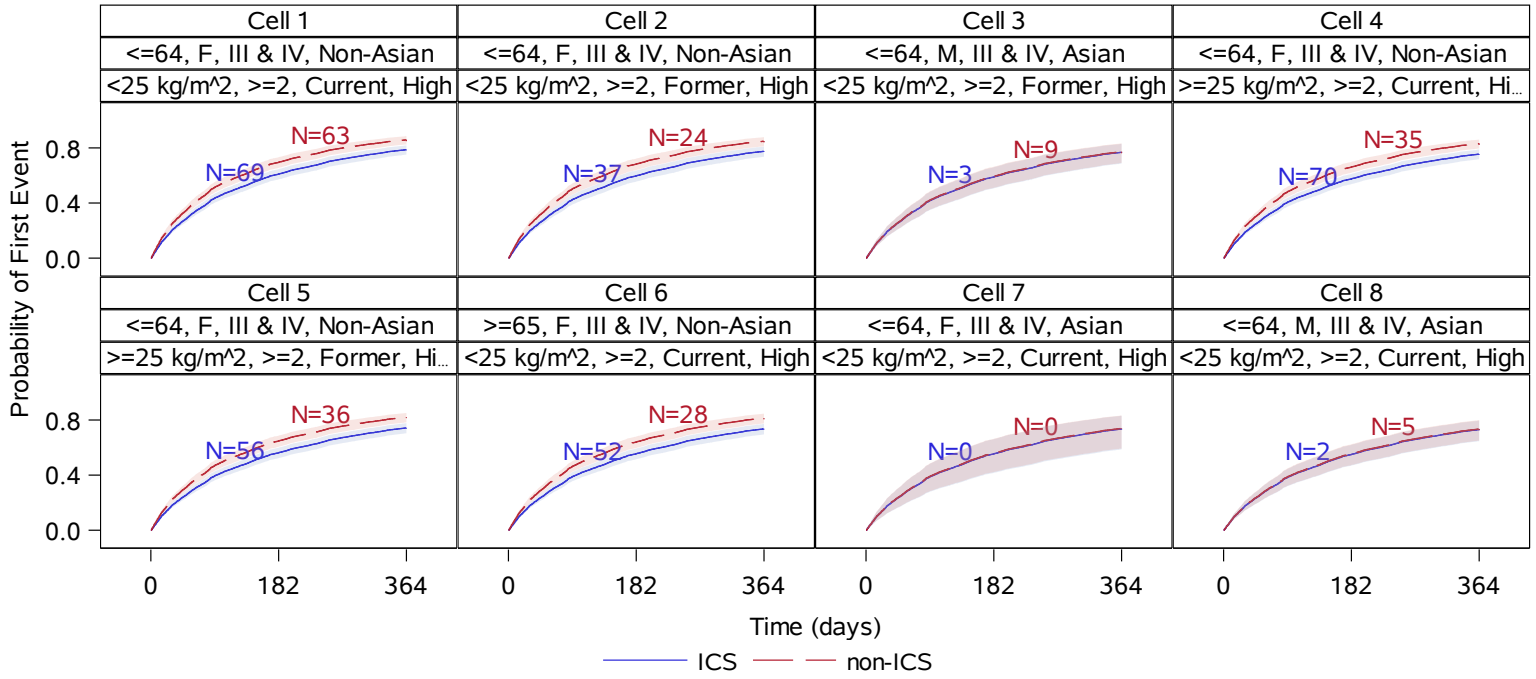


Figure 2.40
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Nine Covariates)



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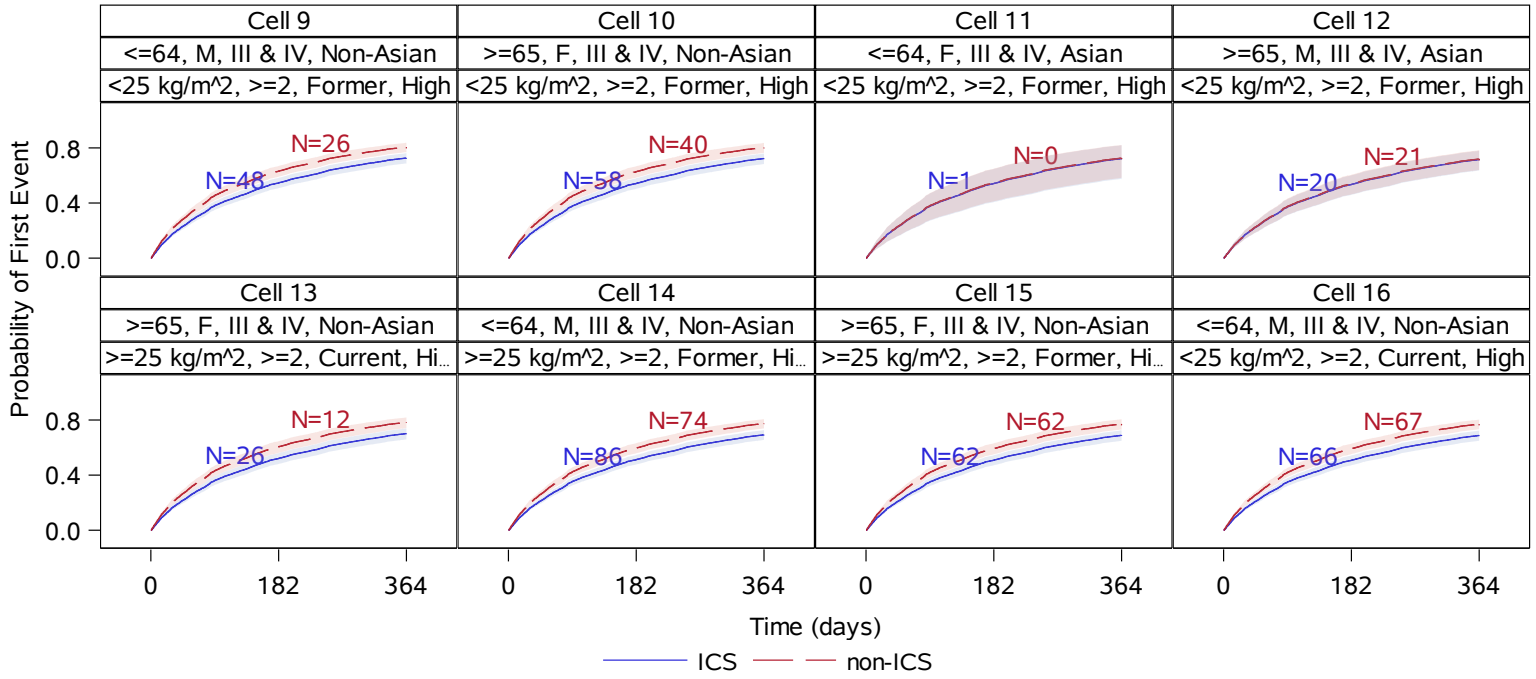

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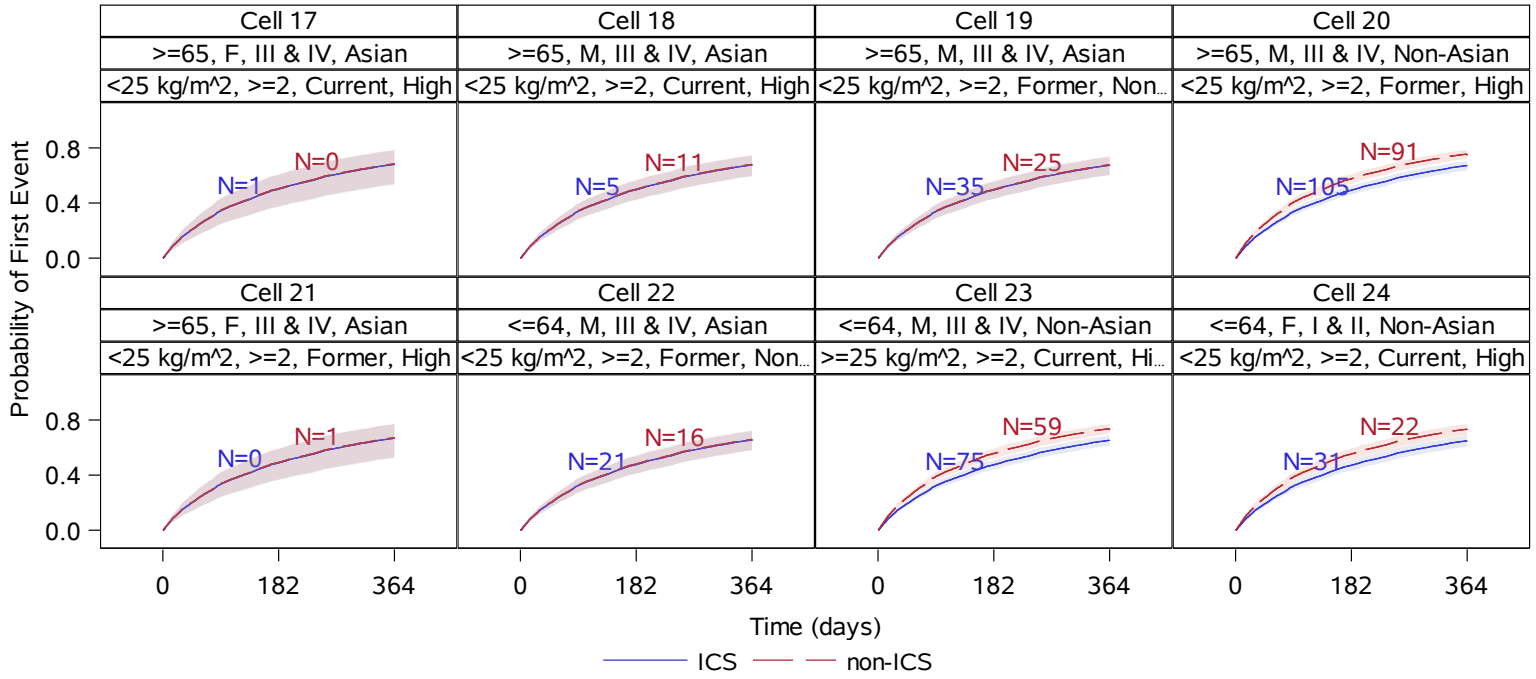

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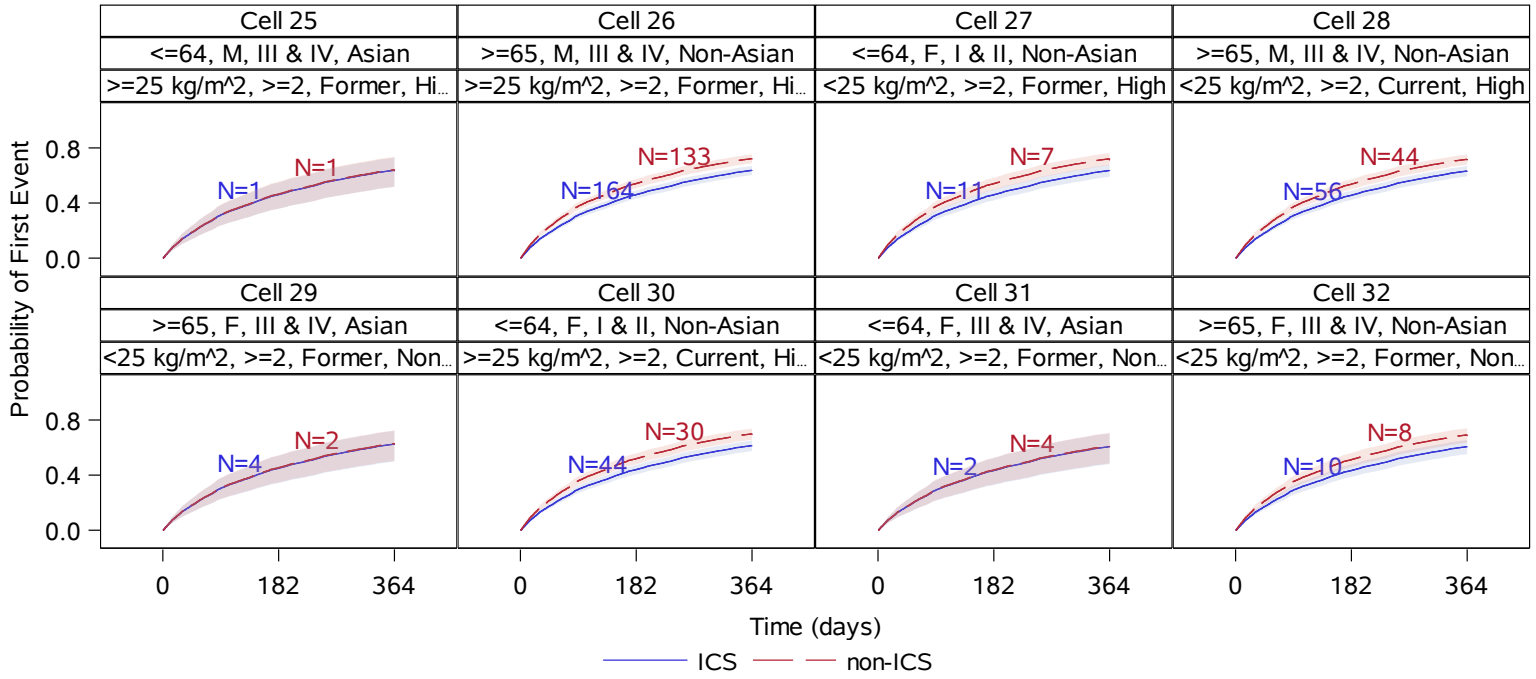

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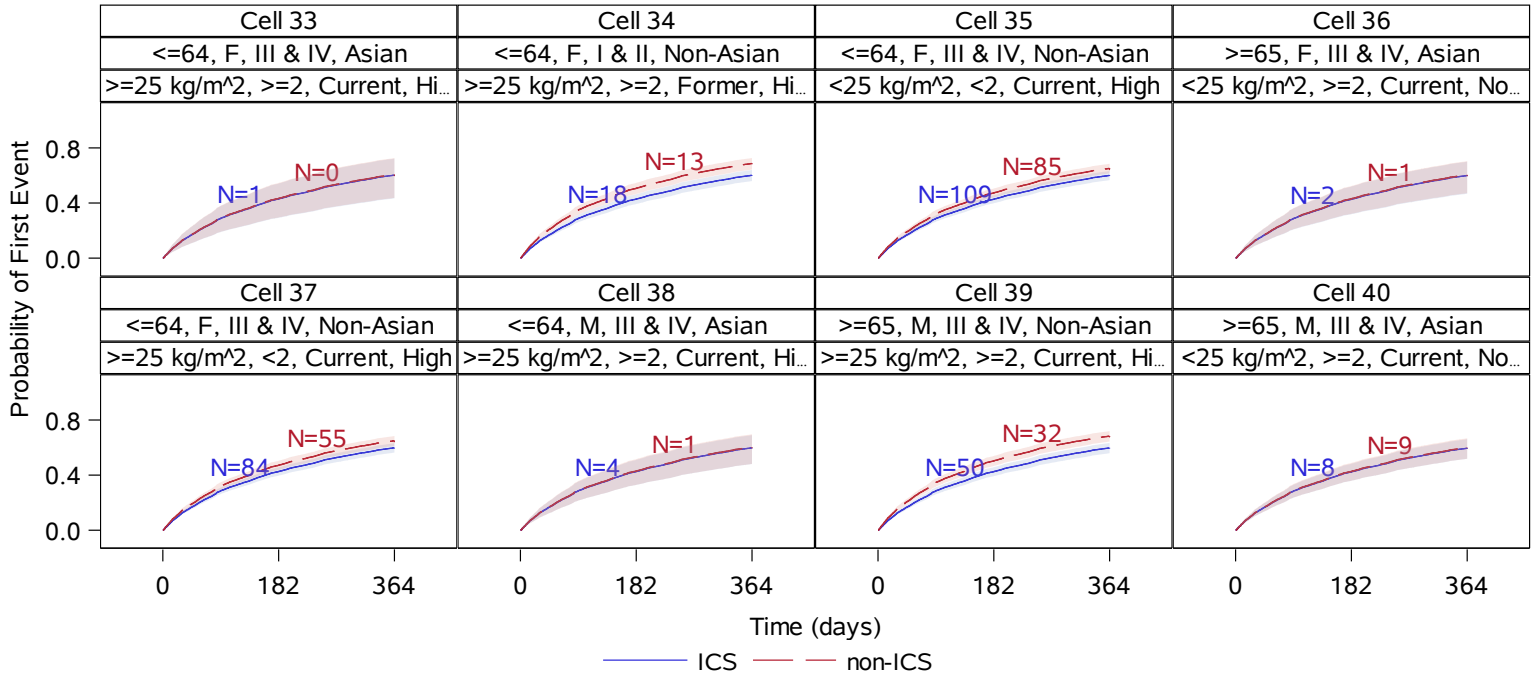

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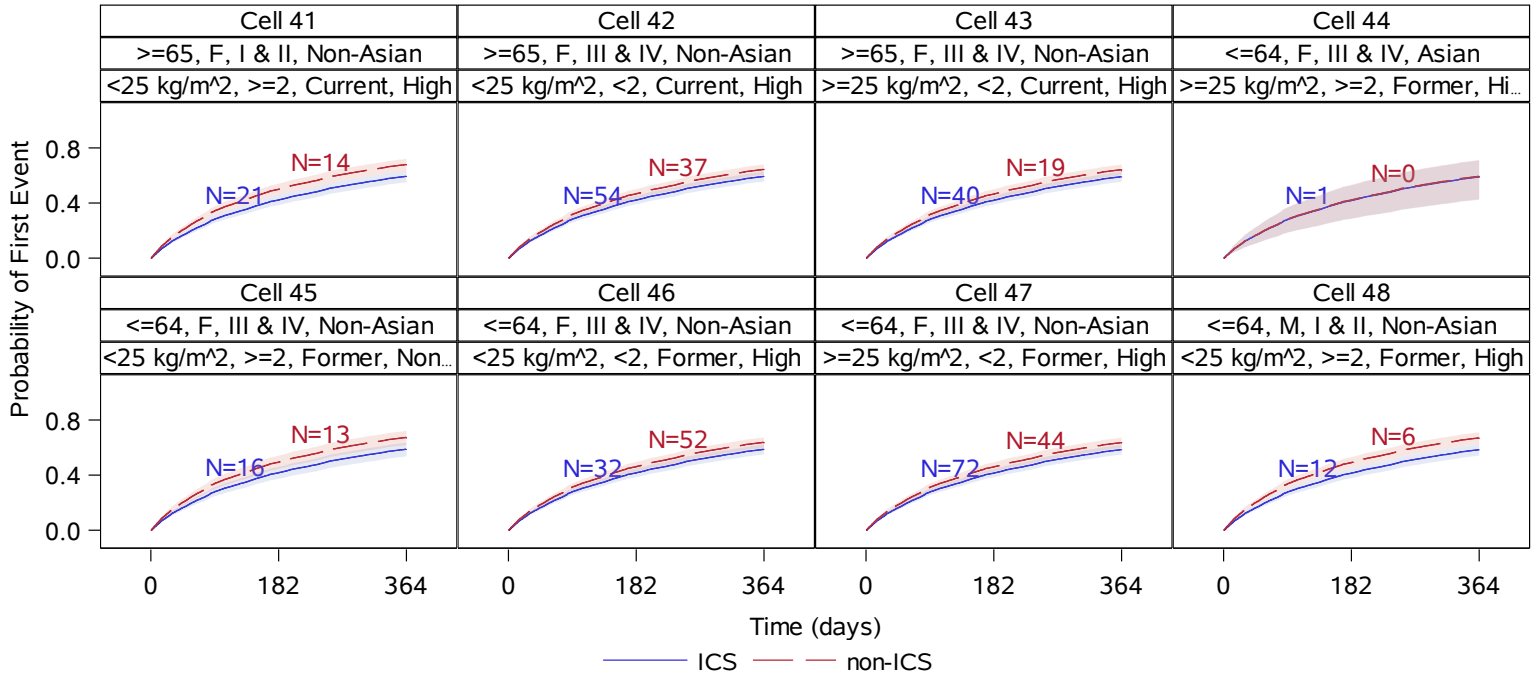

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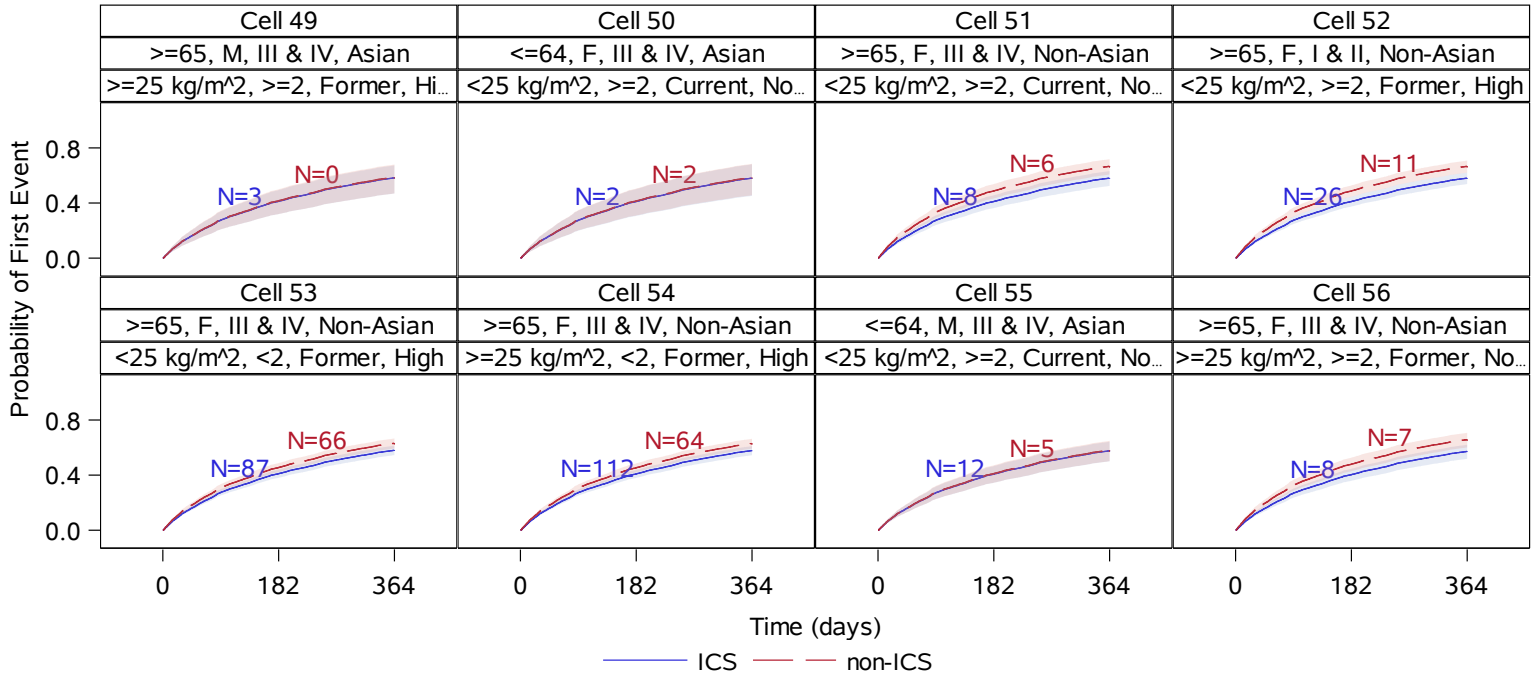

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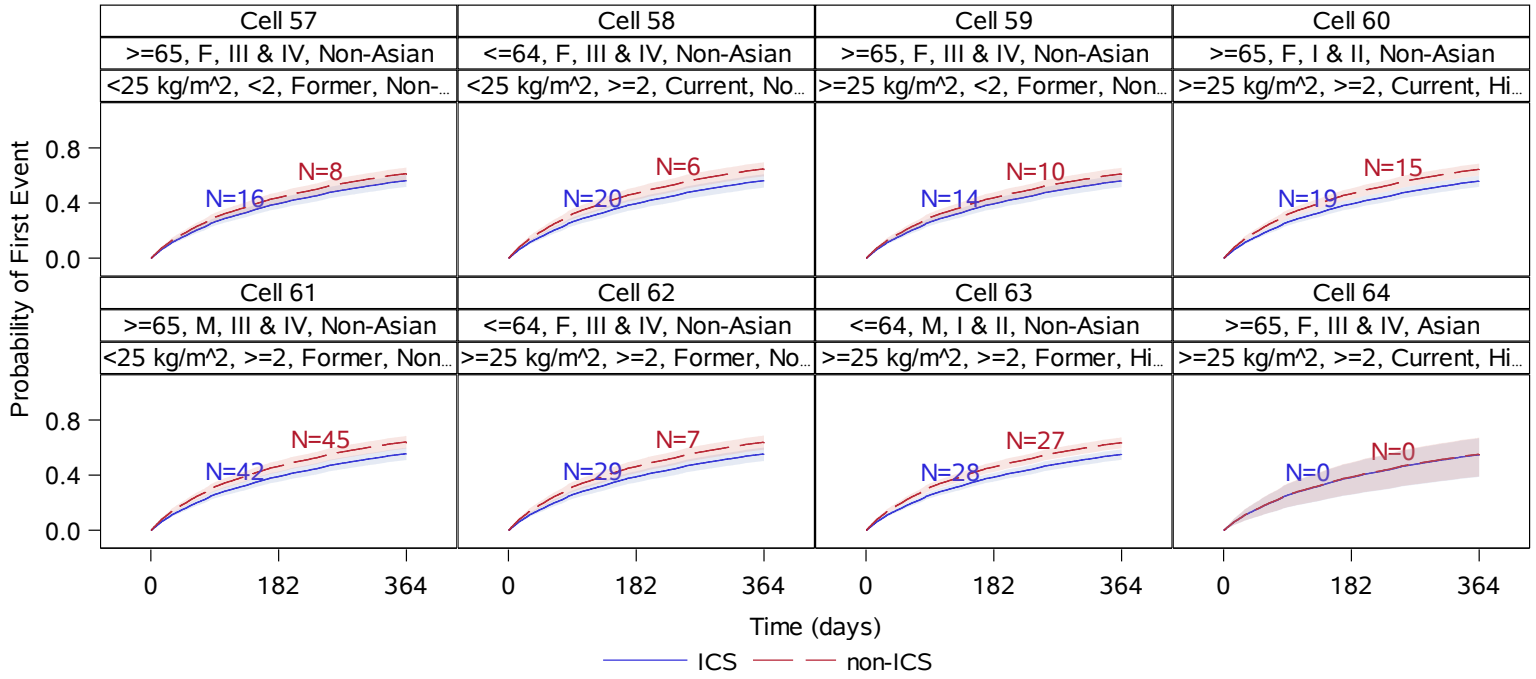
(Based on Nine Covariates)



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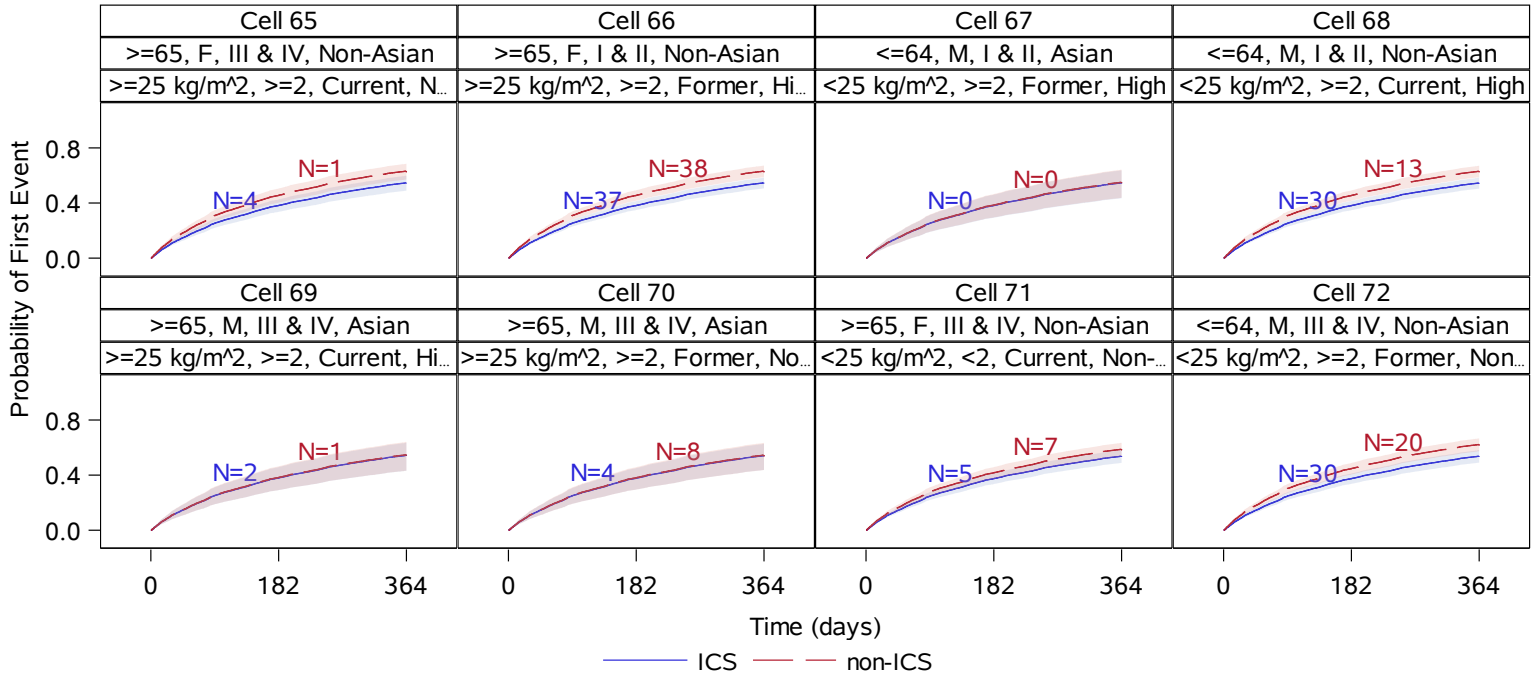
PPD

Figure 2.40
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Nine Covariates)



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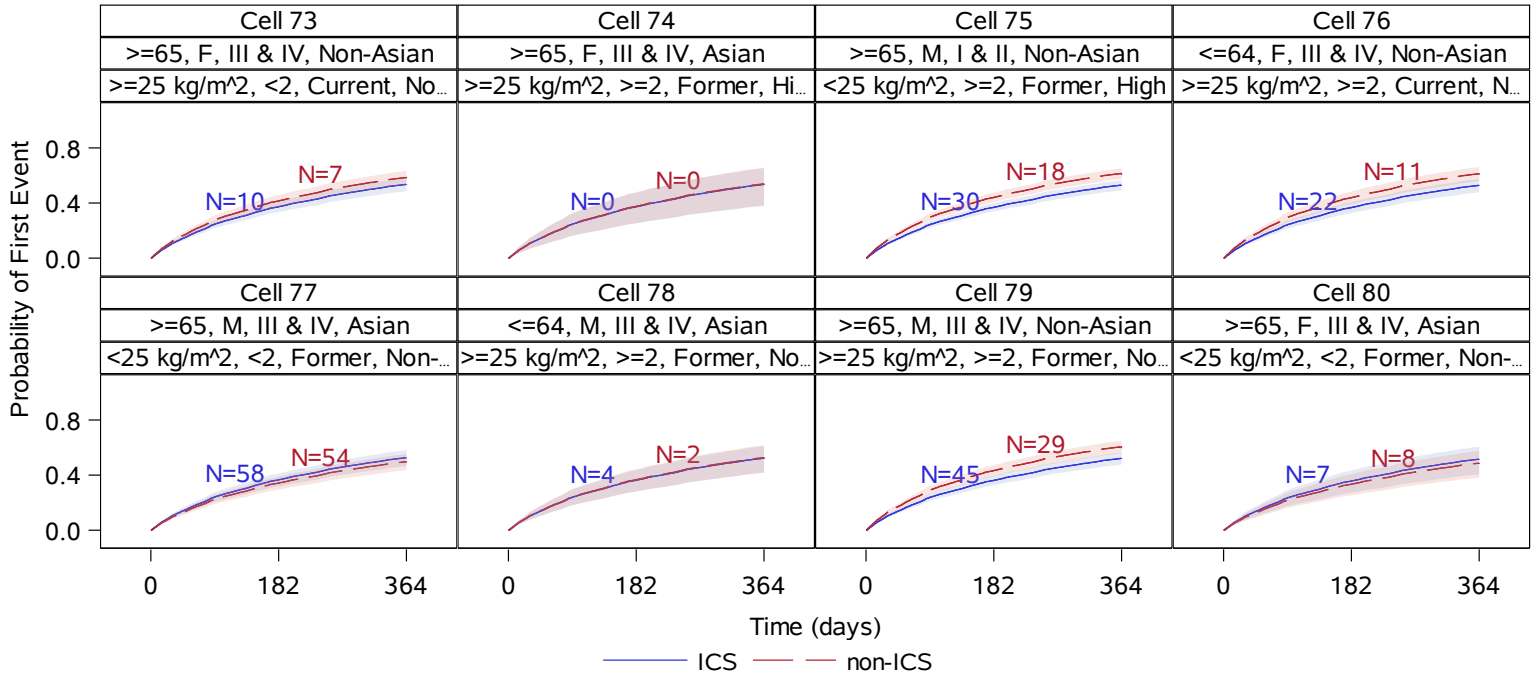

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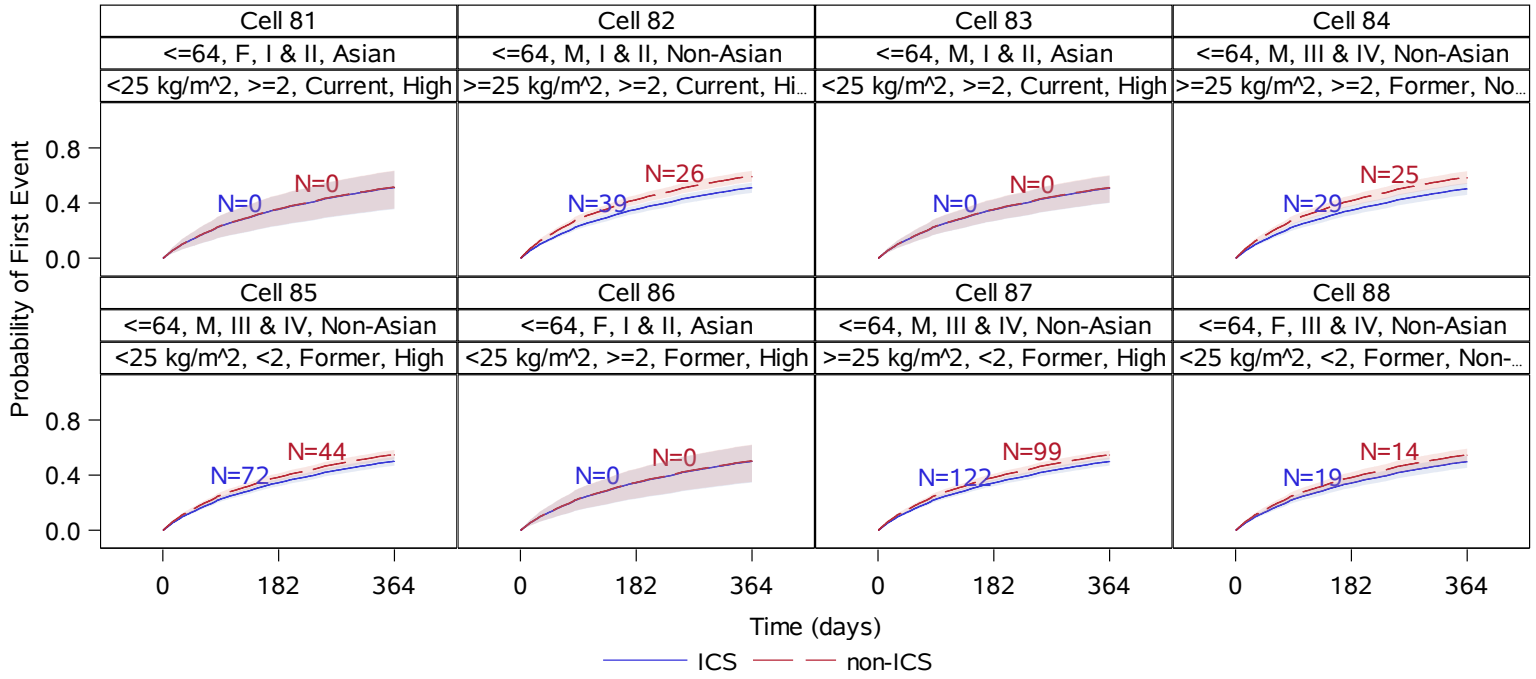

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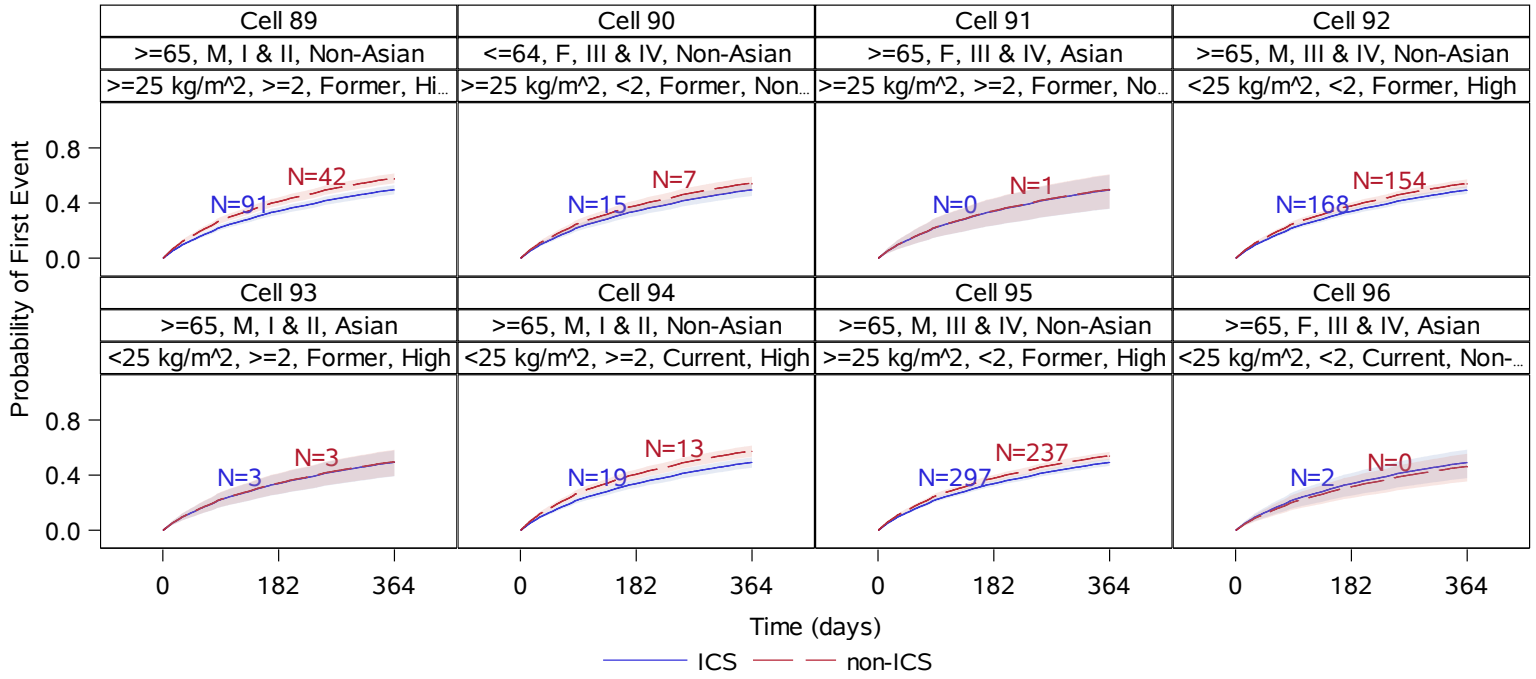

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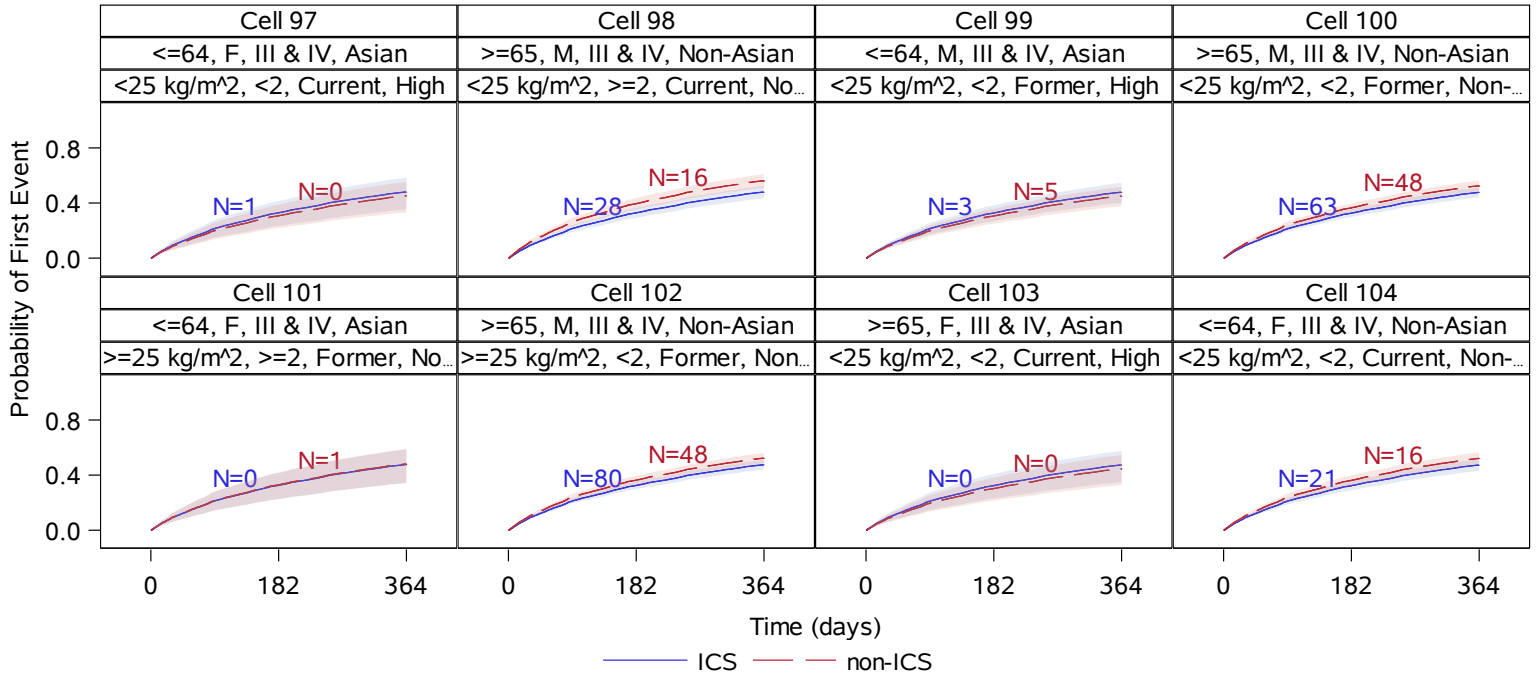

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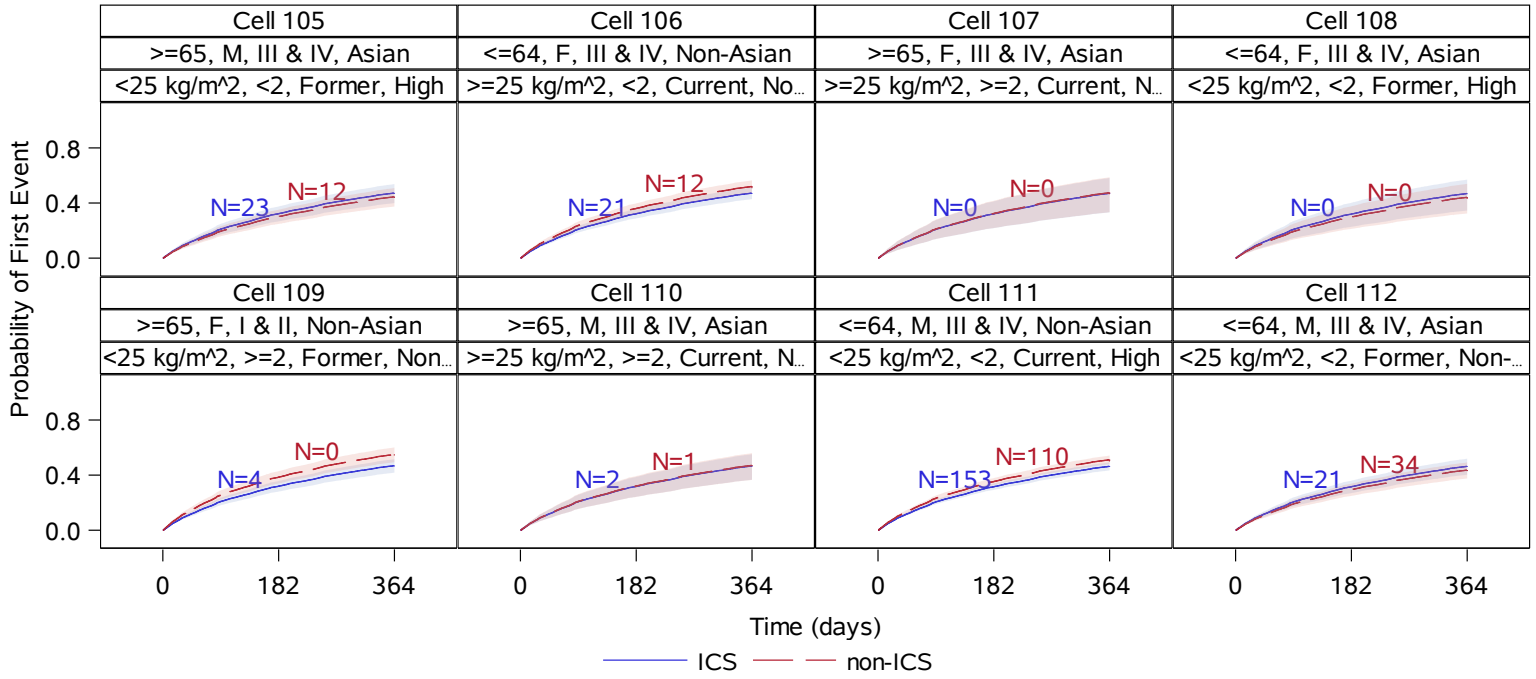

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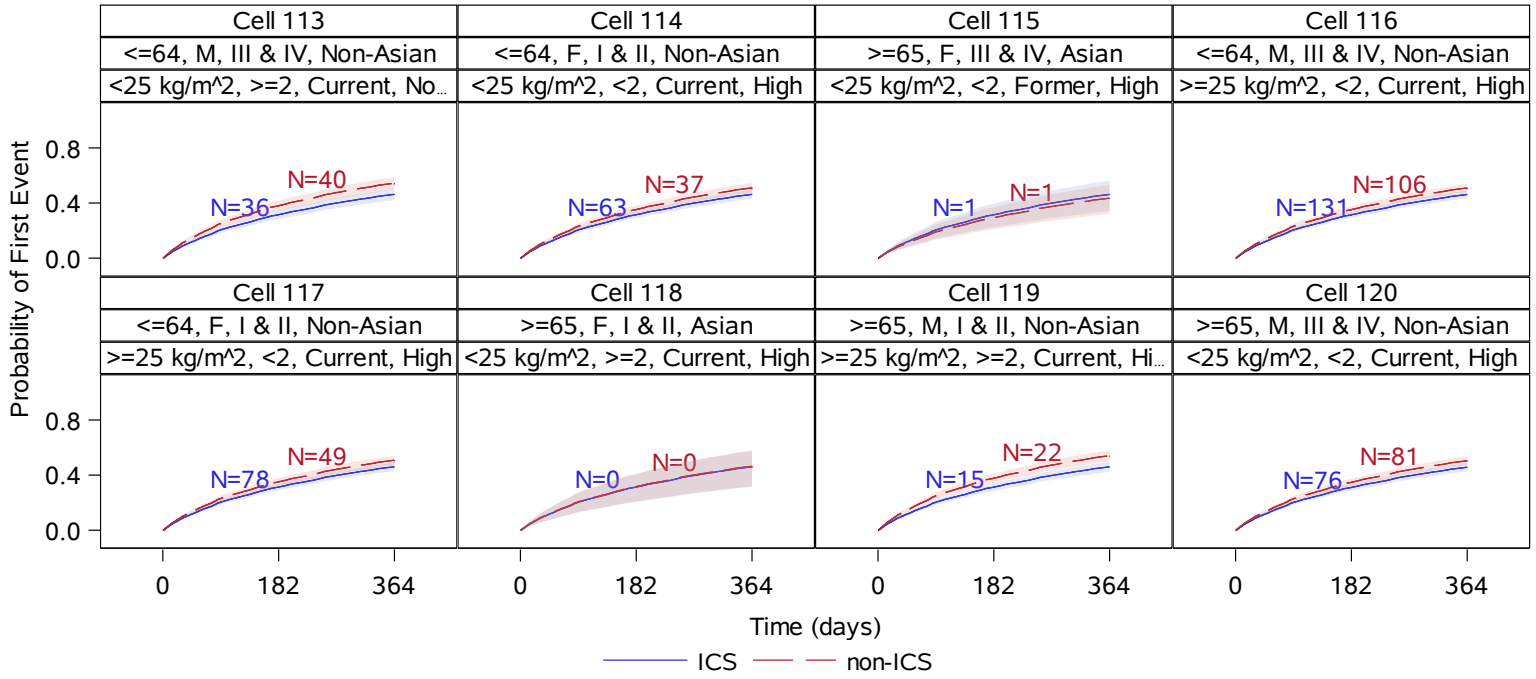

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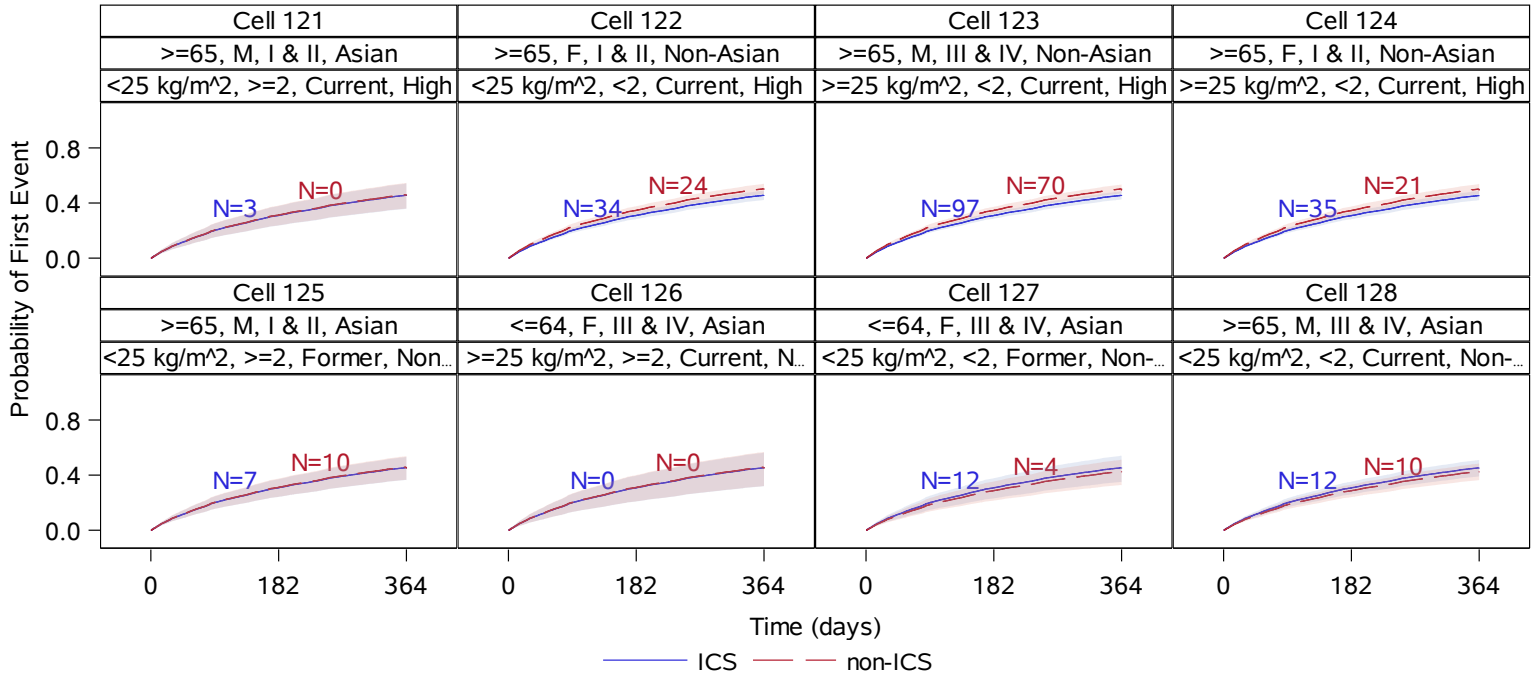

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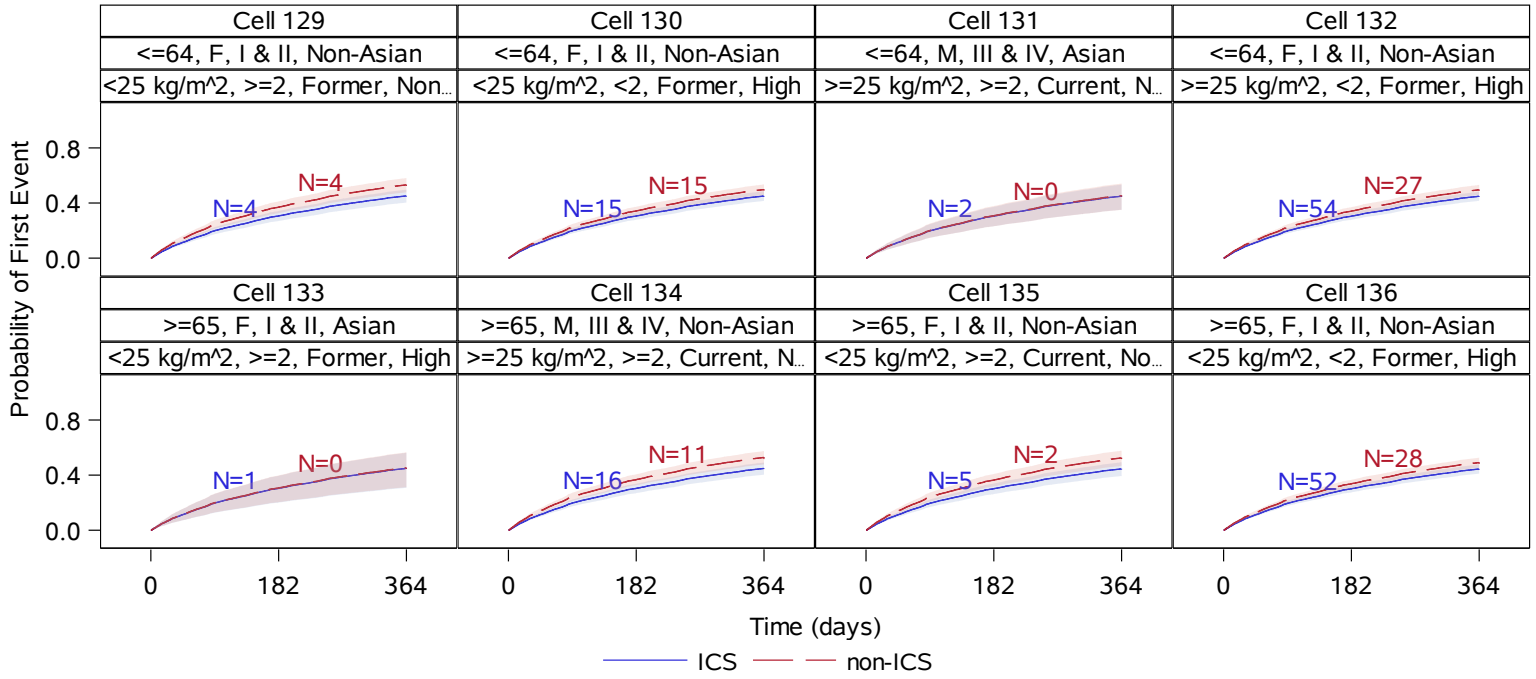

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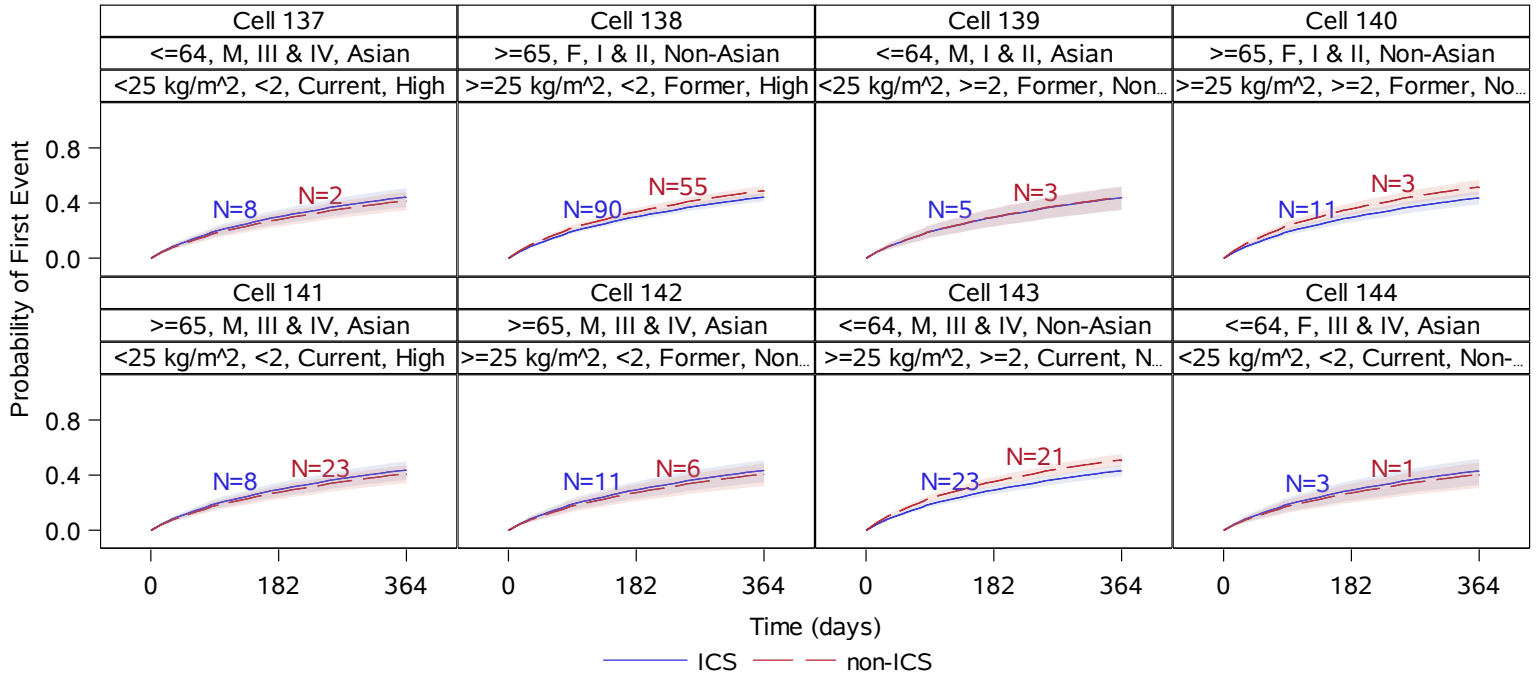

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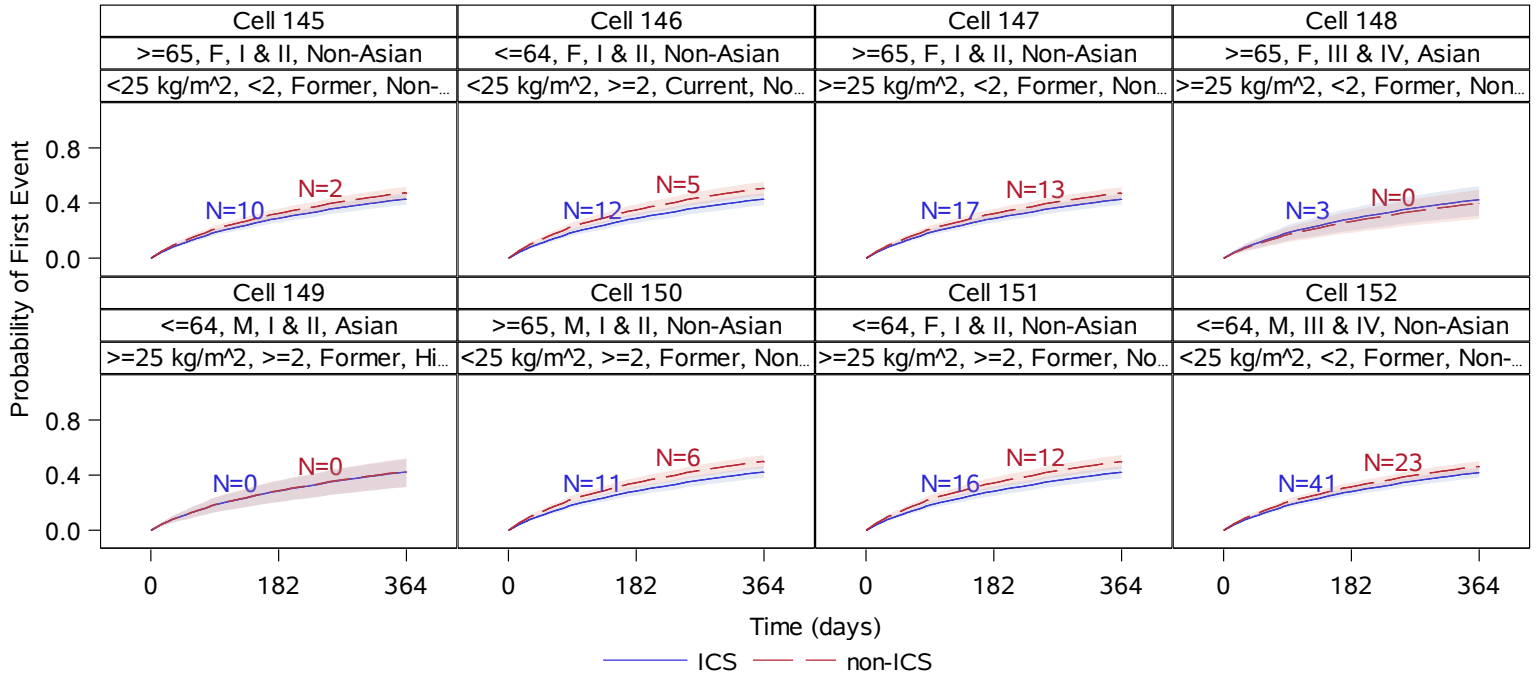

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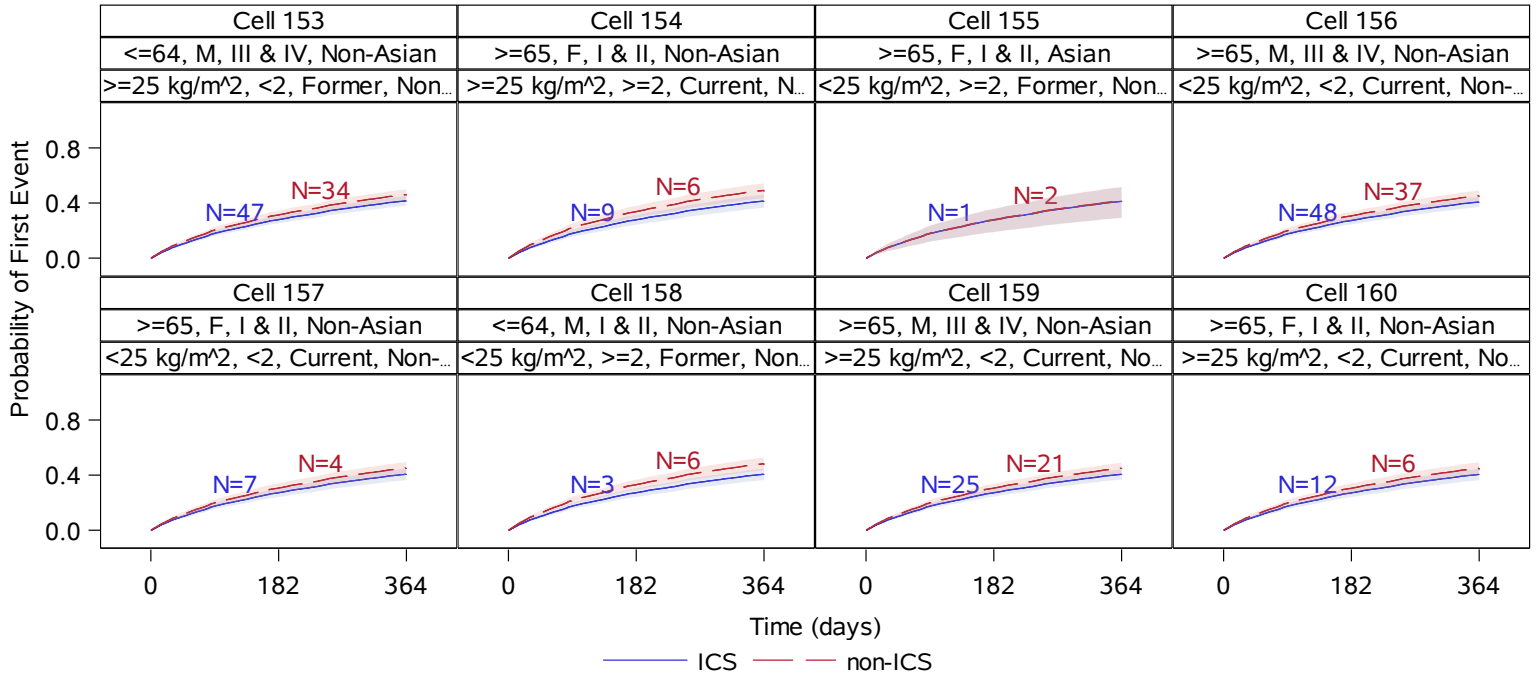

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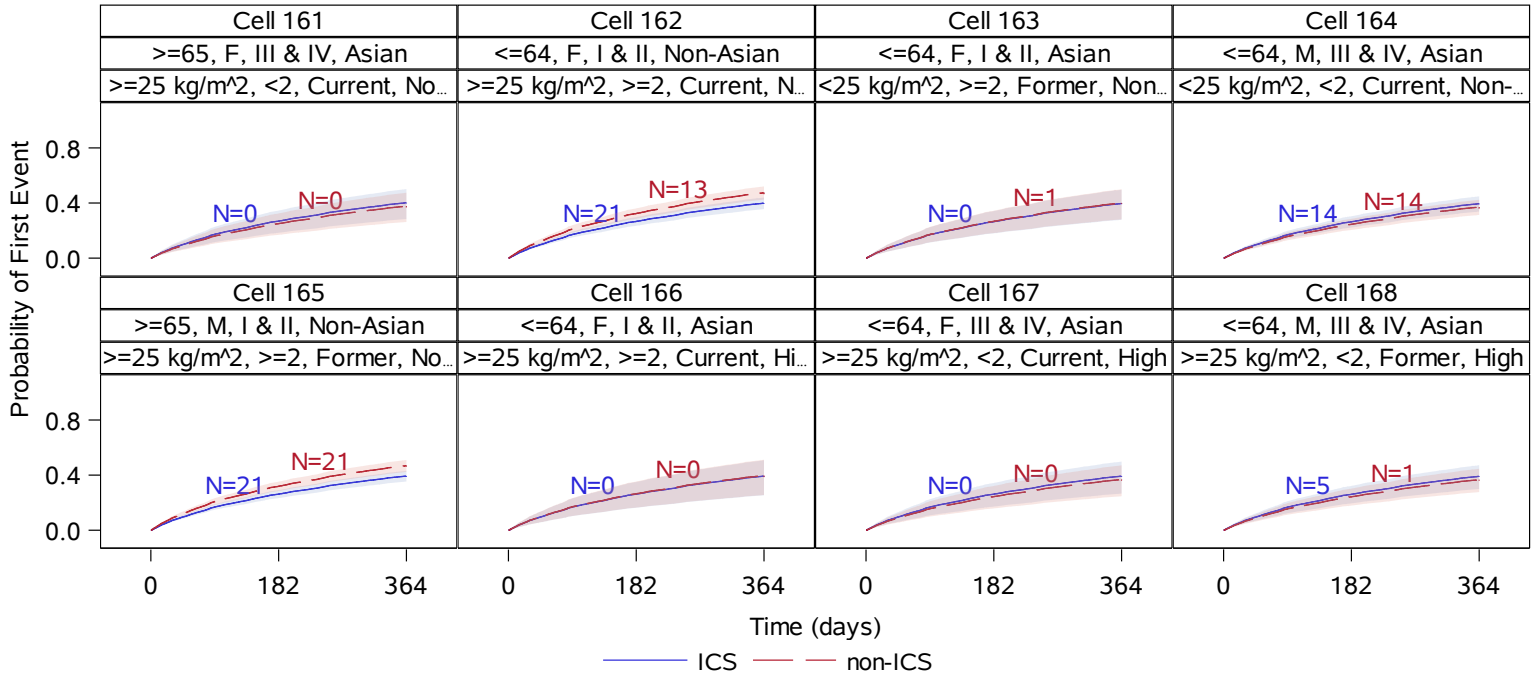

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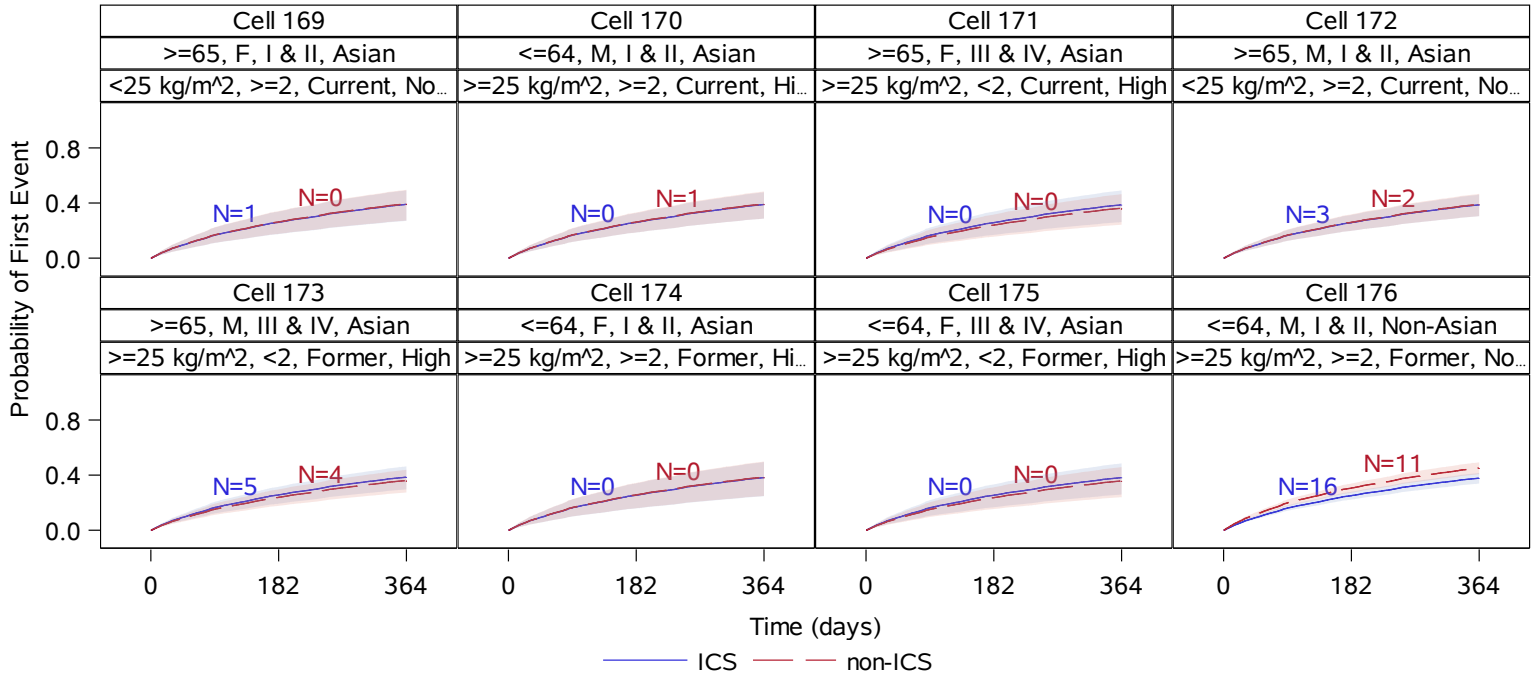

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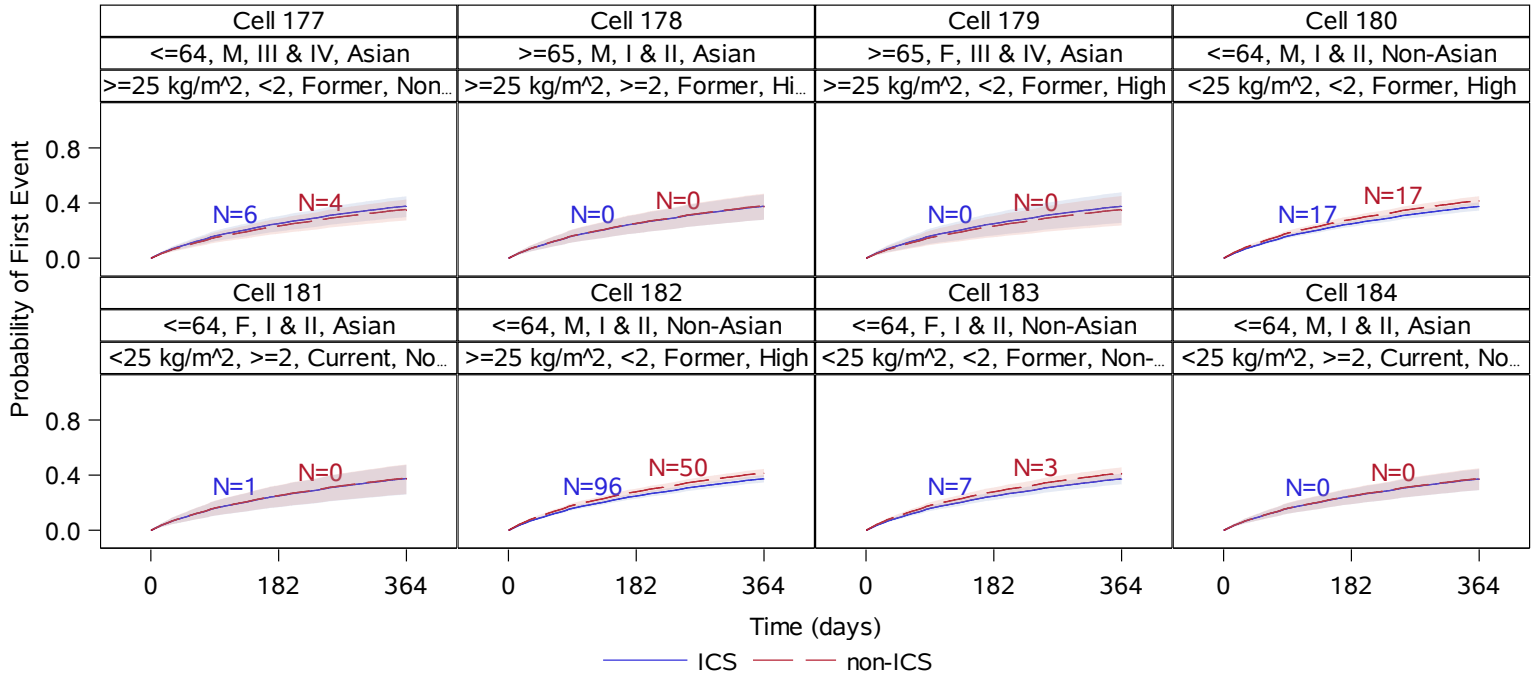

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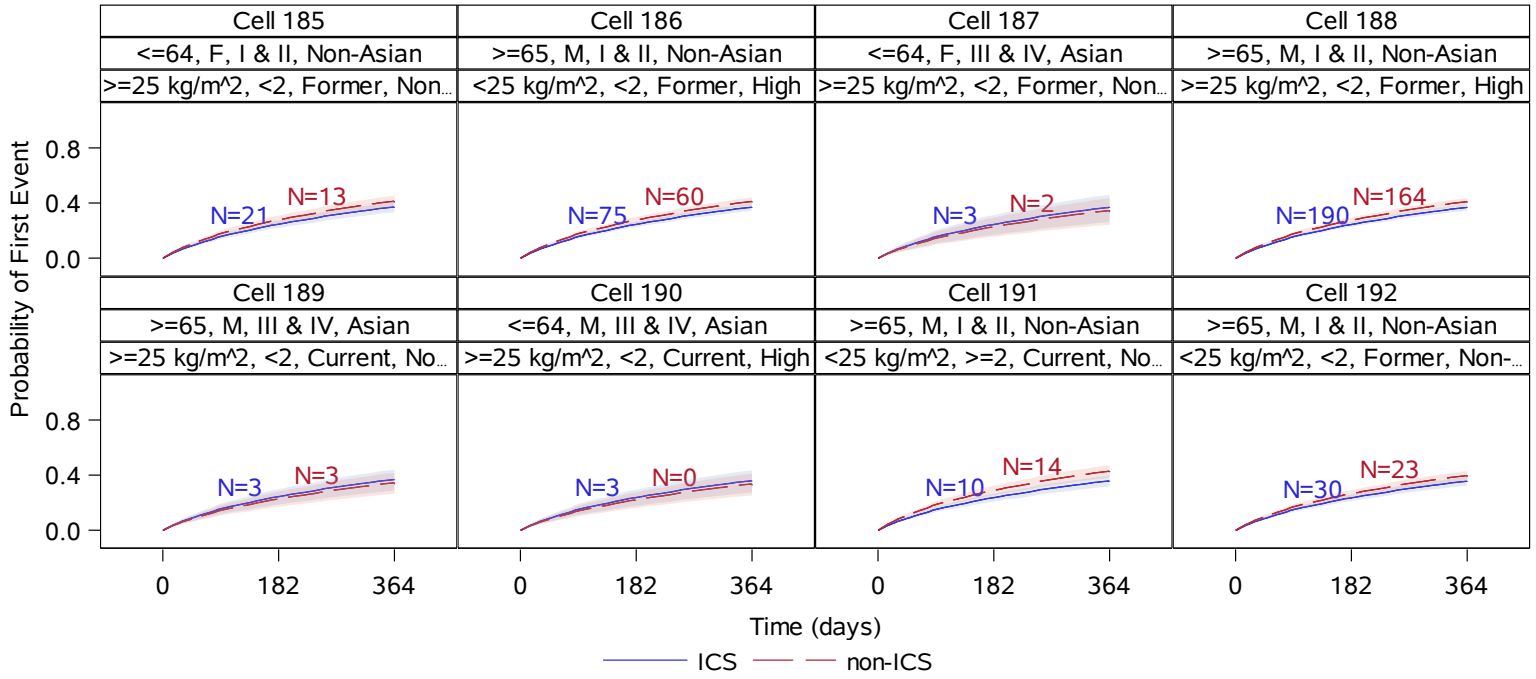

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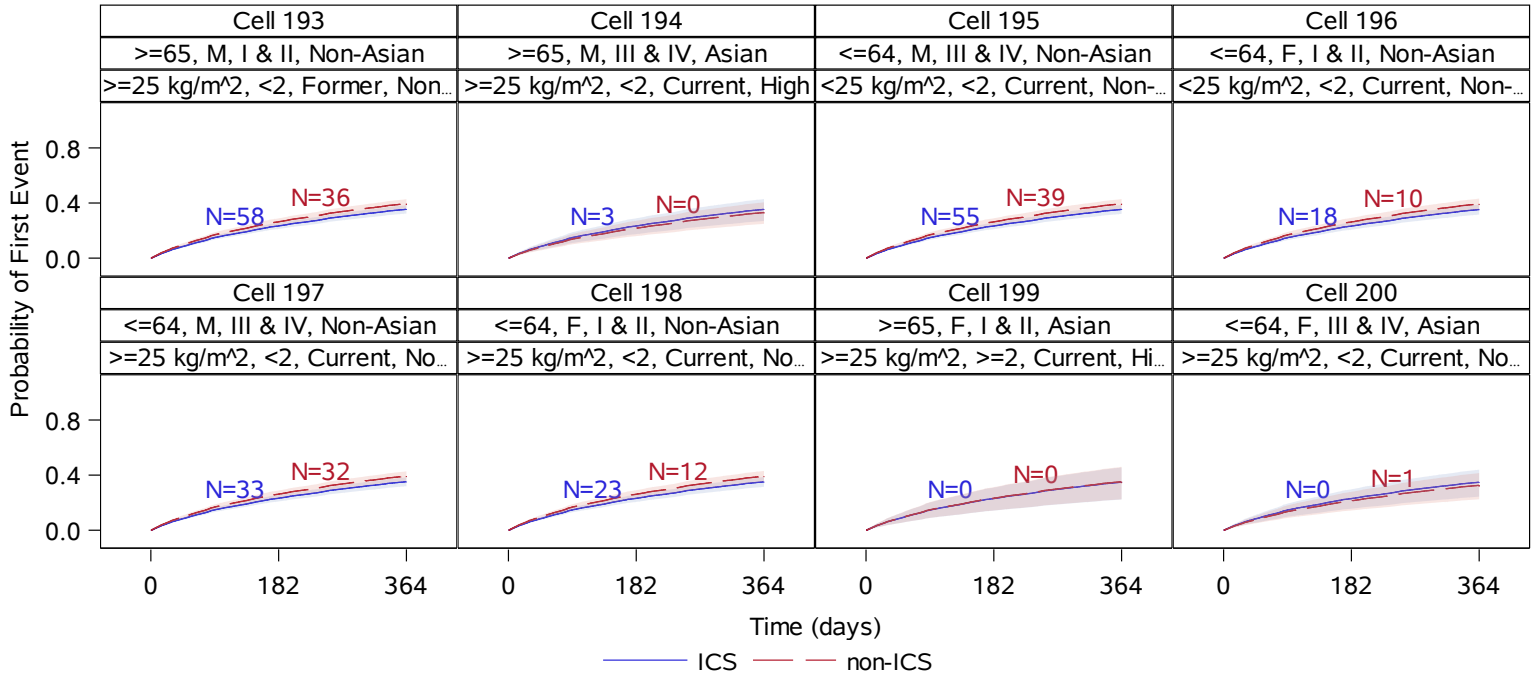

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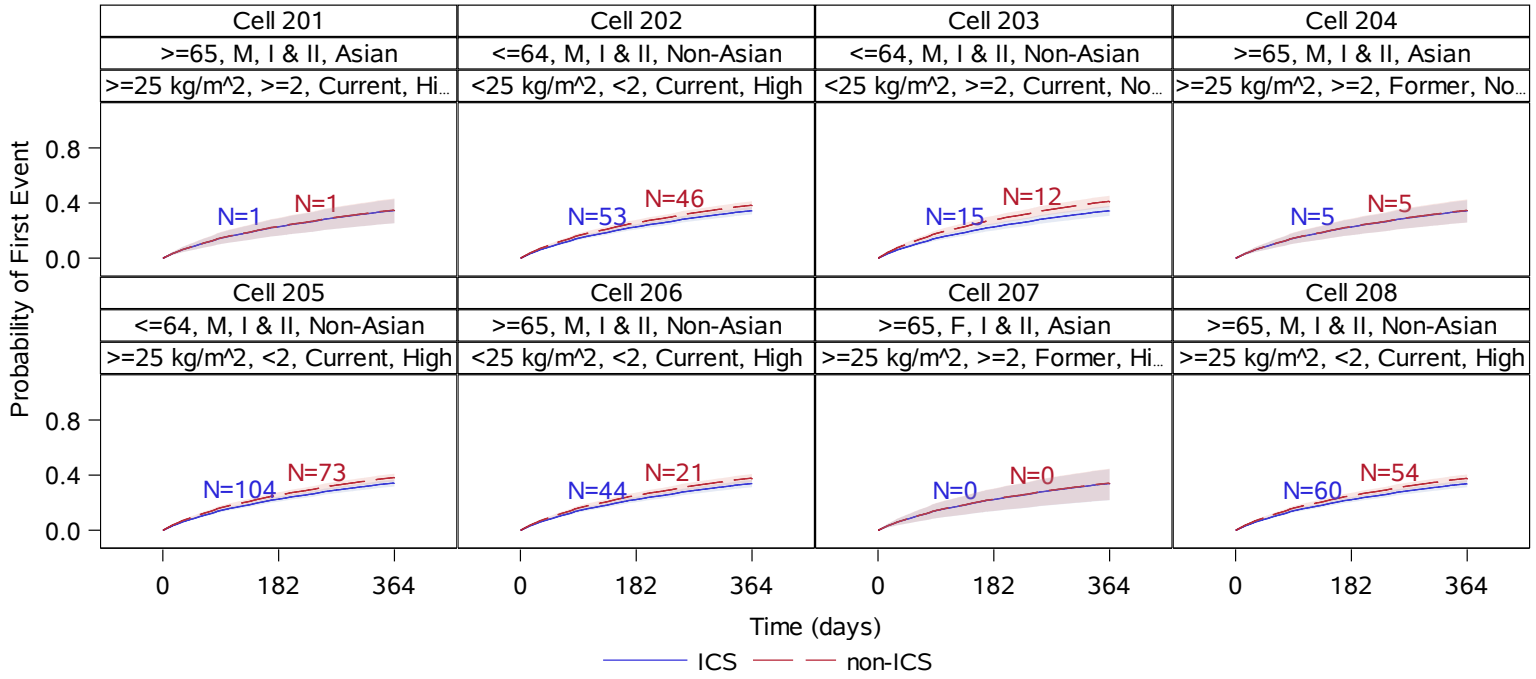

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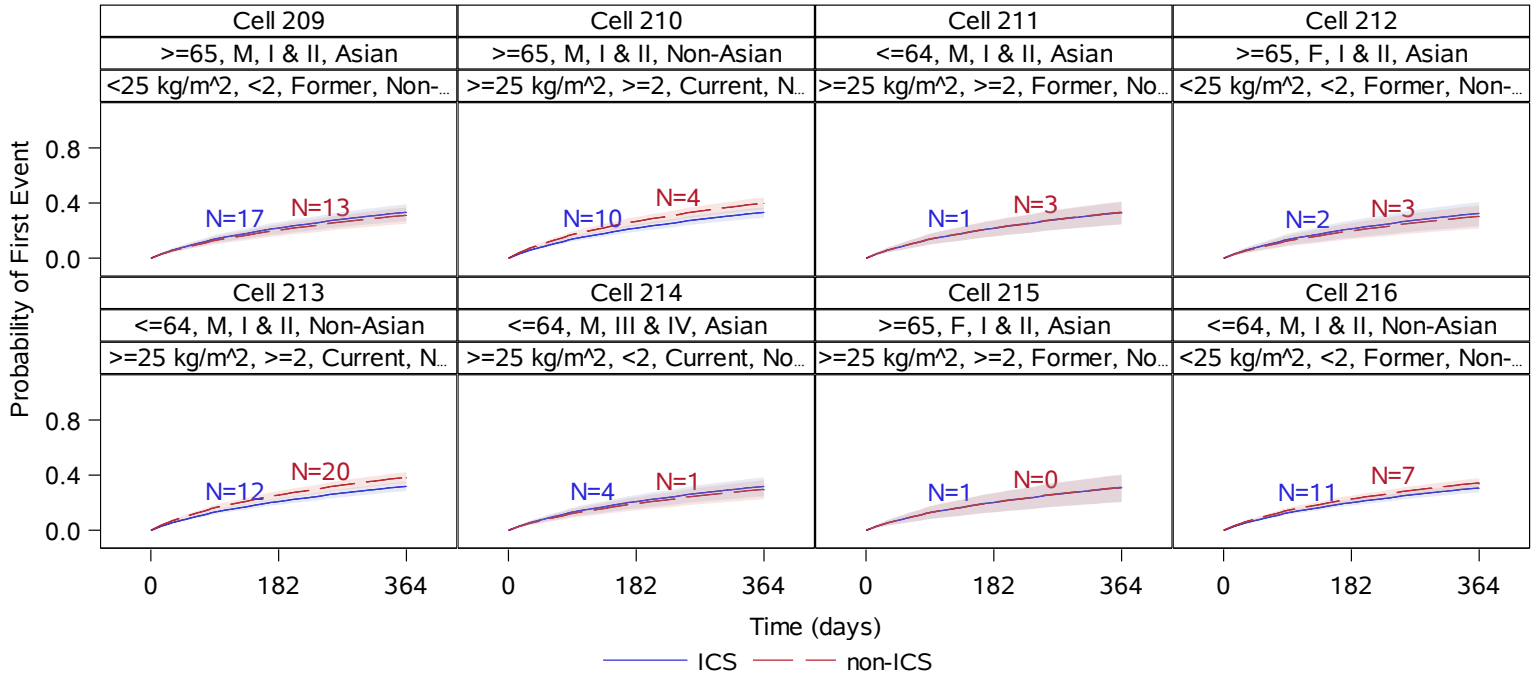

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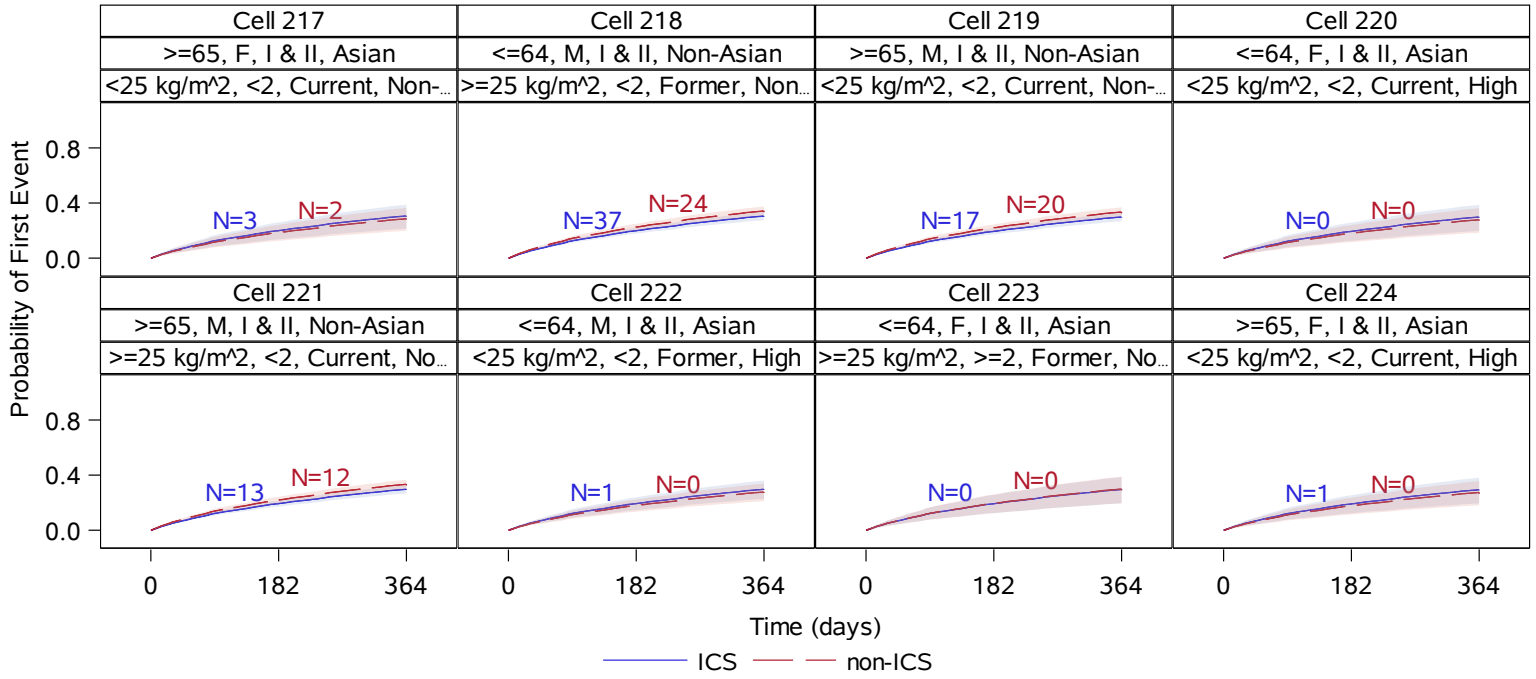

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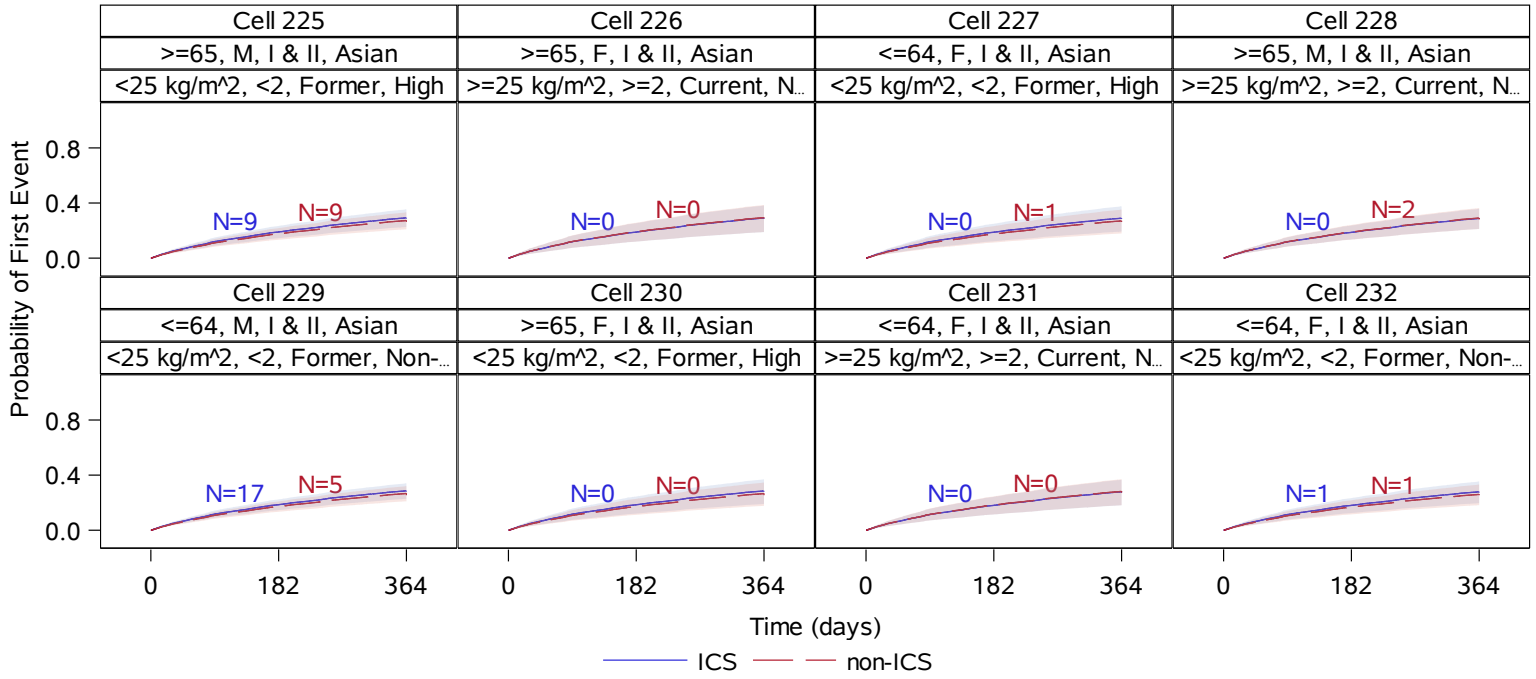

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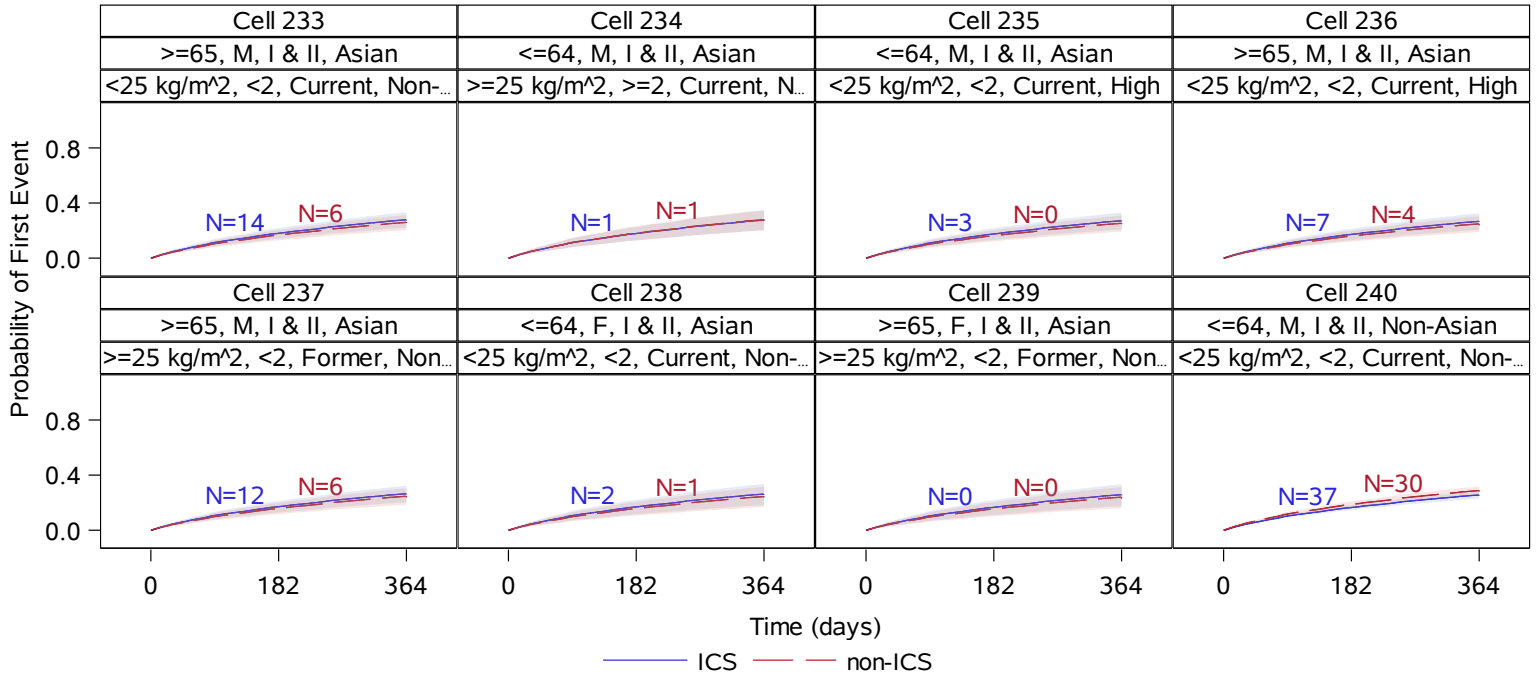

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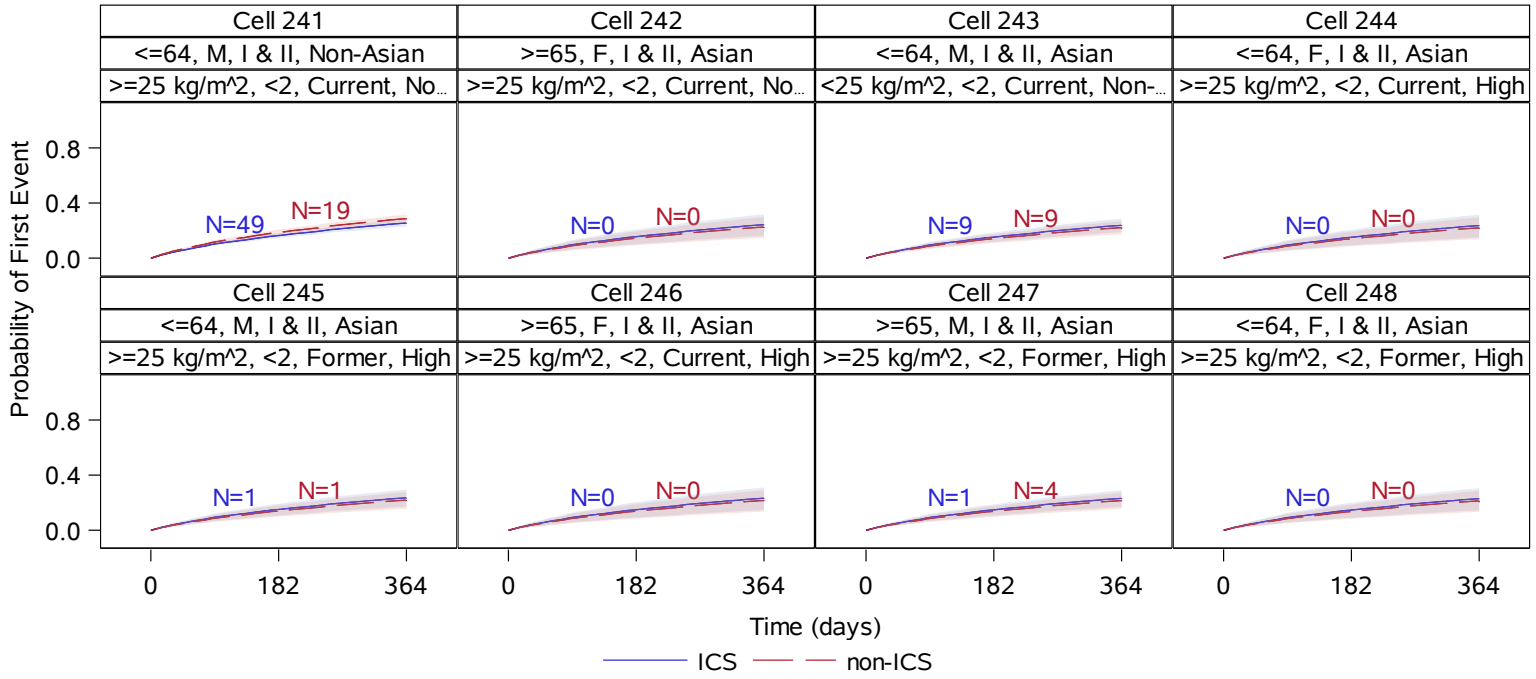

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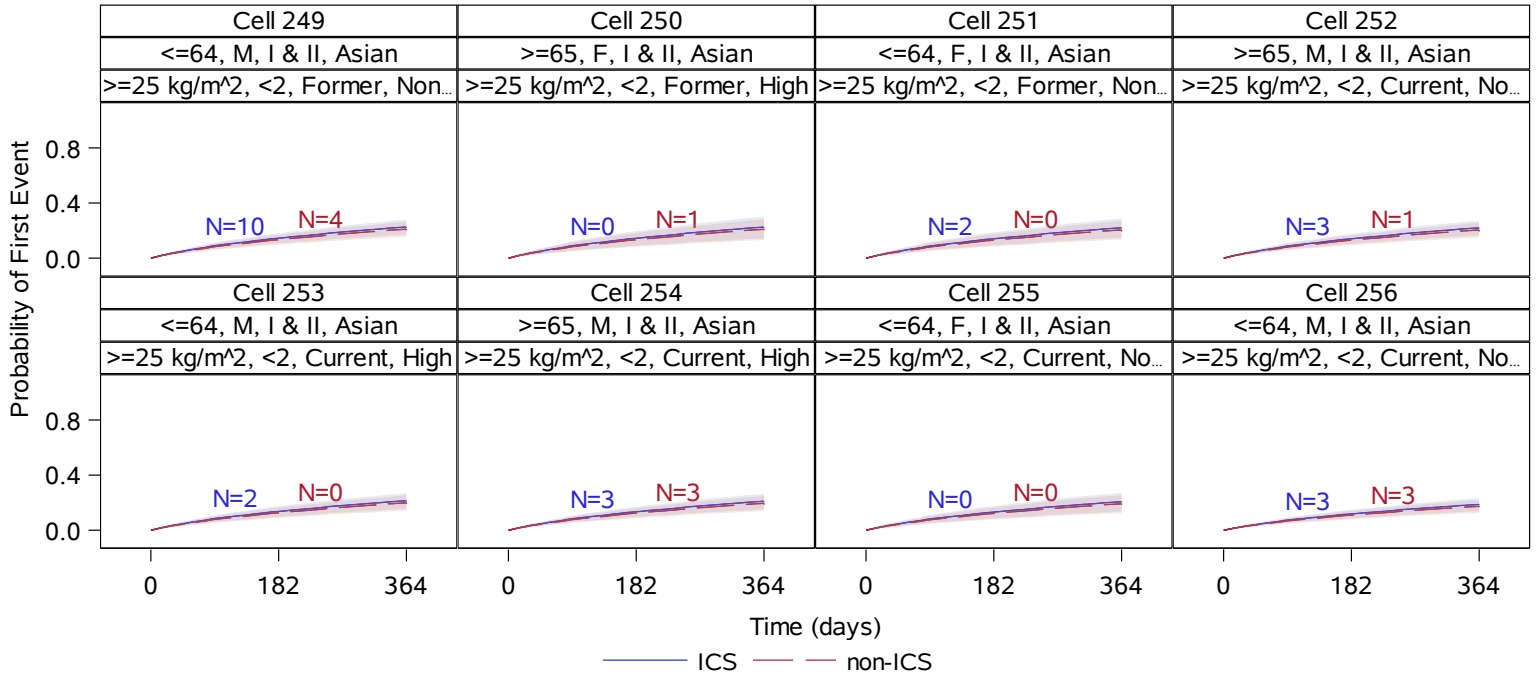

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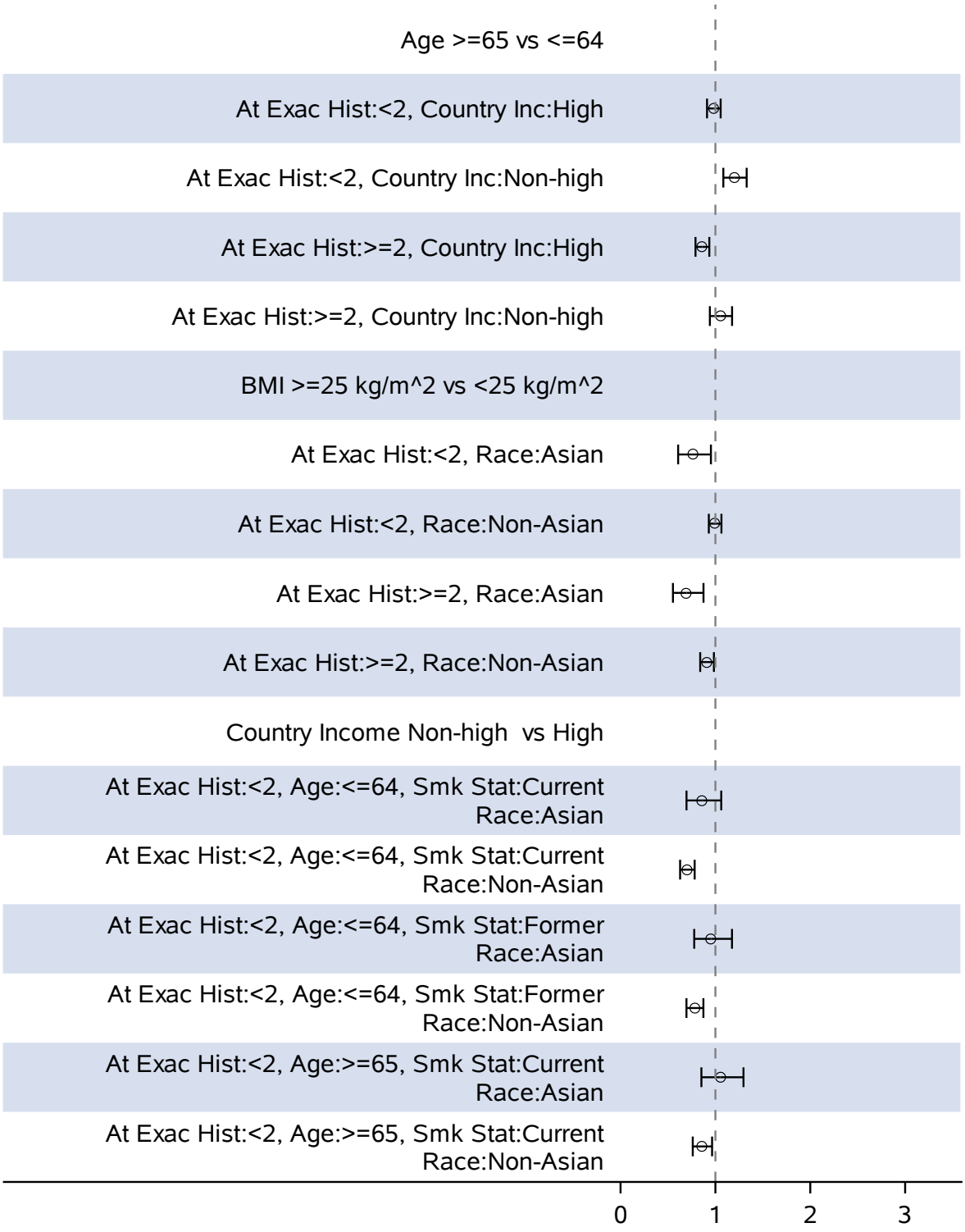
PPD

Figure 2.50
Hazard Ratios from Selected Exacerbation Cox Model (Based on Nine Covariates)



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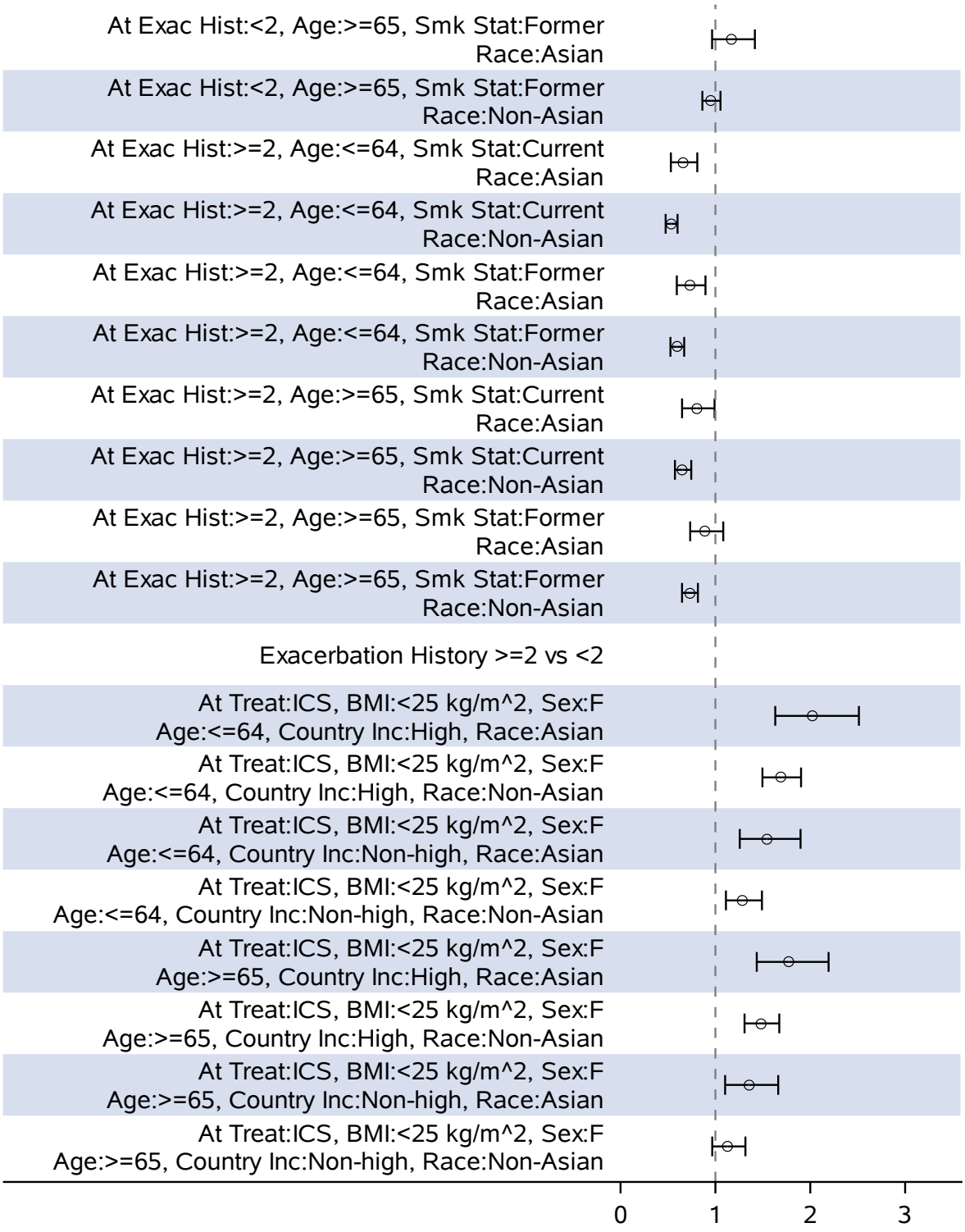
Hazard Ratios from Selected Exacerbation Cox Model (Based on Nine Covariates)



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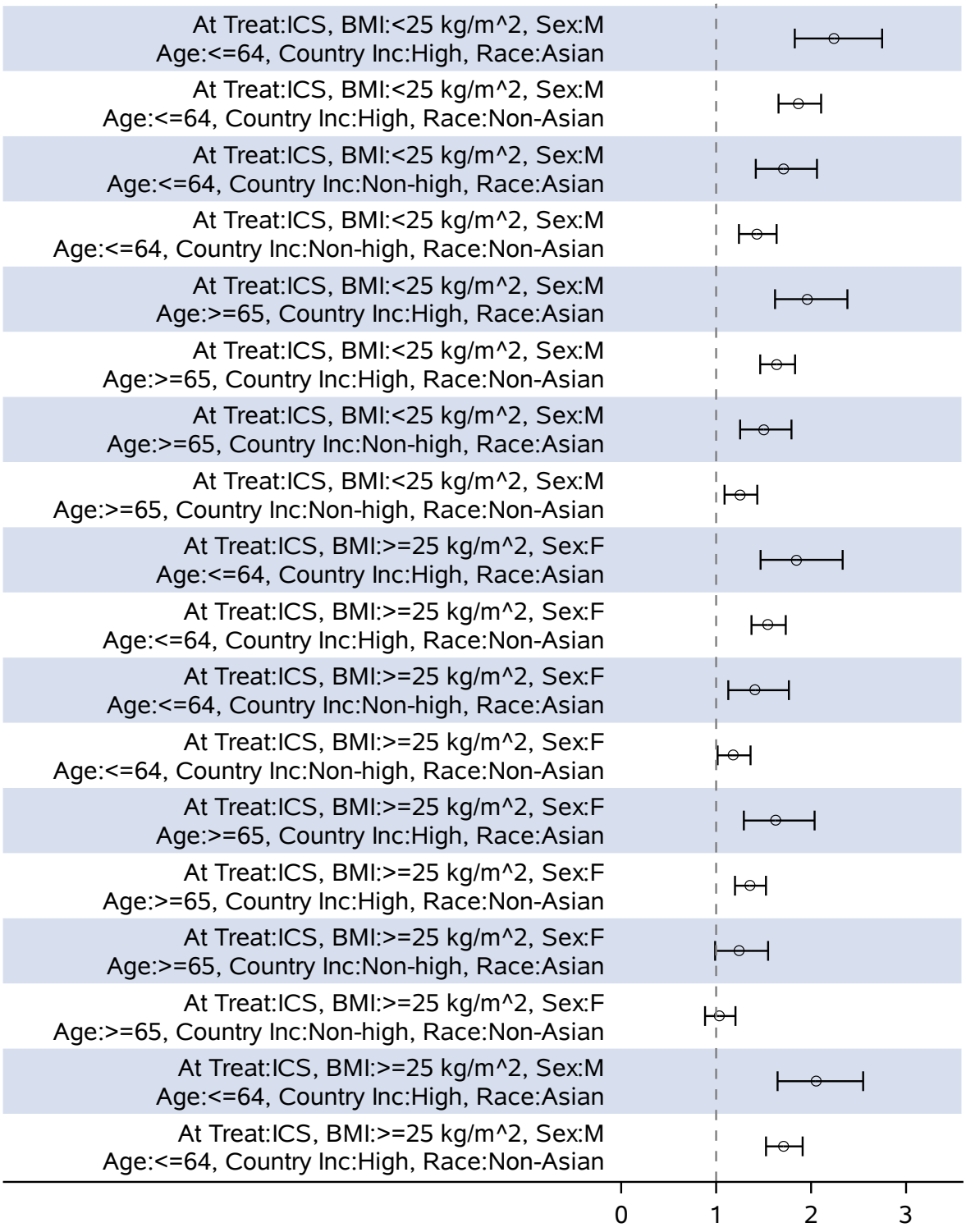

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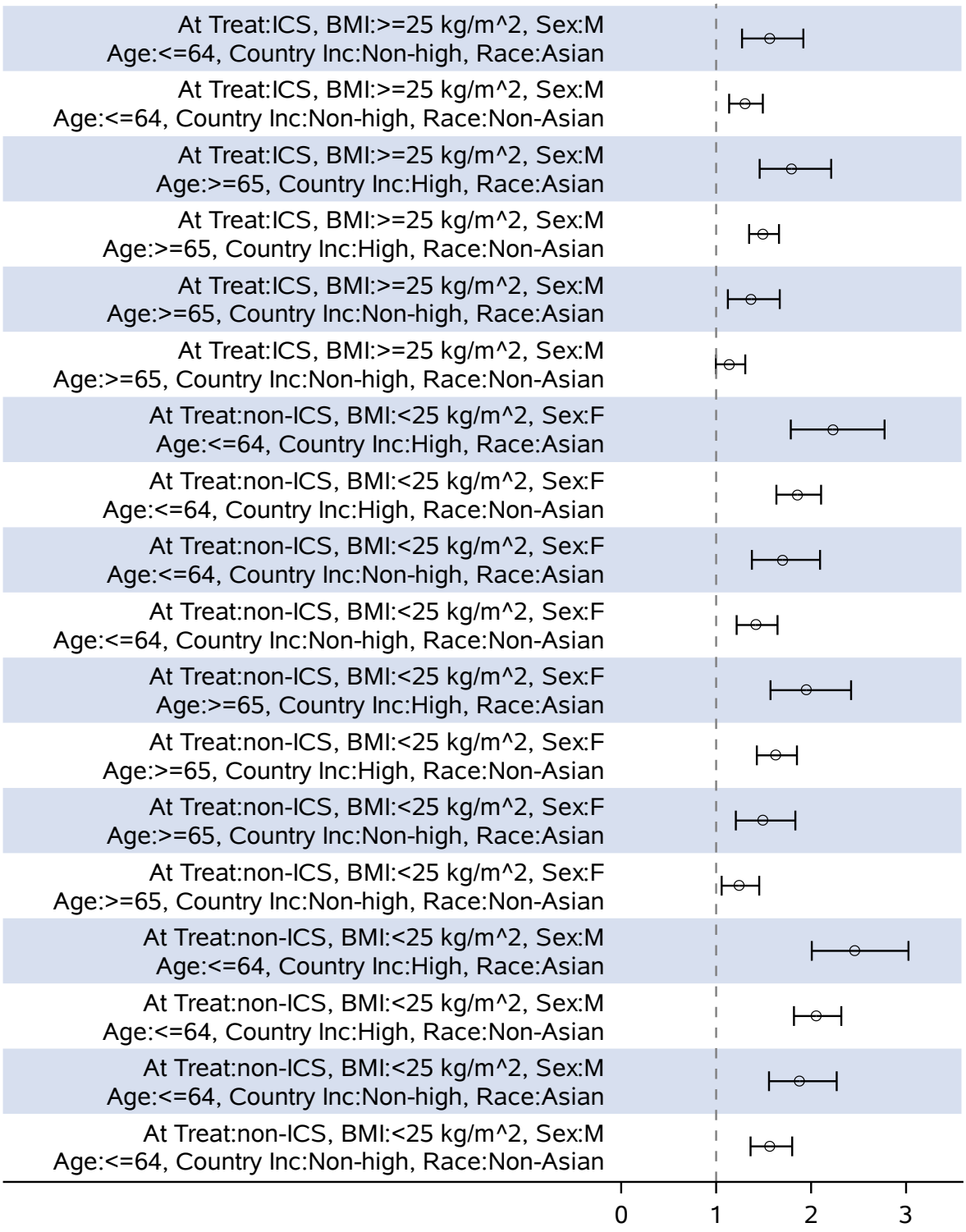

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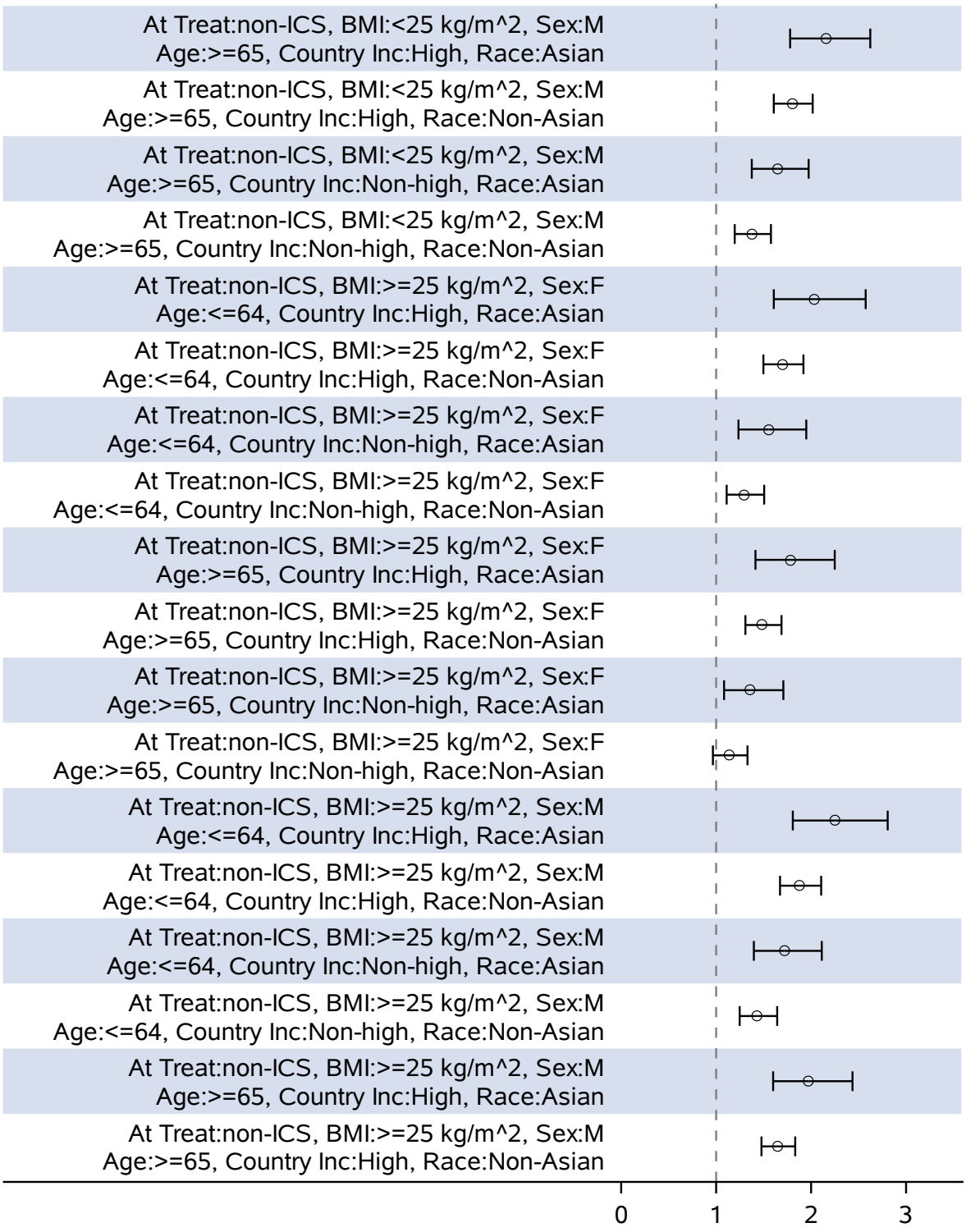

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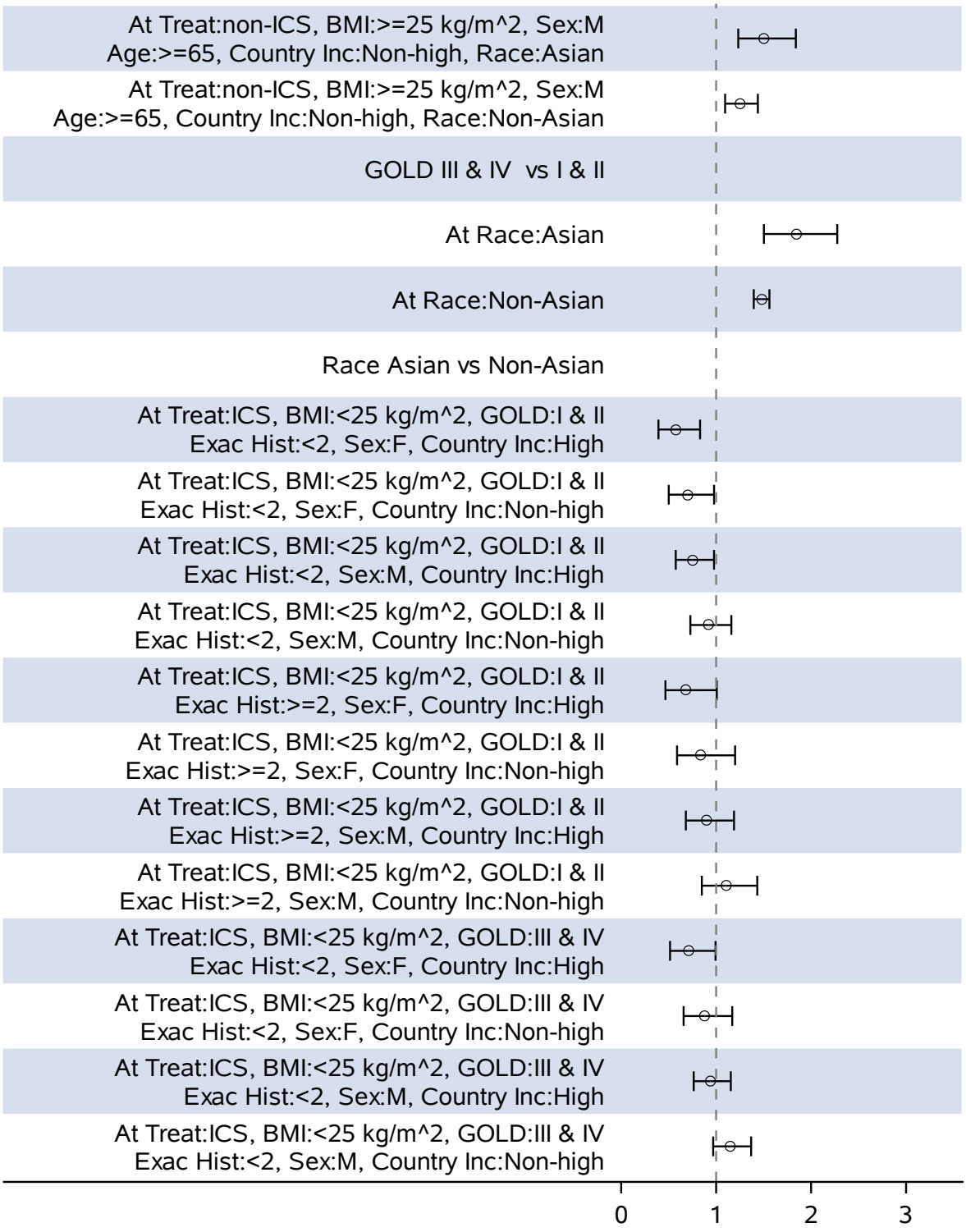

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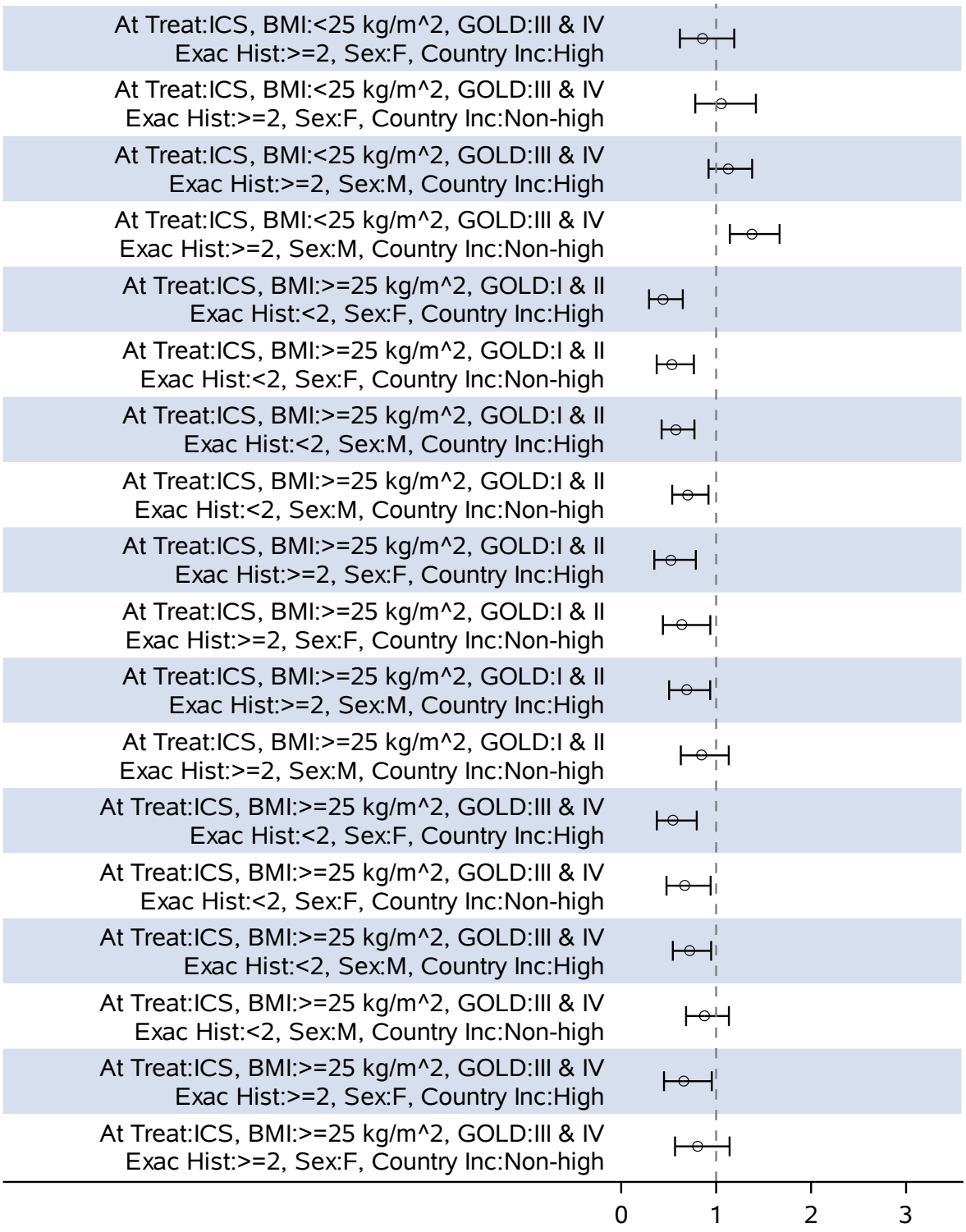

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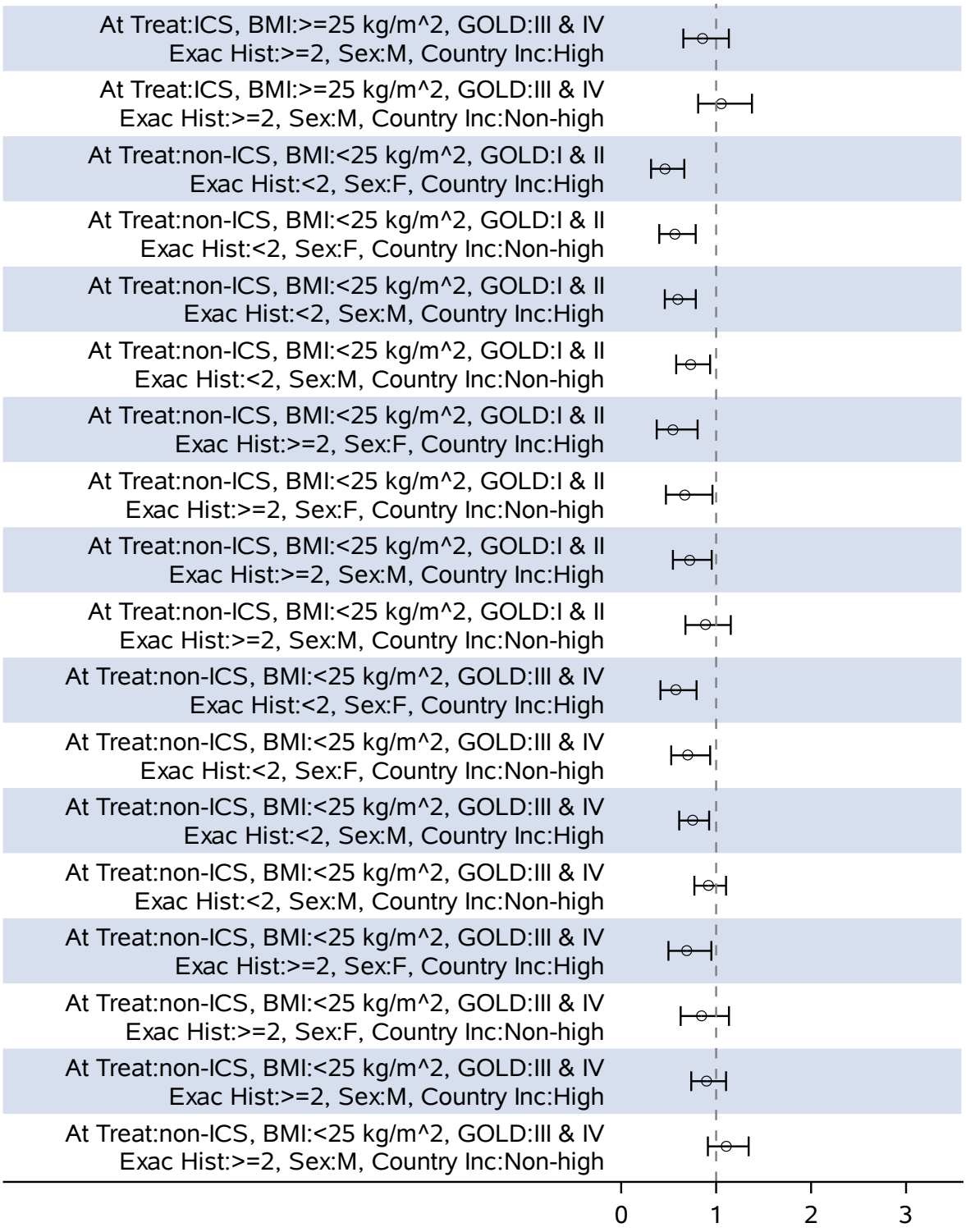

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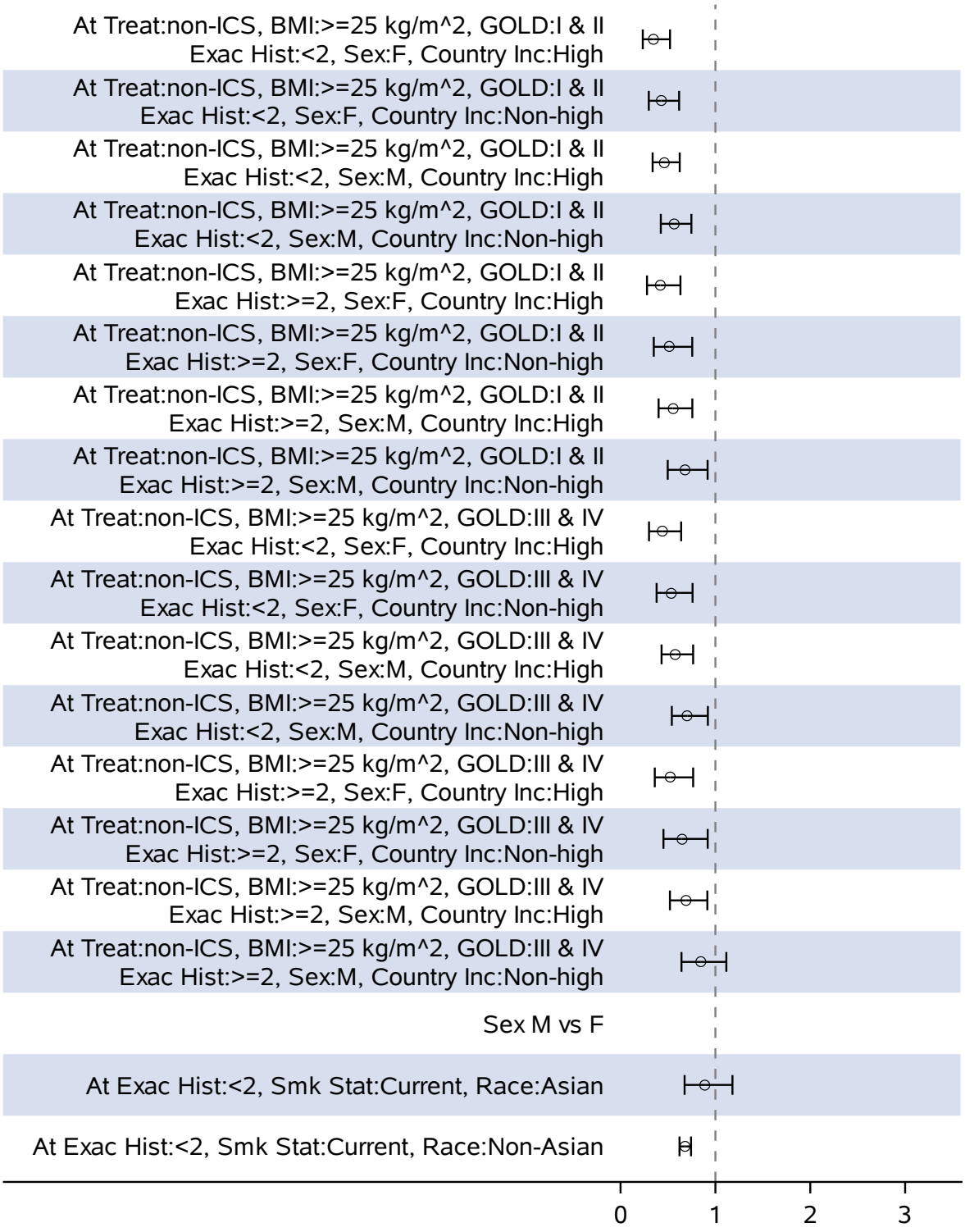


Figure 2.50
Hazard Ratios from Selected Exacerbation Cox Model (Based on Nine Covariates)

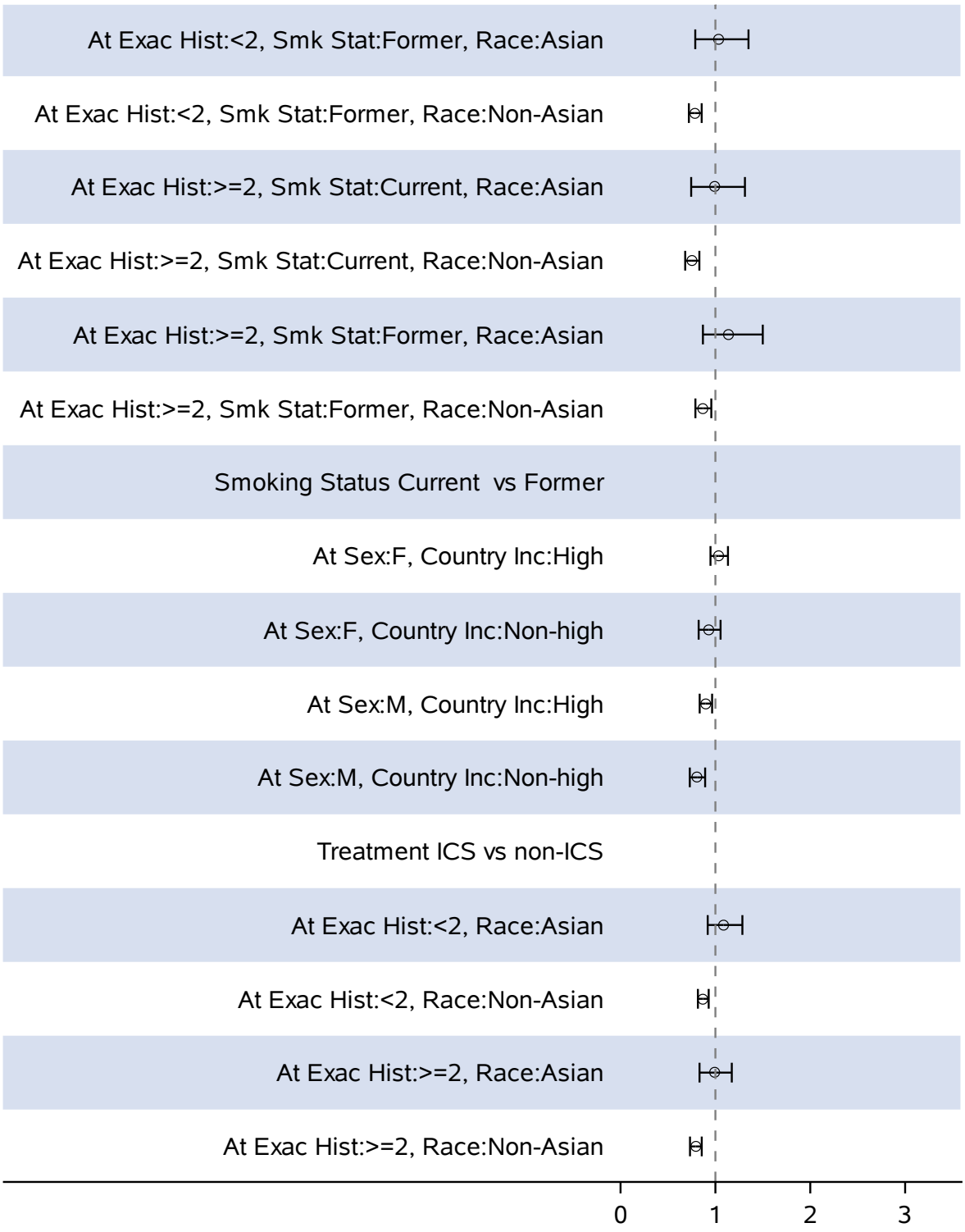


Figure 9.3
Hazard Ratios from Selected Exacerbation Cox Model (Based on Seven Covariates Pneumonia Model)

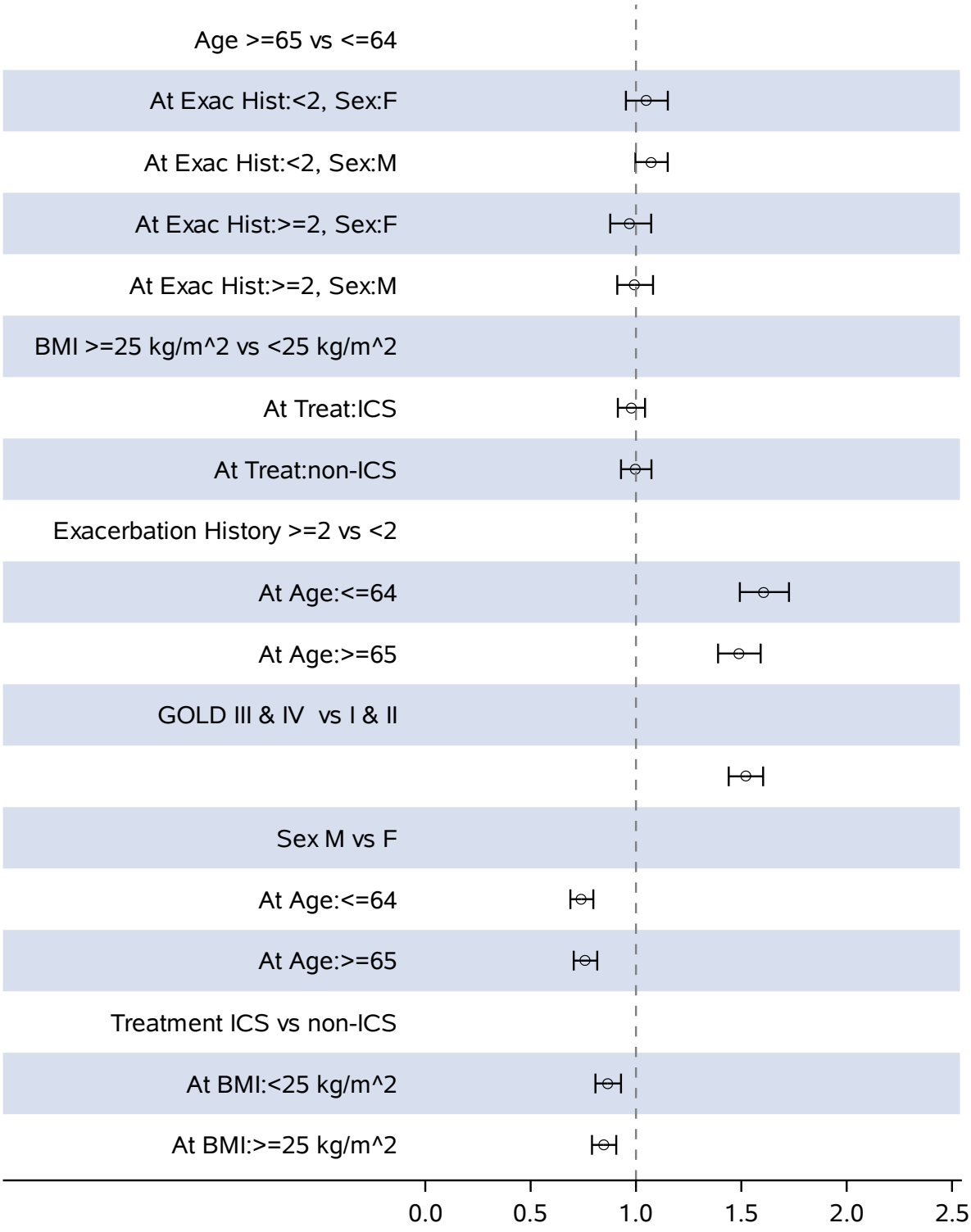
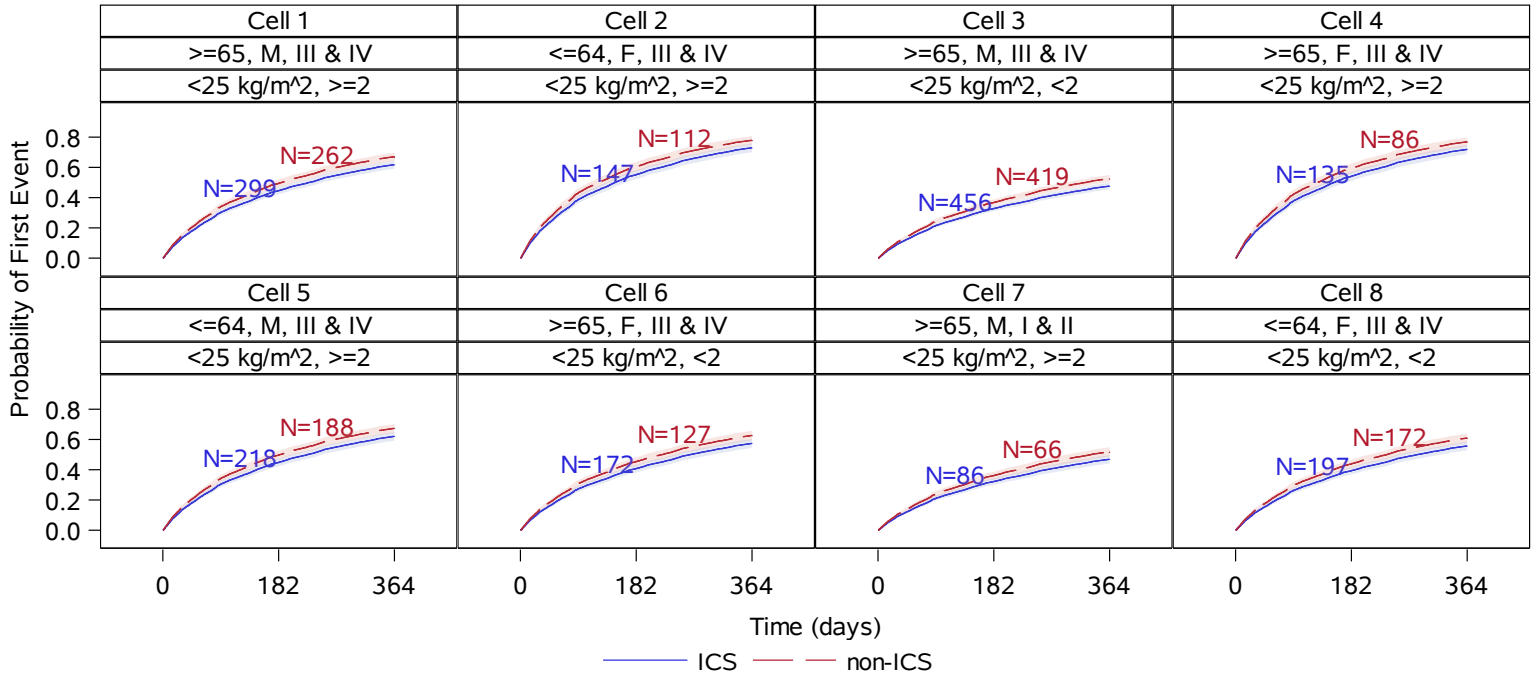


Figure 9.4
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Seven Covariates Pneumonia Model)



Cell Header Line 1: Age, Sex, GOLD
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Note: Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

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Probability of First Exacerbation During Year on Study Treatment Survival Curves
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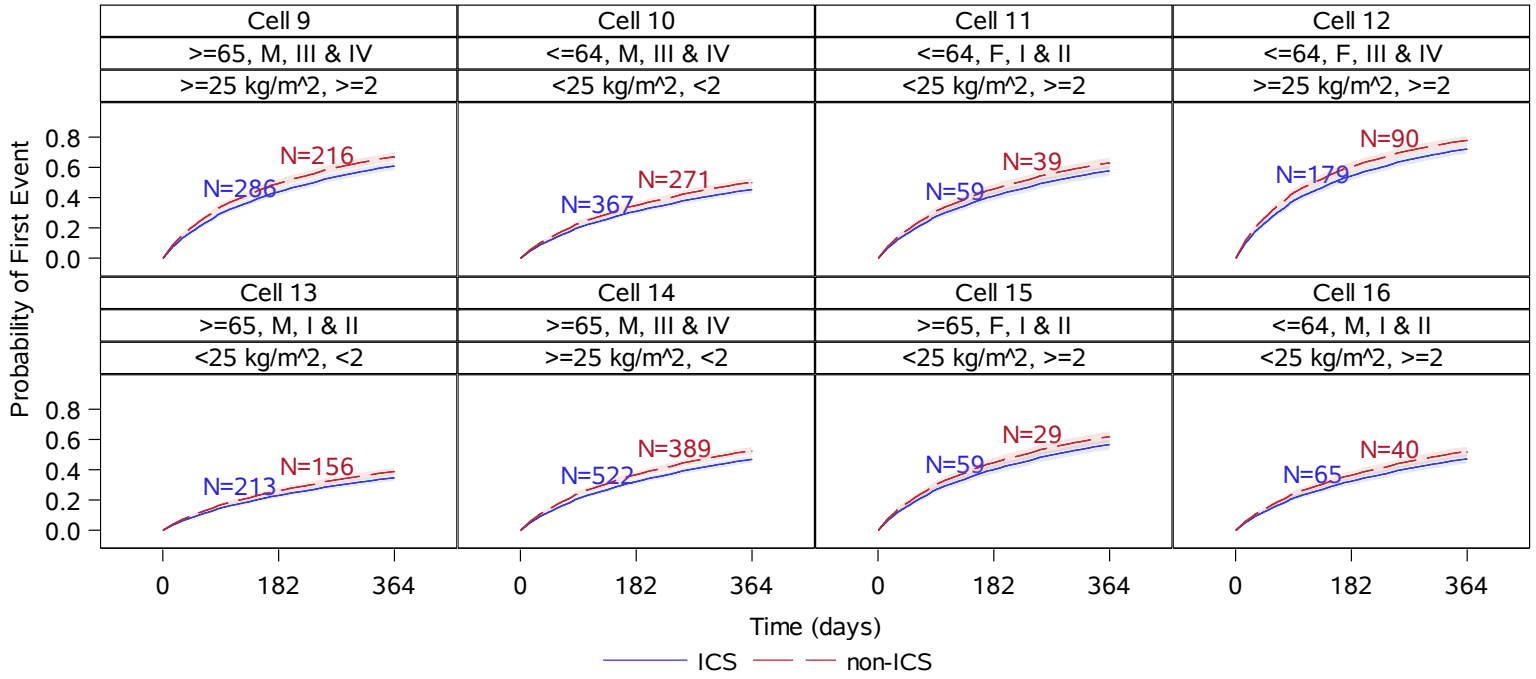

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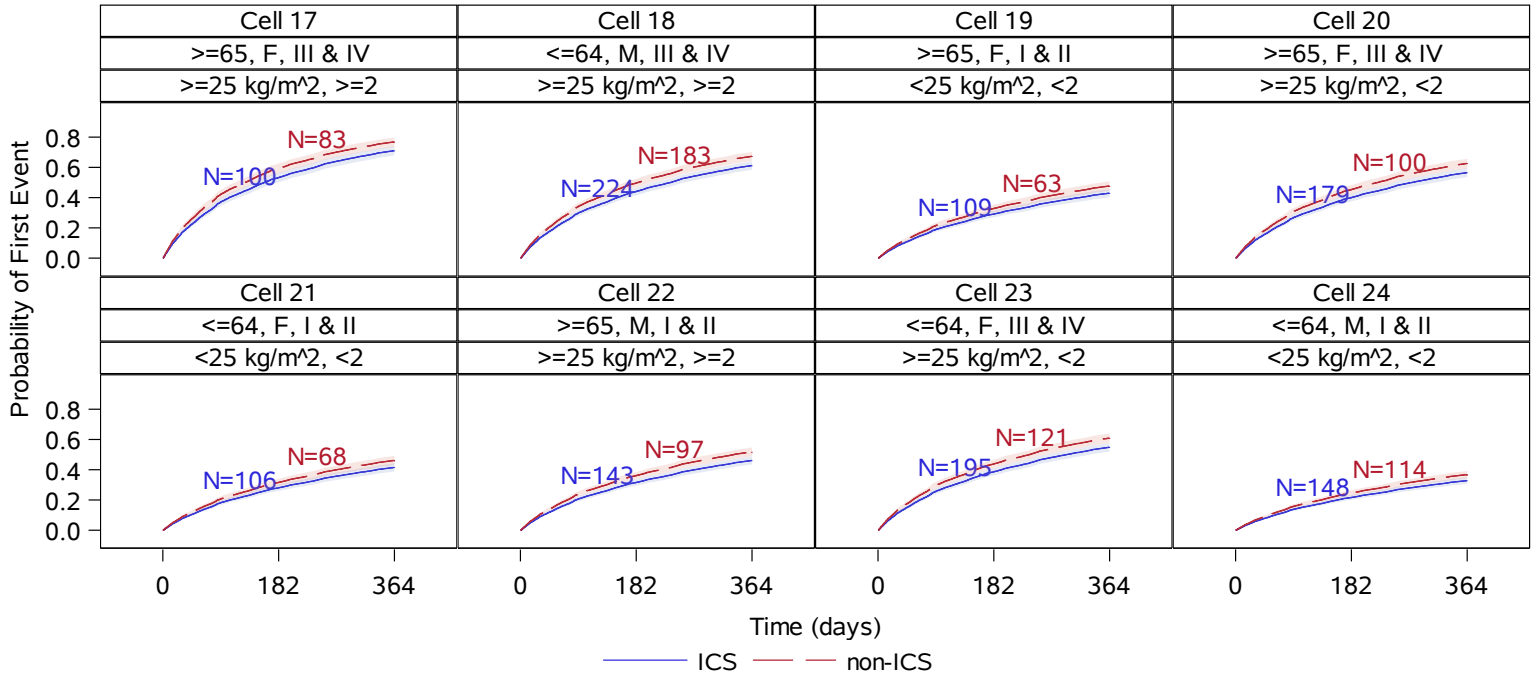
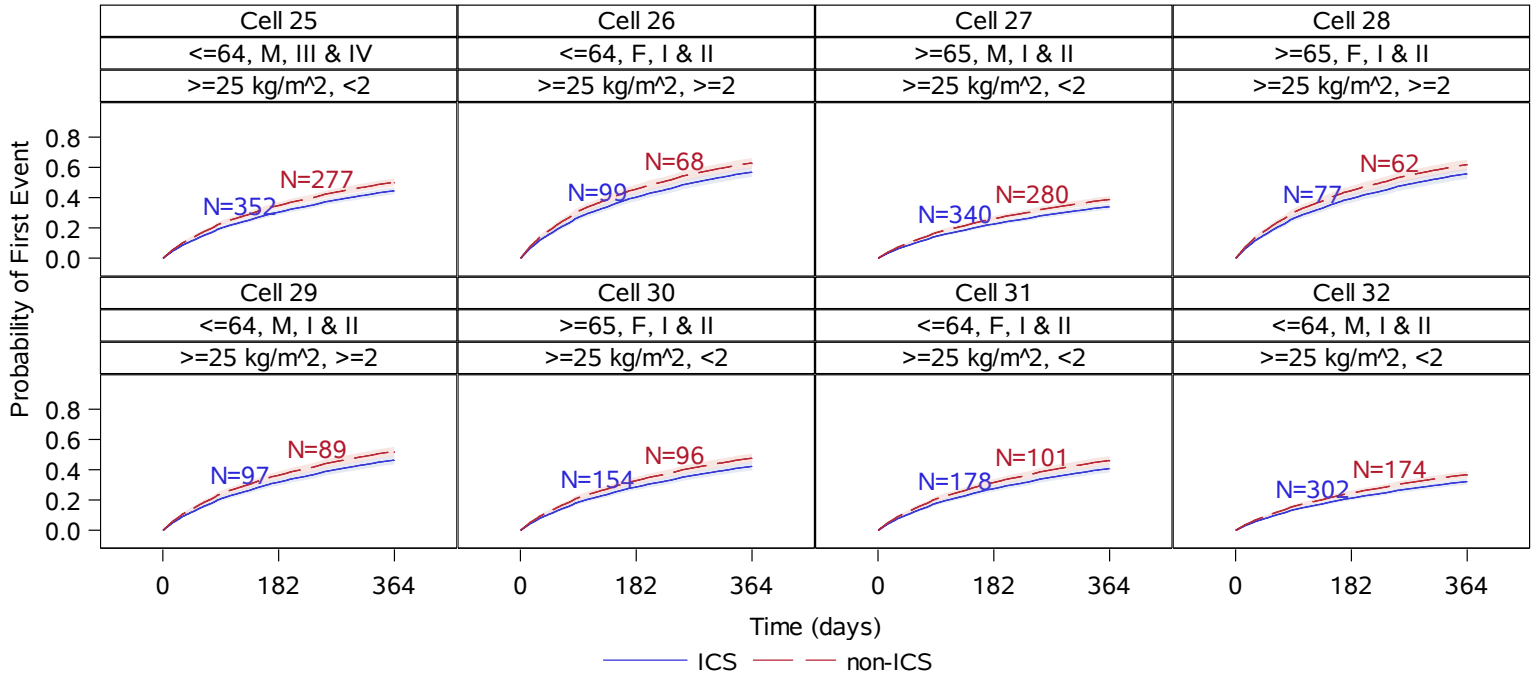
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Seven Covariates Pneumonia Model)



Cell Header Line 1: Age, Sex, GOLD
Cell Header Line 2: BMI, Exac.
Note: Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

Figure 9.4
Probability of First Exacerbation During Year on Study Treatment Survival Curves
(Based on Seven Covariates Pneumonia Model)



Cell Header Line 1: Age, Sex, GOLD
Cell Header Line 2: BMI, Exac.
Note: Ns presented are subgroup numbers, subjects without covariates will not contribute to the model.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 1	AIC	18469.0	
Iteration 1	Type 3 Wald p-values	SUSMHS*TREAT	0.981
		EBHIS2*GOLDGR	0.936
		SUSMHS	0.920
		SEX	0.857
		BMIGRP*GOLDGR	0.850
		BMIGRP*SUSMHS	0.847
		AGEGRP1*BMIGRP	0.809
		GOLDGR*SUSMHS	0.793
		AGEGRP1*TREAT	0.775
		AGEGRP1*GOLDGR	0.633
		AGEGRP1*SUSMHS	0.609
		GOLDGR*SEX	0.581
		BMIGRP*EBHIS2	0.451
		GOLDGR*TREAT	0.449
		SEX*TREAT	0.357
		SEX*SUSMHS	0.343
		EBHIS2*SUSMHS	0.277
		EBHIS2*SEX	0.228
		AGEGRP1*SEX	0.154
		EBHIS2*TREAT	0.144
		BMIGRP*SEX	0.136
		AGEGRP1*EBHIS2	0.101
		AGEGRP1	0.041*
		BMIGRP*TREAT	0.013*
		BMIGRP	0.004*
		EBHIS2	0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 1	Removed Effect	SUSMHS*TREAT	0.981
Iteration 1	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 2	AIC	18467.0	
Iteration 2	Type 3 Wald p-values	EBHIS2*GOLDGR	0.936
		SUSMHS	0.922
		SEX	0.857
		BMIGRP*GOLDGR	0.850
		BMIGRP*SUSMHS	0.848
		AGEGRP1*BMIGRP	0.810
		GOLDGR*SUSMHS	0.793
		AGEGRP1*TREAT	0.763
		AGEGRP1*GOLDGR	0.633
		AGEGRP1*SUSMHS	0.609
		GOLDGR*SEX	0.581
		BMIGRP*EBHIS2	0.451
		GOLDGR*TREAT	0.447
		SEX*TREAT	0.356
		SEX*SUSMHS	0.343
		EBHIS2*SUSMHS	0.277
		EBHIS2*SEX	0.228
		AGEGRP1*SEX	0.154
		EBHIS2*TREAT	0.144
		BMIGRP*SEX	0.136
		AGEGRP1*EBHIS2	0.101
		AGEGRP1	0.040*
		BMIGRP*TREAT	0.012*
		BMIGRP	0.004*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 2	Removed Effect	EBHIS2*GOLDGR	0.936

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

PPD

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description	
Iteration 2	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 3	AIC	18465.0	
Iteration 3	Type 3 Wald p-values	SUSMHS	0.923
		SEX	0.853
		BMIGRP*GOLDGR	0.851
		BMIGRP*SUSMHS	0.848
		AGEGRP1*BMIGRP	0.808
		GOLDGR*SUSMHS	0.794
		AGEGRP1*TREAT	0.762
		AGEGRP1*GOLDGR	0.629
		AGEGRP1*SUSMHS	0.609
		GOLDGR*SEX	0.584
		GOLDGR*TREAT	0.449
		BMIGRP*EBHIS2	0.442
		SEX*TREAT	0.356
		SEX*SUSMHS	0.342
		EBHIS2*SUSMHS	0.273
		EBHIS2*SEX	0.229
		AGEGRP1*SEX	0.154
		EBHIS2*TREAT	0.144
		BMIGRP*SEX	0.136
		AGEGRP1*EBHIS2	0.100*
		AGEGRP1	0.040*
		BMIGRP*TREAT	0.012*
		BMIGRP	0.004*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 3	Removed Effect	BMIGRP*GOLDGR	0.851

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description	
Iteration 3	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

PPD

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 4	AIC	18463.0	
Iteration 4	Type 3 Wald p-values	SUSMHS	0.913
		SEX	0.851
		BMIGRP*SUSMHS	0.837
		GOLDGR*SUSMHS	0.815
		AGEGRP1*BMIGRP	0.801
		AGEGRP1*TREAT	0.761
		AGEGRP1*GOLDGR	0.620
		AGEGRP1*SUSMHS	0.607
		GOLDGR*SEX	0.587
		GOLDGR*TREAT	0.455
		BMIGRP*EBHIS2	0.449
		SEX*TREAT	0.355
		SEX*SUSMHS	0.345
		EBHIS2*SUSMHS	0.274
		EBHIS2*SEX	0.230
		AGEGRP1*SEX	0.153
		EBHIS2*TREAT	0.145
		BMIGRP*SEX	0.139
		AGEGRP1*EBHIS2	0.099*
		AGEGRP1	0.040*
		BMIGRP*TREAT	0.013*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 4	Removed Effect	BMIGRP*SUSMHS	0.837
Iteration 4	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 5	AIC	18461.1	
Iteration 5	Type 3 Wald p-values	SUSMHS	0.902
		SEX	0.848
		AGEGRP1*BMIGRP	0.837
		GOLDGR*SUSMHS	0.794
		AGEGRP1*TREAT	0.761
		AGEGRP1*GOLDGR	0.625
		AGEGRP1*SUSMHS	0.617
		GOLDGR*SEX	0.588
		GOLDGR*TREAT	0.457
		BMIGRP*EBHIS2	0.452
		SEX*TREAT	0.354
		SEX*SUSMHS	0.348
		EBHIS2*SUSMHS	0.277
		EBHIS2*SEX	0.229
		AGEGRP1*SEX	0.153
		EBHIS2*TREAT	0.144
		BMIGRP*SEX	0.142
		AGEGRP1*EBHIS2	0.100*
		AGEGRP1	0.039*
		BMIGRP*TREAT	0.013*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 5	Removed Effect	AGEGRP1*BMIGRP	0.837
Iteration 5	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 6	AIC	18459.1	
Iteration 6	Type 3 Wald p-values	SUSMHS	0.903
		SEX	0.849
		GOLDGR*SUSMHS	0.793
		AGEGRP1*TREAT	0.751
		AGEGRP1*GOLDGR	0.641
		AGEGRP1*SUSMHS	0.633
		GOLDGR*SEX	0.592
		BMIGRP*EBHIS2	0.460
		GOLDGR*TREAT	0.458
		SEX*TREAT	0.351
		SEX*SUSMHS	0.345
		EBHIS2*SUSMHS	0.278
		EBHIS2*SEX	0.228
		AGEGRP1*SEX	0.151
		EBHIS2*TREAT	0.144
		BMIGRP*SEX	0.129
		AGEGRP1*EBHIS2	0.101
		AGEGRP1	0.038*
		BMIGRP*TREAT	0.013*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 6	Removed Effect	GOLDGR*SUSMHS	0.793
Iteration 6	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 7	AIC	18457.2	
Iteration 7	Type 3 Wald p-values	SEX	0.840
		SUSMHS	0.804
		AGEGRP1*TREAT	0.750
		AGEGRP1*SUSMHS	0.623
		GOLDGR*SEX	0.604
		AGEGRP1*GOLDGR	0.576
		BMIGRP*EBHIS2	0.459
		GOLDGR*TREAT	0.457
		SEX*SUSMHS	0.354
		SEX*TREAT	0.351
		EBHIS2*SUSMHS	0.286
		EBHIS2*SEX	0.228
		AGEGRP1*SEX	0.149
		EBHIS2*TREAT	0.145
		BMIGRP*SEX	0.130
		AGEGRP1*EBHIS2	0.102
		AGEGRP1	0.035*
		BMIGRP*TREAT	0.013*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 7	Removed Effect	AGEGRP1*TREAT	0.750
Iteration 7	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 8	AIC	18455.3	
Iteration 8	Type 3 Wald p-values	SEX	0.851
		SUSMHS	0.804
		AGEGRP1*SUSMHS	0.624
		GOLDGR*SEX	0.607
		AGEGRP1*GOLDGR	0.583
		GOLDGR*TREAT	0.463
		BMIGRP*EBHIS2	0.459
		SEX*TREAT	0.372
		SEX*SUSMHS	0.354
		EBHIS2*SUSMHS	0.287
		EBHIS2*SEX	0.231
		AGEGRP1*SEX	0.154
		EBHIS2*TREAT	0.140
		BMIGRP*SEX	0.131
		AGEGRP1*EBHIS2	0.100*
		AGEGRP1	0.023*
		BMIGRP*TREAT	0.013*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 8	Removed Effect	AGEGRP1*SUSMHS	0.624
Iteration 8	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 9	AIC	18453.5	
Iteration 9	Type 3 Wald p-values	SEX	0.851
		SUSMHS	0.822
		GOLDGR*SEX	0.612
		AGEGRP1*GOLDGR	0.601
		GOLDGR*TREAT	0.464
		BMIGRP*EBHIS2	0.461
		SEX*TREAT	0.373
		SEX*SUSMHS	0.322
		EBHIS2*SUSMHS	0.299
		EBHIS2*SEX	0.234
		AGEGRP1*SEX	0.145
		EBHIS2*TREAT	0.138
		BMIGRP*SEX	0.131
		AGEGRP1*EBHIS2	0.102
		AGEGRP1	0.022*
		BMIGRP*TREAT	0.013*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 9	Removed Effect	GOLDGR*SEX	0.612
Iteration 9	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 10	AIC	18451.8	
Iteration 10	Type 3 Wald p-values	SUSMHS	0.806
		SEX	0.690
		AGEGRP1*GOLDGR	0.652
		GOLDGR*TREAT	0.483
		BMIGRP*EBHIS2	0.465
		SEX*TREAT	0.382
		SEX*SUSMHS	0.302
		EBHIS2*SUSMHS	0.298
		EBHIS2*SEX	0.247
		AGEGRP1*SEX	0.153
		EBHIS2*TREAT	0.137
		BMIGRP*SEX	0.113
		AGEGRP1*EBHIS2	0.100
		AGEGRP1	0.023*
		BMIGRP*TREAT	0.012*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 10	Removed Effect	AGEGRP1*GOLDGR	0.652
Iteration 10	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 11	AIC	18450.0	
Iteration 11	Type 3 Wald p-values	SUSMHS	0.812
		SEX	0.688
		GOLDGR*TREAT	0.479
		BMIGRP*EBHIS2	0.469
		SEX*TREAT	0.382
		SEX*SUSMHS	0.303
		EBHIS2*SUSMHS	0.297
		EBHIS2*SEX	0.248
		AGEGRP1*SEX	0.160
		EBHIS2*TREAT	0.137
		BMIGRP*SEX	0.115
		AGEGRP1*EBHIS2	0.092*
		AGEGRP1	0.022*
		BMIGRP*TREAT	0.012*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 11	Removed Effect	GOLDGR*TREAT	0.479
Iteration 11	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 12	AIC	18448.5	
Iteration 12	Type 3 Wald p-values	SUSMHS	0.816
		SEX	0.703
		BMIGRP*EBHIS2	0.472
		SEX*TREAT	0.405
		SEX*SUSMHS	0.306
		EBHIS2*SUSMHS	0.302
		EBHIS2*SEX	0.245
		AGEGRP1*SEX	0.160
		EBHIS2*TREAT	0.151
		BMIGRP*SEX	0.113
		AGEGRP1*EBHIS2	0.093*
		AGEGRP1	0.022*
		BMIGRP*TREAT	0.009*
		BMIGRP	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 12	Removed Effect	BMIGRP*EBHIS2	0.472
Iteration 12	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 13	AIC	18447.0	
Iteration 13	Type 3 Wald p-values	SUSMHS	0.803
		SEX	0.690
		SEX*TREAT	0.407
		EBHIS2*SUSMHS	0.339
		SEX*SUSMHS	0.306
		EBHIS2*SEX	0.259
		EBHIS2*TREAT	0.163
		AGEGRP1*SEX	0.162
		BMIGRP*SEX	0.126
		AGEGRP1*EBHIS2	0.099*
		AGEGRP1	0.021*
		BMIGRP*TREAT	0.009*
		BMIGRP	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 13	Removed Effect	SEX*TREAT	0.407
Iteration 13	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 14	AIC	18445.7	
Iteration 14	Type 3 Wald p-values	SEX	0.904
		SUSMHS	0.797
		EBHIS2*SUSMHS	0.339
		SEX*SUSMHS	0.304
		EBHIS2*SEX	0.270
		EBHIS2*TREAT	0.181
		AGEGRP1*SEX	0.166
		BMIGRP*SEX	0.136
		AGEGRP1*EBHIS2	0.095*
		AGEGRP1	0.021*
		BMIGRP*TREAT	0.010*
		BMIGRP	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 14	Removed Effect	EBHIS2*SUSMHS	0.339
Iteration 14	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 15	AIC	18444.6	
Iteration 15	Type 3 Wald p-values	SEX	0.888
		SUSMHS	0.680
		SEX*SUSMHS	0.342
		EBHIS2*SEX	0.304
		EBHIS2*TREAT	0.176
		AGEGRP1*SEX	0.156
		AGEGRP1*EBHIS2	0.138
		BMIGRP*SEX	0.134
		AGEGRP1	0.020*
		BMIGRP*TREAT	0.010*
		BMIGRP	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 15	Removed Effect	SEX*SUSMHS	0.342
Iteration 15	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 16	AIC	18443.5	
Iteration 16	Type 3 Wald p-values	SUSMHS	0.994
		SEX	0.852
		EBHIS2*SEX	0.301
		EBHIS2*TREAT	0.177
		BMIGRP*SEX	0.163
		AGEGRP1*EBHIS2	0.142
		AGEGRP1*SEX	0.089*
		AGEGRP1	0.025*
		BMIGRP*TREAT	0.009*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 16	Removed Effect	SUSMHS	0.994
Iteration 16	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 17	AIC	18441.6	
Iteration 17	Type 3 Wald p-values	SEX	0.853
		EBHIS2*SEX	0.302
		EBHIS2*TREAT	0.177
		BMIGRP*SEX	0.163
		AGEGRP1*EBHIS2	0.141
		AGEGRP1*SEX	0.089*
		AGEGRP1	0.021*
		BMIGRP*TREAT	0.009*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 17	Removed Effect	EBHIS2*SEX	0.302
Iteration 17	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 18	AIC	18440.7	
Iteration 18	Type 3 Wald p-values	SEX	0.712
		EBHIS2*TREAT	0.191
		BMIGRP*SEX	0.167
		AGEGRP1*EBHIS2	0.098*
		AGEGRP1*SEX	0.075*
		AGEGRP1	0.026*
		BMIGRP*TREAT	0.009*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 18	Removed Effect	EBHIS2*TREAT	0.191
Iteration 18	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 19	AIC	18440.4	
Iteration 19	Type 3 Wald p-values	SEX	0.705
		BMIGRP*SEX	0.166
		AGEGRP1*EBHIS2	0.099*
		AGEGRP1*SEX	0.079*
		AGEGRP1	0.026*
		BMIGRP*TREAT	0.010*
		BMIGRP	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 19	Removed Effect	BMIGRP*SEX	0.166
Iteration 19	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 20	AIC	18440.3	
Iteration 20	Type 3 Wald p-values	SEX	0.583
		AGEGRP1*EBHIS2	0.096*
		AGEGRP1*SEX	0.078*
		AGEGRP1	0.027*
		BMIGRP*TREAT	0.012*
		EBHIS2	<0.001*
		BMIGRP	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.06 (0.04,0.07)	0.03 (0.02,0.04)	0.02 (2 / 106)	0.00 (0 / 68)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.08 (0.06,0.09)	0.04 (0.03,0.05)	0.05 (3 / 59)	0.03 (1 / 39)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.04 (0.03,0.05)	0.03 (0.02,0.04)	0.04 (7 / 178)	0.06 (6 / 101)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.05 (5 / 99)	0.09 (6 / 68)

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.05 (0.04,0.06)	0.03 (0.02,0.04)	0.05 (7 / 148)	0.03 (3 / 114)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.07 (0.06,0.09)	0.04 (0.03,0.05)	0.03 (2 / 65)	0.00 (0 / 40)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.03 (0.03,0.04)	0.03 (0.02,0.03)	0.02 (5 / 302)	0.02 (3 / 174)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.04)	0.03 (3 / 97)	0.04 (4 / 89)

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ F	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.08 (0.07,0.10)	0.05 (0.04,0.06)	0.09 (18/ 197)	0.03 (5 / 172)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.11 (0.09,0.14)	0.06 (0.05,0.08)	0.07 (11/ 147)	0.06 (7 / 112)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.06 (0.04,0.07)	0.04 (0.03,0.05)	0.06 (12/ 195)	0.05 (6 / 121)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.08 (0.06,0.09)	0.06 (0.04,0.07)	0.07 (12/ 179)	0.00 (0 / 90)

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.08 (0.06,0.09)	0.04 (0.03,0.05)	0.07 (27/ 367)	0.04 (10/ 271)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.11 (0.09,0.12)	0.06 (0.05,0.07)	0.13 (28/ 218)	0.07 (13/ 188)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.05 (19/ 352)	0.03 (8 / 277)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.07 (0.06,0.08)	0.05 (0.04,0.07)	0.04 (9 / 224)	0.04 (8 / 183)

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.06 (0.05,0.08)	0.04 (0.03,0.04)	0.02 (2 / 109)	0.02 (1 / 63)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.07 (0.06,0.09)	0.04 (0.03,0.05)	0.15 (9 / 59)	0.03 (1 / 29)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.04 (0.03,0.05)	0.03 (0.02,0.04)	0.03 (5 / 154)	0.03 (3 / 96)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.04 (3 / 77)	0.00 (0 / 62)

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.08 (0.06,0.09)	0.04 (0.03,0.05)	0.07 (14/ 213)	0.02 (3 / 156)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.08 (0.07,0.10)	0.05 (0.04,0.06)	0.05 (4 / 86)	0.08 (5 / 66)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.05 (17/ 340)	0.04 (11/ 280)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.06 (0.04,0.07)	0.04 (0.03,0.05)	0.04 (6 / 143)	0.03 (3 / 97)

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.10 (0.08,0.11)	0.05 (0.04,0.07)	0.08 (14/ 172)	0.02 (3 / 127)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.11 (0.09,0.13)	0.06 (0.05,0.07)	0.11 (15/ 135)	0.03 (3 / 86)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.06 (0.05,0.08)	0.05 (0.04,0.06)	0.04 (7 / 179)	0.05 (5 / 100)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.07 (0.06,0.09)	0.05 (0.04,0.07)	0.09 (9 / 100)	0.06 (5 / 83)

Protocol: 207941
Population: Intent-to-Treat

Table 1.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M	<25 kg/m^2/ <2	1.83 (1.54,2.17)	0.11 (0.10,0.13)	0.06 (0.05,0.07)	0.11 (49/ 456)	0.05 (19/ 419)
	<25 kg/m^2/ >=2	1.83 (1.54,2.17)	0.12 (0.11,0.14)	0.07 (0.06,0.08)	0.11 (34/ 299)	0.06 (17/ 262)
	>=25 kg/m^2/ <2	1.32 (1.09,1.59)	0.07 (0.06,0.09)	0.06 (0.05,0.07)	0.06 (33/ 522)	0.04 (14/ 389)
	>=25 kg/m^2/ >=2	1.32 (1.09,1.59)	0.08 (0.07,0.10)	0.06 (0.05,0.08)	0.07 (19/ 286)	0.05 (11/ 216)

Protocol: 207941
Population: Intent-to-Treat

Table 1.3
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Seven Covariates)

Statistic	Level	
Type 3 Wald p-values	Sex	0.583
	Exacerbation History by Age	0.096
	Sex by Age	0.078
	Age	0.027
	Treatment by BMI	0.012
	Exacerbation History	<0.001
	BMI	<0.001
	GOLD	<0.001
	Treatment	<0.001

Protocol: 207941
Population: Intent-to-Treat

Table 1.3
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Seven Covariates)

Statistic	Level	
Hazard Ratio	Age >=65 vs <=64	
95% CI		
	At Exacerbation History:<2 Sex:F	1.15 (0.89, 1.49)
	At Exacerbation History:<2 Sex:M	1.47 (1.24, 1.75)
	At Exacerbation History:>=2 Sex:F	0.93 (0.71, 1.22)
	At Exacerbation History:>=2 Sex:M	1.19 (0.96, 1.47)
	BMI >=25 kg/m^2 vs <25 kg/m^2	
	At Treatment:ICS	0.65 (0.56, 0.76)
	At Treatment:non-ICS	0.90 (0.73, 1.11)
	Exacerbation History >=2 vs <2	
	At Age:<=64	1.39 (1.15, 1.68)
	At Age:>=65	1.12 (0.95, 1.32)
	GOLD III & IV: FEV1<50% predicted vs I & II: FEV1>=50% predicted	1.51 (1.32, 1.73)
	Sex M vs F	
	At Age:<=64	0.92 (0.75, 1.12)
	At Age:>=65	1.18 (0.97, 1.43)
	Treatment ICS vs non-ICS	
	At BMI:<25 kg/m^2	1.83 (1.54, 2.17)
	At BMI:>=25 kg/m^2	1.32 (1.09, 1.59)

Protocol: 207941
Population: Intent-to-Treat

Table 1.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Seven Covariates)
Expanded BMI Category

Statistic	Level	
Type 3 Wald p-values	Sex	0.360
	Exacerbation History by Age	0.082
	Sex by Age	0.054
	Age	0.028
	Treatment by BMI	0.026
	Exacerbation History	0.001
	BMI	<0.001
	GOLD	<0.001
	Treatment	<0.001

Protocol: 207941
Population: Intent-to-Treat

Table 1.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Seven Covariates)
Expanded BMI Category

Statistic	Level	
Hazard Ratio	Age >=65 vs <=64	
95% CI		
	At Exacerbation History:<2 Sex:F	1.14 (0.88, 1.48)
	At Exacerbation History:<2 Sex:M	1.50 (1.26, 1.78)
	At Exacerbation History:>=2 Sex:F	0.91 (0.70, 1.20)
	At Exacerbation History:>=2 Sex:M	1.20 (0.97, 1.48)
	BMI >=20 - <22 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.73 (0.56, 0.96)
	At Treatment:non-ICS	0.70 (0.49, 1.02)
	BMI >=22 - <23 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.80 (0.60, 1.07)
	At Treatment:non-ICS	0.56 (0.35, 0.91)
	BMI >=23 - <24 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.74 (0.55, 1.00)
	At Treatment:non-ICS	0.51 (0.32, 0.82)
	BMI >=24 - <25 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.58 (0.42, 0.79)
	At Treatment:non-ICS	0.56 (0.37, 0.87)
	BMI >=25 - <26 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.69 (0.51, 0.94)
	At Treatment:non-ICS	0.62 (0.40, 0.98)
	BMI >=26 - <28 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.56 (0.43, 0.74)
	At Treatment:non-ICS	0.55 (0.37, 0.80)
	BMI >=28 - <30 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.39 (0.27, 0.54)
	At Treatment:non-ICS	0.68 (0.45, 1.01)
	BMI >=30 - <33 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.43 (0.30, 0.60)
	At Treatment:non-ICS	0.50 (0.33, 0.78)
	BMI >=33 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS	0.49 (0.36, 0.68)

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Protocol: 207941
Population: Intent-to-Treat

Table 1.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Seven Covariates)
Expanded BMI Category

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:non-ICS	0.90 (0.61, 1.32)
	Exacerbation History >=2 vs <2	
	At Age:<=64	1.37 (1.14, 1.66)
	At Age:>=65	1.10 (0.93, 1.30)
	GOLD III & IV: FEV1<50% predicted vs I & II: FEV1>=50% predicted	1.47 (1.28, 1.69)
	Sex M vs F	
	At Age:<=64	0.93 (0.76, 1.14)
	At Age:>=65	1.22 (1.01, 1.48)
	Treatment ICS vs non-ICS	
	At BMI:<20 kg/m^2	1.64 (1.23, 2.19)
	At BMI:>=20 - <22 kg/m^2	1.70 (1.19, 2.44)
	At BMI:>=22 - <23 kg/m^2	2.34 (1.45, 3.77)
	At BMI:>=23 - <24 kg/m^2	2.36 (1.47, 3.78)
	At BMI:>=24 - <25 kg/m^2	1.68 (1.07, 2.64)
	At BMI:>=25 - <26 kg/m^2	1.83 (1.16, 2.89)
	At BMI:>=26 - <28 kg/m^2	1.68 (1.16, 2.43)
	At BMI:>=28 - <30 kg/m^2	0.94 (0.61, 1.45)
	At BMI:>=30 - <33 kg/m^2	1.39 (0.87, 2.21)
	At BMI:>=33 kg/m^2	0.90 (0.59, 1.37)

Protocol: 207941
Population: Intent-to-Treat

Table 1.6
Pneumonia Probabilities by BMI Decile (Direct Adjusted Probabilities)
Based on Seven Covariate Selected Model with Expanded BMI Category

BMI Decile Group	ICS (N=6292)	non-ICS (N=4654)
<20 kg/m^2	0.114 (0.095, 0.134)	0.071 (0.055, 0.088)
>=20 - <22 kg/m^2	0.085 (0.067, 0.103)	0.051 (0.036, 0.065)
>=22 - <23 kg/m^2	0.093 (0.071, 0.114)	0.041 (0.024, 0.058)
>=23 - <24 kg/m^2	0.086 (0.065, 0.106)	0.037 (0.022, 0.052)
>=24 - <25 kg/m^2	0.068 (0.050, 0.086)	0.041 (0.026, 0.056)
>=25 - <26 kg/m^2	0.081 (0.061, 0.100)	0.045 (0.028, 0.062)
>=26 - <28 kg/m^2	0.066 (0.052, 0.080)	0.040 (0.028, 0.052)
>=28 - <30 kg/m^2	0.046 (0.033, 0.059)	0.049 (0.033, 0.064)
>=30 - <33 kg/m^2	0.051 (0.036, 0.065)	0.037 (0.023, 0.050)
>=33 kg/m^2	0.058 (0.042, 0.074)	0.064 (0.044, 0.084)

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 1	AIC	112198.8	
Iteration 1	Type 3 Wald p-values	BMIGRP*SUSMHS	0.791
		SUSMHS*TREAT	0.724
		AGEGRP1	0.701
		AGEGRP1*SEX	0.700
		EBHIS2*GOLDGR	0.641
		BMIGRP*TREAT	0.635
		GOLDGR*SUSMHS	0.616
		EBHIS2*SUSMHS	0.583
		AGEGRP1*TREAT	0.560
		GOLDGR*TREAT	0.534
		BMIGRP*GOLDGR	0.509
		AGEGRP1*BMIGRP	0.443
		GOLDGR*SEX	0.408
		BMIGRP	0.293
		AGEGRP1*GOLDGR	0.274
		SUSMHS	0.172
		BMIGRP*SEX	0.151
		EBHIS2*TREAT	0.145
		EBHIS2*SEX	0.143
		AGEGRP1*EBHIS2	0.069*
		BMIGRP*EBHIS2	0.052*
		SEX*TREAT	0.035*
		AGEGRP1*SUSMHS	0.021*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 1	Removed Effect	BMIGRP*SUSMHS	0.791
Iteration 1	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 2	AIC	112196.9	
Iteration 2	Type 3 Wald p-values	SUSMHS*TREAT	0.728
		AGEGRP1*SEX	0.700
		AGEGRP1	0.698
		EBHIS2*GOLDGR	0.638
		BMIGRP*TREAT	0.636
		GOLDGR*SUSMHS	0.583
		EBHIS2*SUSMHS	0.580
		AGEGRP1*TREAT	0.561
		GOLDGR*TREAT	0.536
		BMIGRP*GOLDGR	0.492
		GOLDGR*SEX	0.407
		AGEGRP1*BMIGRP	0.380
		BMIGRP	0.287
		AGEGRP1*GOLDGR	0.268
		SUSMHS	0.176
		BMIGRP*SEX	0.156
		EBHIS2*TREAT	0.146
		EBHIS2*SEX	0.142
		AGEGRP1*EBHIS2	0.068*
		BMIGRP*EBHIS2	0.051*
		SEX*TREAT	0.035*
		AGEGRP1*SUSMHS	0.019*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 2	Removed Effect	SUSMHS*TREAT	0.728

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description	
Iteration 2	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 3	AIC	112195.0	
Iteration 3	Type 3 Wald p-values	AGEGRP1	0.704
		AGEGRP1*SEX	0.702
		BMIGRP*TREAT	0.666
		EBHIS2*GOLDGR	0.634
		AGEGRP1*TREAT	0.614
		GOLDGR*SUSMHS	0.581
		EBHIS2*SUSMHS	0.577
		GOLDGR*TREAT	0.551
		BMIGRP*GOLDGR	0.491
		GOLDGR*SEX	0.407
		AGEGRP1*BMIGRP	0.380
		BMIGRP	0.285
		AGEGRP1*GOLDGR	0.266
		SUSMHS	0.165
		BMIGRP*SEX	0.156
		EBHIS2*TREAT	0.147
		EBHIS2*SEX	0.142
		AGEGRP1*EBHIS2	0.067*
		BMIGRP*EBHIS2	0.051*
		SEX*TREAT	0.032*
		AGEGRP1*SUSMHS	0.019*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 3	Removed Effect	AGEGRP1*SEX	0.702

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description	
Iteration 3	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 4	AIC	112193.2	
Iteration 4	Type 3 Wald p-values	AGEGRP1	0.768
		BMIGRP*TREAT	0.661
		EBHIS2*GOLDGR	0.636
		AGEGRP1*TREAT	0.622
		EBHIS2*SUSMHS	0.585
		GOLDGR*SUSMHS	0.573
		GOLDGR*TREAT	0.552
		BMIGRP*GOLDGR	0.488
		GOLDGR*SEX	0.396
		AGEGRP1*BMIGRP	0.376
		BMIGRP	0.281
		AGEGRP1*GOLDGR	0.253
		SUSMHS	0.158
		BMIGRP*SEX	0.149
		EBHIS2*TREAT	0.145
		EBHIS2*SEX	0.139
		AGEGRP1*EBHIS2	0.070*
		BMIGRP*EBHIS2	0.050*
		SEX*TREAT	0.032*
		AGEGRP1*SUSMHS	0.020*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 4	Removed Effect	BMIGRP*TREAT	0.661
Iteration 4	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 5	AIC	112191.4	
Iteration 5	Type 3 Wald p-values	AGEGRP1	0.765
		EBHIS2*GOLDGR	0.631
		AGEGRP1*TREAT	0.626
		GOLDGR*TREAT	0.591
		EBHIS2*SUSMHS	0.581
		GOLDGR*SUSMHS	0.571
		BMIGRP*GOLDGR	0.488
		GOLDGR*SEX	0.392
		AGEGRP1*BMIGRP	0.376
		BMIGRP	0.261
		AGEGRP1*GOLDGR	0.250
		SUSMHS	0.158
		EBHIS2*TREAT	0.146
		BMIGRP*SEX	0.144
		EBHIS2*SEX	0.141
		AGEGRP1*EBHIS2	0.071*
		BMIGRP*EBHIS2	0.050*
		SEX*TREAT	0.033*
		AGEGRP1*SUSMHS	0.020*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 5	Removed Effect	EBHIS2*GOLDGR	0.631
Iteration 5	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 6	AIC	112189.6	
Iteration 6	Type 3 Wald p-values	AGEGRP1	0.763
		AGEGRP1*TREAT	0.631
		EBHIS2*SUSMHS	0.605
		GOLDGR*TREAT	0.594
		GOLDGR*SUSMHS	0.567
		BMIGRP*GOLDGR	0.485
		AGEGRP1*BMIGRP	0.382
		GOLDGR*SEX	0.377
		BMIGRP	0.269
		AGEGRP1*GOLDGR	0.253
		SUSMHS	0.163
		EBHIS2*SEX	0.150
		EBHIS2*TREAT	0.146
		BMIGRP*SEX	0.144
		AGEGRP1*EBHIS2	0.073*
		BMIGRP*EBHIS2	0.057*
		SEX*TREAT	0.033*
		AGEGRP1*SUSMHS	0.020*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 6	Removed Effect	AGEGRP1*TREAT	0.631
Iteration 6	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 7	AIC	112187.8	
Iteration 7	Type 3 Wald p-values	AGEGRP1	0.789
		EBHIS2*SUSMHS	0.600
		GOLDGR*TREAT	0.599
		GOLDGR*SUSMHS	0.564
		BMIGRP*GOLDGR	0.480
		AGEGRP1*BMIGRP	0.376
		GOLDGR*SEX	0.376
		BMIGRP	0.273
		AGEGRP1*GOLDGR	0.253
		SUSMHS	0.163
		EBHIS2*SEX	0.153
		EBHIS2*TREAT	0.149
		BMIGRP*SEX	0.146
		AGEGRP1*EBHIS2	0.074*
		BMIGRP*EBHIS2	0.057*
		SEX*TREAT	0.036*
		AGEGRP1*SUSMHS	0.020*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 7	Removed Effect	EBHIS2*SUSMHS	0.600
Iteration 7	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 8	AIC	112186.1	
Iteration 8	Type 3 Wald p-values	AGEGRP1	0.771
		GOLDGR*TREAT	0.593
		GOLDGR*SUSMHS	0.537
		BMIGRP*GOLDGR	0.481
		GOLDGR*SEX	0.379
		AGEGRP1*BMIGRP	0.378
		BMIGRP	0.277
		AGEGRP1*GOLDGR	0.247
		SUSMHS	0.186
		EBHIS2*TREAT	0.147
		BMIGRP*SEX	0.147
		EBHIS2*SEX	0.139
		AGEGRP1*EBHIS2	0.088*
		BMIGRP*EBHIS2	0.064*
		SEX*TREAT	0.036*
		AGEGRP1*SUSMHS	0.021*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 8	Removed Effect	GOLDGR*TREAT	0.593
Iteration 8	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 9	AIC	112184.4	
Iteration 9	Type 3 Wald p-values	AGEGRP1	0.774
		GOLDGR*SUSMHS	0.539
		BMIGRP*GOLDGR	0.481
		AGEGRP1*BMIGRP	0.373
		GOLDGR*SEX	0.368
		BMIGRP	0.270
		AGEGRP1*GOLDGR	0.247
		SUSMHS	0.184
		BMIGRP*SEX	0.145
		EBHIS2*SEX	0.139
		EBHIS2*TREAT	0.135
		AGEGRP1*EBHIS2	0.089*
		BMIGRP*EBHIS2	0.063*
		SEX*TREAT	0.039*
		AGEGRP1*SUSMHS	0.020*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 9	Removed Effect	GOLDGR*SUSMHS	0.539
Iteration 9	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 10	AIC	112182.8	
Iteration 10	Type 3 Wald p-values	AGEGRP1	0.830
		BMIGRP*GOLDGR	0.532
		AGEGRP1*BMIGRP	0.374
		GOLDGR*SEX	0.339
		AGEGRP1*GOLDGR	0.305
		BMIGRP	0.255
		BMIGRP*SEX	0.149
		EBHIS2*SEX	0.139
		EBHIS2*TREAT	0.132
		SUSMHS	0.093*
		AGEGRP1*EBHIS2	0.088*
		BMIGRP*EBHIS2	0.064*
		SEX*TREAT	0.039*
		AGEGRP1*SUSMHS	0.021*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 10	Removed Effect	BMIGRP*GOLDGR	0.532
Iteration 10	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 11	AIC	112181.2	
Iteration 11	Type 3 Wald p-values	AGEGRP1	0.842
		AGEGRP1*BMIGRP	0.381
		GOLDGR*SEX	0.350
		AGEGRP1*GOLDGR	0.312
		BMIGRP*SEX	0.161
		EBHIS2*SEX	0.139
		BMIGRP	0.132
		EBHIS2*TREAT	0.130
		SUSMHS	0.092*
		AGEGRP1*EBHIS2	0.090*
		BMIGRP*EBHIS2	0.057*
		SEX*TREAT	0.039*
		AGEGRP1*SUSMHS	0.021*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 11	Removed Effect	AGEGRP1*BMIGRP	0.381
Iteration 11	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 12	AIC	112179.9	
Iteration 12	Type 3 Wald p-values	AGEGRP1	0.888
		AGEGRP1*GOLDGR	0.371
		GOLDGR*SEX	0.359
		BMIGRP*SEX	0.192
		EBHIS2*SEX	0.141
		EBHIS2*TREAT	0.133
		BMIGRP	0.125
		AGEGRP1*EBHIS2	0.093*
		SUSMHS	0.092*
		BMIGRP*EBHIS2	0.060*
		SEX*TREAT	0.040*
		AGEGRP1*SUSMHS	0.028*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 12	Removed Effect	AGEGRP1*GOLDGR	0.371
Iteration 12	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 13	AIC	112178.7	
Iteration 13	Type 3 Wald p-values	AGEGRP1	0.823
		GOLDGR*SEX	0.413
		BMIGRP*SEX	0.191
		EBHIS2*SEX	0.136
		EBHIS2*TREAT	0.135
		BMIGRP	0.122
		SUSMHS	0.090*
		AGEGRP1*EBHIS2	0.079*
		BMIGRP*EBHIS2	0.062*
		SEX*TREAT	0.040*
		AGEGRP1*SUSMHS	0.031*
		SEX*SUSMHS	0.002*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 13	Removed Effect	GOLDGR*SEX	0.413
Iteration 13	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 14	AIC	112177.4	
Iteration 14	Type 3 Wald p-values	AGEGRP1	0.833
		BMIGRP*SEX	0.229
		EBHIS2*TREAT	0.133
		BMIGRP	0.131
		EBHIS2*SEX	0.121
		SUSMHS	0.096*
		AGEGRP1*EBHIS2	0.078*
		BMIGRP*EBHIS2	0.063*
		SEX*TREAT	0.039*
		AGEGRP1*SUSMHS	0.031*
		SEX*SUSMHS	0.001*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 14	Removed Effect	BMIGRP*SEX	0.229
Iteration 14	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 15	AIC	112176.9	
Iteration 15	Type 3 Wald p-values	AGEGRP1	0.844
		BMIGRP	0.233
		EBHIS2*TREAT	0.138
		EBHIS2*SEX	0.123
		SUSMHS	0.108
		AGEGRP1*EBHIS2	0.080*
		BMIGRP*EBHIS2	0.057*
		SEX*TREAT	0.037*
		AGEGRP1*SUSMHS	0.031*
		SEX*SUSMHS	<0.001*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 15	Removed Effect	EBHIS2*TREAT	0.138
Iteration 15	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 16	AIC	112177.1	
Iteration 16	Type 3 Wald p-values	AGEGRP1	0.837
		BMIGRP	0.235
		EBHIS2*SEX	0.110
		SUSMHS	0.100
		AGEGRP1*EBHIS2	0.080*
		BMIGRP*EBHIS2	0.053*
		SEX*TREAT	0.032*
		AGEGRP1*SUSMHS	0.029*
		SEX*SUSMHS	<0.001*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 16	Removed Effect	EBHIS2*SEX	0.110
Iteration 16	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 17	AIC	112177.6	
Iteration 17	Type 3 Wald p-values	AGEGRP1	0.873
		BMIGRP	0.219
		AGEGRP1*EBHIS2	0.118
		SUSMHS	0.099*
		BMIGRP*EBHIS2	0.050*
		SEX*TREAT	0.031*
		AGEGRP1*SUSMHS	0.028*
		SEX*SUSMHS	<0.001*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 17	Removed Effect	AGEGRP1*EBHIS2	0.118
Iteration 17	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Seven Covariates)

Iteration	Description		
Iteration 18	AIC	112178.1	
Iteration 18	Type 3 Wald p-values	AGEGRP1	0.915
		BMIGRP	0.232
		SUSMHS	0.095*
		BMIGRP*EBHIS2	0.052*
		SEX*TREAT	0.033*
		AGEGRP1*SUSMHS	0.028*
		SEX*SUSMHS	<0.001*
		TREAT	<0.001*
		SEX	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F	<25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.42 (0.39,0.45)	0.50 (0.46,0.53)	0.31 (26 / 83)	0.50 (24 / 48)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.59 (0.55,0.62)	0.67 (0.63,0.71)	0.55 (24 / 44)	0.74 (20 / 27)
	<25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.39 (0.36,0.42)	0.46 (0.43,0.50)	0.26 (6 / 23)	0.35 (7 / 20)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.55 (0.51,0.59)	0.63 (0.59,0.67)	0.53 (8 / 15)	0.92 (11 / 12)
	>=25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.43 (0.40,0.45)	0.50 (0.47,0.53)	0.42 (42 / 101)	0.51 (31 / 61)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.56 (0.52,0.59)	0.64 (0.60,0.68)	0.52 (34 / 65)	0.58 (25 / 43)
	>=25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.39 (0.37,0.42)	0.47 (0.43,0.50)	0.36 (28 / 77)	0.40 (16 / 40)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.52 (0.49,0.56)	0.61 (0.57,0.64)	0.32 (11 / 34)	0.44 (11 / 25)

Protocol: 207941
Population: Intent-to-Treat

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M	<25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.32 (0.30,0.34)	0.35 (0.33,0.38)	0.31 (32 / 102)	0.25 (21 / 85)
	<25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.47 (0.43,0.50)	0.51 (0.47,0.54)	0.47 (21 / 45)	0.44 (11 / 25)
	<25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.34 (0.32,0.37)	0.38 (0.35,0.40)	0.22 (10 / 46)	0.21 (6 / 29)
	<25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.49 (0.46,0.53)	0.53 (0.50,0.57)	0.40 (8 / 20)	0.40 (6 / 15)
	>=25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.33 (0.30,0.35)	0.36 (0.33,0.38)	0.26 (41 / 158)	0.27 (26 / 95)
	>=25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.44 (0.41,0.47)	0.48 (0.45,0.51)	0.42 (22 / 52)	0.50 (24 / 48)
	>=25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.35 (0.32,0.37)	0.38 (0.36,0.41)	0.28 (41 / 144)	0.24 (19 / 79)
	>=25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.47 (0.43,0.50)	0.51 (0.47,0.54)	0.53 (24 / 45)	0.59 (24 / 41)

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ F	<25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.56 (0.53,0.59)	0.65 (0.61,0.68)	0.55 (74 / 134)	0.60 (61 / 102)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.74 (0.71,0.77)	0.82 (0.78,0.84)	0.66 (60 / 91)	0.77 (55 / 71)
	<25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.53 (0.49,0.56)	0.61 (0.57,0.64)	0.46 (29 / 63)	0.66 (46 / 70)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.70 (0.67,0.73)	0.78 (0.75,0.81)	0.68 (38 / 56)	0.73 (30 / 41)
	>=25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.57 (0.54,0.60)	0.65 (0.62,0.69)	0.51 (54 / 105)	0.62 (42 / 68)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.71 (0.68,0.74)	0.79 (0.76,0.82)	0.68 (63 / 93)	0.72 (33 / 46)
	>=25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.53 (0.50,0.56)	0.62 (0.58,0.65)	0.42 (38 / 90)	0.51 (27 / 53)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.67 (0.64,0.71)	0.76 (0.72,0.79)	0.56 (48 / 86)	0.57 (25 / 44)

Protocol: 207941
Population: Intent-to-Treat

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M	<25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.44 (0.42,0.47)	0.48 (0.46,0.51)	0.42 (97 / 230)	0.41 (68 / 165)
	<25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.61 (0.58,0.64)	0.66 (0.63,0.69)	0.54 (63 / 116)	0.67 (78 / 117)
	<25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.47 (0.44,0.50)	0.51 (0.48,0.54)	0.46 (63 / 137)	0.41 (43 / 106)
	<25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.64 (0.61,0.67)	0.69 (0.65,0.72)	0.67 (68 / 102)	0.61 (43 / 71)
	>=25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.45 (0.42,0.48)	0.49 (0.46,0.52)	0.49 (83 / 171)	0.47 (65 / 139)
	>=25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.59 (0.55,0.61)	0.63 (0.60,0.66)	0.48 (50 / 104)	0.64 (52 / 81)
	>=25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.48 (0.45,0.50)	0.52 (0.49,0.54)	0.50 (90 / 180)	0.43 (59 / 138)
	>=25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.61 (0.58,0.64)	0.66 (0.62,0.69)	0.63 (75 / 120)	0.66 (67 / 102)

Protocol: 207941
Population: Intent-to-Treat

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F	<25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.40 (0.37,0.43)	0.48 (0.44,0.51)	0.49 (22 / 45)	0.37 (11 / 30)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.57 (0.53,0.60)	0.65 (0.61,0.69)	0.56 (15 / 27)	0.75 (12 / 16)
	<25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.41 (0.38,0.44)	0.48 (0.45,0.52)	0.38 (24 / 64)	0.55 (18 / 33)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.57 (0.53,0.61)	0.66 (0.62,0.69)	0.41 (13 / 32)	0.62 (8 / 13)
	>=25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.41 (0.38,0.44)	0.48 (0.45,0.52)	0.40 (19 / 47)	0.41 (11 / 27)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.54 (0.50,0.57)	0.62 (0.58,0.66)	0.54 (15 / 28)	0.38 (8 / 21)
	>=25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.41 (0.38,0.44)	0.49 (0.45,0.52)	0.39 (42 / 107)	0.48 (33 / 69)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.54 (0.51,0.58)	0.63 (0.59,0.66)	0.57 (28 / 49)	0.61 (25 / 41)

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M	<25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.31 (0.28,0.33)	0.34 (0.31,0.36)	0.27 (22 / 82)	0.27 (14 / 51)
	<25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.45 (0.42,0.48)	0.49 (0.45,0.52)	0.46 (16 / 35)	0.55 (16 / 29)
	<25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.36 (0.34,0.38)	0.39 (0.37,0.42)	0.27 (36 / 131)	0.38 (40 / 105)
	<25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.51 (0.48,0.54)	0.56 (0.52,0.59)	0.35 (18 / 51)	0.59 (22 / 37)
	>=25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.31 (0.29,0.33)	0.34 (0.32,0.37)	0.32 (25 / 79)	0.29 (20 / 70)
	>=25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.42 (0.39,0.45)	0.46 (0.43,0.49)	0.27 (7 / 26)	0.48 (14 / 29)
	>=25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.36 (0.34,0.38)	0.40 (0.38,0.42)	0.35 (91 / 261)	0.40 (85 / 210)
	>=25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.49 (0.46,0.51)	0.53 (0.50,0.56)	0.48 (56 / 117)	0.53 (36 / 68)

Protocol: 207941
Population: Intent-to-Treat

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F	<25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.54 (0.51,0.58)	0.63 (0.59,0.66)	0.52 (32 / 61)	0.45 (20 / 44)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.72 (0.68,0.75)	0.80 (0.76,0.83)	0.70 (44 / 63)	0.66 (23 / 35)
	<25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.55 (0.52,0.58)	0.63 (0.60,0.66)	0.55 (61 / 111)	0.49 (41 / 83)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.72 (0.69,0.75)	0.80 (0.77,0.83)	0.64 (46 / 72)	0.65 (33 / 51)
	>=25 kg/m^2/ Current/<2	0.79 (0.73,0.86)	0.55 (0.51,0.58)	0.63 (0.59,0.67)	0.56 (28 / 50)	0.54 (14 / 26)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.69 (0.65,0.73)	0.77 (0.73,0.81)	0.73 (22 / 30)	0.54 (7 / 13)
	>=25 kg/m^2/ Former/<2	0.79 (0.73,0.86)	0.55 (0.52,0.58)	0.64 (0.60,0.67)	0.50 (65 / 129)	0.61 (45 / 74)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.70 (0.66,0.73)	0.78 (0.74,0.81)	0.53 (37 / 70)	0.69 (48 / 70)

Protocol: 207941
Population: Intent-to-Treat

Table 1.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates)

Age/GOLD/ Sex	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M	<25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.43 (0.40,0.45)	0.47 (0.44,0.49)	0.40 (57 / 144)	0.43 (65 / 151)
	<25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.59 (0.56,0.62)	0.64 (0.60,0.67)	0.51 (49 / 97)	0.63 (50 / 80)
	<25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.49 (0.47,0.51)	0.53 (0.51,0.56)	0.48 (149/ 312)	0.50 (135/ 268)
	<25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.67 (0.64,0.69)	0.71 (0.68,0.73)	0.57 (116/ 202)	0.64 (116/ 182)
	>=25 kg/m^2/ Current/<2	0.89 (0.84,0.94)	0.43 (0.40,0.46)	0.47 (0.44,0.50)	0.35 (45 / 128)	0.44 (41 / 94)
	>=25 kg/m^2/ Current/>=2	0.89 (0.84,0.94)	0.57 (0.53,0.60)	0.61 (0.57,0.64)	0.41 (29 / 70)	0.64 (29 / 45)
	>=25 kg/m^2/ Former/<2	0.89 (0.84,0.94)	0.50 (0.47,0.52)	0.54 (0.51,0.56)	0.43 (170/ 394)	0.44 (130/ 295)
	>=25 kg/m^2/ Former/>=2	0.89 (0.84,0.94)	0.64 (0.61,0.66)	0.68 (0.65,0.71)	0.59 (128/ 216)	0.66 (113/ 171)

Protocol: 207941
Population: Intent-to-Treat

Table 1.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Seven Covariates)

Statistic	Level	
Type 3 Wald p-values	Age	0.915
	BMI	0.232
	Smoking Status	0.095
	Exacerbation History by BMI	0.052
	Treatment by Sex	0.033
	Smoking Status by Age	0.028
	Sex by Smoking Status	<0.001
	Treatment	<0.001
	Sex	<0.001
	GOLD	<0.001
	Exacerbation History	<0.001

Protocol: 207941
Population: Intent-to-Treat

Table 1.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Seven Covariates)

Statistic	Level	
Hazard Ratio	Age >=65 vs <=64	
95% CI		
	At Smoking Status:Current smoker	0.95 (0.88, 1.02)
	At Smoking Status:Former smoker	1.06 (0.99, 1.14)
	BMI >=25 kg/m^2 vs <25 kg/m^2	
	At Exacerbation History:<2	1.02 (0.96, 1.09)
	At Exacerbation History:>=2	0.92 (0.86, 1.00)
	Exacerbation History >=2 vs <2	
	At BMI:<25 kg/m^2	1.62 (1.51, 1.74)
	At BMI:>=25 kg/m^2	1.47 (1.37, 1.58)
	GOLD III & IV: FEV1<50% predicted vs I & II: FEV1>=50% predicted	1.52 (1.44, 1.60)
	Sex M vs F	
	At Treatment:ICS Smoking Status:Current smoker	0.71 (0.65, 0.78)
	At Treatment:ICS Smoking Status:Former smoker	0.85 (0.78, 0.93)
	At Treatment:non-ICS Smoking Status:Current smoker	0.64 (0.58, 0.70)
	At Treatment:non-ICS Smoking Status:Former smoker	0.76 (0.69, 0.83)
	Smoking Status Former smoker vs Current smoker	
	At Sex:F Age:<=64	0.90 (0.82, 0.99)
	At Sex:F Age:>=65	1.01 (0.92, 1.12)
	At Sex:M Age:<=64	1.08 (0.99, 1.18)
	At Sex:M Age:>=65	1.21 (1.12, 1.31)
	Treatment ICS vs non-ICS	
	At Sex:F	0.79 (0.73, 0.86)
	At Sex:M	0.89 (0.84, 0.94)

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 1	AIC	18438.0	
Iteration 1	Type 3 Wald p-values	EBHIS2*GOLDGR	0.949
		AGEGRP1*TREAT	0.803
		BMIGRP*GOLDGR	0.801
		GOLDGR*RACEGRP2	0.782
		SEX	0.781
		AGEGRP1	0.747
		GOLDGR*SUSMHS	0.747
		SUSMHS*TREAT	0.738
		SEX*SUSMHS	0.723
		AGEGRP1*GOLDGR	0.684
		AGEGRP1*INCGRP1	0.622
		GOLDGR*SEX	0.611
		AGEGRP1*SUSMHS	0.576
		BMIGRP*EBHIS2	0.488
		INCGRP1*TREAT	0.480
		GOLDGR*TREAT	0.455
		INCGRP1*SUSMHS	0.412
		RACEGRP2*SEX	0.395
		BMIGRP*SUSMHS	0.390
		AGEGRP1*BMIGRP	0.367
		SEX*TREAT	0.357
		AGEGRP1*RACEGRP2	0.346
		RACEGRP2*TREAT	0.335
		EBHIS2*SUSMHS	0.311
		EBHIS2*SEX	0.309
		GOLDGR*INCGRP1	0.241
		BMIGRP*SEX	0.202
		BMIGRP*RACEGRP2	0.191
		EBHIS2*RACEGRP2	0.185

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 1	Type 3 Wald p-values	RACEGRP2	0.177
		EBHIS2*TREAT	0.137
		BMIGRP	0.113
		SUSMHS	0.092*
		AGEGRP1*EBHIS2	0.057*
		AGEGRP1*SEX	0.052*
		INCGRP1*SEX	0.049*
		EBHIS2*INCGRP1	0.041*
		RACEGRP2*SUSMHS	0.028*
		INCGRP1*RACEGRP2	0.014*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		EBHIS2	0.004*
		BMIGRP*INCGRP1	0.002*
		GOLDGR	0.002*
		TREAT	<0.001*
Iteration 1	Removed Effect	EBHIS2*GOLDGR	0.949
Iteration 1	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 2	AIC	18436.0	
Iteration 2	Type 3 Wald p-values	AGEGRP1*TREAT	0.803
		BMIGRP*GOLDGR	0.802
		GOLDGR*RACEGRP2	0.783
		SEX	0.779
		AGEGRP1	0.748
		GOLDGR*SUSMHS	0.747
		SUSMHS*TREAT	0.738
		SEX*SUSMHS	0.722
		AGEGRP1*GOLDGR	0.681
		AGEGRP1*INCGRP1	0.621
		GOLDGR*SEX	0.613
		AGEGRP1*SUSMHS	0.575
		BMIGRP*EBHIS2	0.482
		INCGRP1*TREAT	0.479
		GOLDGR*TREAT	0.456
		INCGRP1*SUSMHS	0.412
		RACEGRP2*SEX	0.395
		BMIGRP*SUSMHS	0.390
		AGEGRP1*BMIGRP	0.365
		SEX*TREAT	0.357
		AGEGRP1*RACEGRP2	0.345
		RACEGRP2*TREAT	0.335
		EBHIS2*SEX	0.309
		EBHIS2*SUSMHS	0.308
		GOLDGR*INCGRP1	0.242
		BMIGRP*SEX	0.202
		BMIGRP*RACEGRP2	0.191
		EBHIS2*RACEGRP2	0.185
		RACEGRP2	0.177

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 2	Type 3 Wald p-values	EBHIS2*TREAT	0.137
		BMIGRP	0.113
		SUSMHS	0.092*
		AGEGRP1*EBHIS2	0.057*
		AGEGRP1*SEX	0.052*
		INCGRP1*SEX	0.048*
		EBHIS2*INCGRP1	0.041*
		RACEGRP2*SUSMHS	0.028*
		INCGRP1*RACEGRP2	0.014*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		GOLDGR	0.002*
		TREAT	<0.001*
Iteration 2	Removed Effect	AGEGRP1*TREAT	0.803
Iteration 2	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 3	AIC	18434.0	
Iteration 3	Type 3 Wald p-values	BMIGRP*GOLDGR	0.801
		GOLDGR*RACEGRP2	0.783
		SEX	0.783
		GOLDGR*SUSMHS	0.745
		SEX*SUSMHS	0.719
		AGEGRP1	0.715
		AGEGRP1*GOLDGR	0.685
		SUSMHS*TREAT	0.679
		AGEGRP1*INCGRP1	0.624
		GOLDGR*SEX	0.615
		AGEGRP1*SUSMHS	0.573
		INCGRP1*TREAT	0.491
		BMIGRP*EBHIS2	0.480
		GOLDGR*TREAT	0.462
		INCGRP1*SUSMHS	0.412
		RACEGRP2*SEX	0.396
		BMIGRP*SUSMHS	0.387
		SEX*TREAT	0.371
		AGEGRP1*BMIGRP	0.355
		AGEGRP1*RACEGRP2	0.338
		RACEGRP2*TREAT	0.337
		EBHIS2*SEX	0.311
		EBHIS2*SUSMHS	0.308
		GOLDGR*INCGRP1	0.242
		BMIGRP*SEX	0.204
		BMIGRP*RACEGRP2	0.192
		EBHIS2*RACEGRP2	0.186
		RACEGRP2	0.177
		EBHIS2*TREAT	0.132

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 3	Type 3 Wald p-values	BMIGRP	0.113
		SUSMHS	0.093*
		AGEGRP1*EBHIS2	0.055*
		AGEGRP1*SEX	0.053*
		INCGRP1*SEX	0.048*
		EBHIS2*INCGRP1	0.041*
		RACEGRP2*SUSMHS	0.028*
		INCGRP1*RACEGRP2	0.014*
		BMIGRP*TREAT	0.011*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		GOLDGR	0.002*
		TREAT	<0.001*
Iteration 3	Removed Effect	BMIGRP*GOLDGR	0.801
Iteration 3	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 4	AIC	18432.1	
Iteration 4	Type 3 Wald p-values	SEX	0.784
		GOLDGR*SUSMHS	0.777
		GOLDGR*RACEGRP2	0.752
		SEX*SUSMHS	0.726
		AGEGRP1	0.713
		SUSMHS*TREAT	0.681
		AGEGRP1*GOLDGR	0.670
		AGEGRP1*INCGRP1	0.622
		GOLDGR*SEX	0.609
		AGEGRP1*SUSMHS	0.570
		INCGRP1*TREAT	0.492
		BMIGRP*EBHIS2	0.491
		GOLDGR*TREAT	0.472
		INCGRP1*SUSMHS	0.413
		RACEGRP2*SEX	0.395
		BMIGRP*SUSMHS	0.377
		SEX*TREAT	0.371
		AGEGRP1*BMIGRP	0.349
		RACEGRP2*TREAT	0.338
		AGEGRP1*RACEGRP2	0.337
		EBHIS2*SEX	0.313
		EBHIS2*SUSMHS	0.310
		GOLDGR*INCGRP1	0.251
		BMIGRP*SEX	0.210
		BMIGRP*RACEGRP2	0.195
		EBHIS2*RACEGRP2	0.183
		RACEGRP2	0.174
		EBHIS2*TREAT	0.134
		BMIGRP	0.118

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 4	Type 3 Wald p-values	SUSMHS	0.095*
		AGEGRP1*EBHIS2	0.055*
		AGEGRP1*SEX	0.053*
		INCGRP1*SEX	0.048*
		EBHIS2*INCGRP1	0.041*
		RACEGRP2*SUSMHS	0.028*
		INCGRP1*RACEGRP2	0.014*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		GOLDGR	0.002*
		TREAT	<0.001*
Iteration 4	Removed Effect	GOLDGR*SUSMHS	0.777
Iteration 4	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 5	AIC	18430.2	
Iteration 5	Type 3 Wald p-values	SEX	0.775
		SEX*SUSMHS	0.740
		GOLDGR*RACEGRP2	0.727
		AGEGRP1	0.698
		SUSMHS*TREAT	0.686
		AGEGRP1*INCGRP1	0.624
		GOLDGR*SEX	0.620
		AGEGRP1*GOLDGR	0.602
		AGEGRP1*SUSMHS	0.558
		BMIGRP*EBHIS2	0.491
		INCGRP1*TREAT	0.490
		GOLDGR*TREAT	0.472
		INCGRP1*SUSMHS	0.416
		RACEGRP2*SEX	0.398
		SEX*TREAT	0.372
		BMIGRP*SUSMHS	0.357
		AGEGRP1*BMIGRP	0.343
		RACEGRP2*TREAT	0.337
		AGEGRP1*RACEGRP2	0.334
		EBHIS2*SUSMHS	0.319
		EBHIS2*SEX	0.312
		GOLDGR*INCGRP1	0.251
		BMIGRP*SEX	0.212
		BMIGRP*RACEGRP2	0.196
		EBHIS2*RACEGRP2	0.180
		RACEGRP2	0.172
		EBHIS2*TREAT	0.134
		BMIGRP	0.117
		SUSMHS	0.098*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 5	Type 3 Wald p-values	AGEGRP1*EBHIS2	0.055*
		AGEGRP1*SEX	0.052*
		INCGRP1*SEX	0.048*
		EBHIS2*INCGRP1	0.041*
		RACEGRP2*SUSMHS	0.027*
		INCGRP1*RACEGRP2	0.014*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		GOLDGR	0.002*
		TREAT	<0.001*
Iteration 5	Removed Effect	SEX*SUSMHS	0.740
Iteration 5	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 6	AIC	18428.3	
Iteration 6	Type 3 Wald p-values	SEX	0.735
		AGEGRP1	0.726
		GOLDGR*RACEGRP2	0.724
		SUSMHS*TREAT	0.702
		AGEGRP1*INCGRP1	0.614
		GOLDGR*SEX	0.602
		AGEGRP1*GOLDGR	0.599
		AGEGRP1*SUSMHS	0.527
		BMIGRP*EBHIS2	0.493
		INCGRP1*TREAT	0.492
		GOLDGR*TREAT	0.472
		RACEGRP2*SEX	0.420
		INCGRP1*SUSMHS	0.383
		SEX*TREAT	0.374
		BMIGRP*SUSMHS	0.355
		RACEGRP2*TREAT	0.340
		AGEGRP1*BMIGRP	0.336
		EBHIS2*SUSMHS	0.331
		AGEGRP1*RACEGRP2	0.326
		EBHIS2*SEX	0.315
		GOLDGR*INCGRP1	0.252
		BMIGRP*SEX	0.227
		BMIGRP*RACEGRP2	0.199
		RACEGRP2	0.181
		EBHIS2*RACEGRP2	0.178
		EBHIS2*TREAT	0.135
		BMIGRP	0.111
		AGEGRP1*EBHIS2	0.056*
		SUSMHS	0.055*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 6	Type 3 Wald p-values	INCGRP1*SEX	0.046*
		EBHIS2*INCGRP1	0.041*
		AGEGRP1*SEX	0.035*
		RACEGRP2*SUSMHS	0.025*
		INCGRP1*RACEGRP2	0.015*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		GOLDGR	0.002*
		TREAT	<0.001*
Iteration 6	Removed Effect	GOLDGR*RACEGRP2	0.724
Iteration 6	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 7	AIC	18426.4	
Iteration 7	Type 3 Wald p-values	SEX	0.729
		SUSMHS*TREAT	0.706
		AGEGRP1	0.705
		GOLDGR*SEX	0.619
		AGEGRP1*INCGRP1	0.609
		AGEGRP1*GOLDGR	0.578
		AGEGRP1*SUSMHS	0.531
		INCGRP1*TREAT	0.491
		BMIGRP*EBHIS2	0.488
		GOLDGR*TREAT	0.467
		RACEGRP2*SEX	0.417
		INCGRP1*SUSMHS	0.380
		SEX*TREAT	0.374
		BMIGRP*SUSMHS	0.357
		RACEGRP2*TREAT	0.338
		AGEGRP1*RACEGRP2	0.337
		AGEGRP1*BMIGRP	0.335
		EBHIS2*SUSMHS	0.326
		EBHIS2*SEX	0.313
		GOLDGR*INCGRP1	0.273
		BMIGRP*SEX	0.227
		RACEGRP2	0.197
		EBHIS2*RACEGRP2	0.187
		BMIGRP*RACEGRP2	0.177
		EBHIS2*TREAT	0.133
		BMIGRP	0.117
		AGEGRP1*EBHIS2	0.057*
		SUSMHS	0.056*
		INCGRP1*SEX	0.045*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 7	Type 3 Wald p-values	EBHIS2*INCGRP1	0.042*
		AGEGRP1*SEX	0.035*
		RACEGRP2*SUSMHS	0.026*
		INCGRP1*RACEGRP2	0.014*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.008*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 7	Removed Effect	SUSMHS*TREAT	0.706
Iteration 7	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 8	AIC	18424.5	
Iteration 8	Type 3 Wald p-values	SEX	0.728
		AGEGRP1	0.699
		GOLDGR*SEX	0.621
		AGEGRP1*INCGRP1	0.609
		AGEGRP1*GOLDGR	0.578
		AGEGRP1*SUSMHS	0.536
		INCGRP1*TREAT	0.488
		BMIGRP*EBHIS2	0.486
		GOLDGR*TREAT	0.456
		RACEGRP2*SEX	0.419
		SEX*TREAT	0.388
		INCGRP1*SUSMHS	0.379
		BMIGRP*SUSMHS	0.368
		RACEGRP2*TREAT	0.364
		AGEGRP1*RACEGRP2	0.341
		AGEGRP1*BMIGRP	0.337
		EBHIS2*SUSMHS	0.328
		EBHIS2*SEX	0.316
		GOLDGR*INCGRP1	0.274
		BMIGRP*SEX	0.228
		RACEGRP2	0.202
		EBHIS2*RACEGRP2	0.187
		BMIGRP*RACEGRP2	0.178
		EBHIS2*TREAT	0.135
		BMIGRP	0.115
		AGEGRP1*EBHIS2	0.057*
		SUSMHS	0.046*
		INCGRP1*SEX	0.045*
		EBHIS2*INCGRP1	0.042*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 8	Type 3 Wald p-values	AGEGRP1*SEX	0.035*
		RACEGRP2*SUSMHS	0.027*
		INCGRP1*RACEGRP2	0.014*
		BMIGRP*TREAT	0.013*
		INCGRP1	0.008*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 8	Removed Effect	GOLDGR*SEX	0.621
Iteration 8	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 9	AIC	18422.8	
Iteration 9	Type 3 Wald p-values	AGEGRP1	0.710
		SEX	0.631
		AGEGRP1*GOLDGR	0.630
		AGEGRP1*INCGRP1	0.616
		AGEGRP1*SUSMHS	0.538
		BMIGRP*EBHIS2	0.493
		INCGRP1*TREAT	0.487
		GOLDGR*TREAT	0.474
		RACEGRP2*SEX	0.432
		SEX*TREAT	0.397
		INCGRP1*SUSMHS	0.379
		BMIGRP*SUSMHS	0.373
		RACEGRP2*TREAT	0.364
		AGEGRP1*BMIGRP	0.345
		AGEGRP1*RACEGRP2	0.339
		EBHIS2*SEX	0.331
		EBHIS2*SUSMHS	0.329
		GOLDGR*INCGRP1	0.225
		RACEGRP2	0.208
		BMIGRP*SEX	0.207
		EBHIS2*RACEGRP2	0.185
		BMIGRP*RACEGRP2	0.180
		EBHIS2*TREAT	0.133
		BMIGRP	0.117
		AGEGRP1*EBHIS2	0.056*
		SUSMHS	0.046*
		INCGRP1*SEX	0.045*
		EBHIS2*INCGRP1	0.042*
		AGEGRP1*SEX	0.037*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 9	Type 3 Wald p-values	RACEGRP2*SUSMHS	0.027*
		INCGRP1*RACEGRP2	0.015*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 9	Removed Effect	AGEGRP1*GOLDGR	0.630
Iteration 9	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 10	AIC	18421.0	
Iteration 10	Type 3 Wald p-values	AGEGRP1	0.807
		SEX	0.634
		AGEGRP1*INCGRP1	0.617
		AGEGRP1*SUSMHS	0.558
		BMIGRP*EBHIS2	0.501
		INCGRP1*TREAT	0.486
		GOLDGR*TREAT	0.469
		RACEGRP2*SEX	0.431
		SEX*TREAT	0.396
		INCGRP1*SUSMHS	0.378
		BMIGRP*SUSMHS	0.373
		AGEGRP1*BMIGRP	0.372
		RACEGRP2*TREAT	0.363
		AGEGRP1*RACEGRP2	0.335
		EBHIS2*SEX	0.330
		EBHIS2*SUSMHS	0.330
		GOLDGR*INCGRP1	0.219
		BMIGRP*SEX	0.206
		RACEGRP2	0.204
		EBHIS2*RACEGRP2	0.182
		BMIGRP*RACEGRP2	0.179
		EBHIS2*TREAT	0.133
		BMIGRP	0.116
		AGEGRP1*EBHIS2	0.051*
		SUSMHS	0.046*
		INCGRP1*SEX	0.046*
		EBHIS2*INCGRP1	0.042*
		AGEGRP1*SEX	0.039*
		RACEGRP2*SUSMHS	0.027*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 10	Type 3 Wald p-values	INCGRP1*RACEGRP2	0.015*
		BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.002*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 10	Removed Effect	AGEGRP1*INCGRP1	0.617
Iteration 10	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 11	AIC	18419.3	
Iteration 11	Type 3 Wald p-values	AGEGRP1	0.781
		SEX	0.635
		AGEGRP1*SUSMHS	0.575
		BMIGRP*EBHIS2	0.502
		INCGRP1*TREAT	0.485
		GOLDGR*TREAT	0.469
		RACEGRP2*SEX	0.448
		INCGRP1*SUSMHS	0.429
		AGEGRP1*BMIGRP	0.411
		SEX*TREAT	0.395
		BMIGRP*SUSMHS	0.387
		RACEGRP2*TREAT	0.364
		EBHIS2*SUSMHS	0.333
		EBHIS2*SEX	0.326
		GOLDGR*INCGRP1	0.215
		AGEGRP1*RACEGRP2	0.213
		BMIGRP*SEX	0.203
		RACEGRP2	0.203
		EBHIS2*RACEGRP2	0.187
		BMIGRP*RACEGRP2	0.186
		EBHIS2*TREAT	0.133
		BMIGRP	0.113
		AGEGRP1*EBHIS2	0.053*
		INCGRP1*SEX	0.052*
		SUSMHS	0.046*
		EBHIS2*INCGRP1	0.045*
		AGEGRP1*SEX	0.044*
		RACEGRP2*SUSMHS	0.025*
		INCGRP1*RACEGRP2	0.016*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 11	Type 3 Wald p-values	BMIGRP*TREAT	0.012*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	0.002*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 11	Removed Effect	AGEGRP1*SUSMHS	0.575
Iteration 11	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 12	AIC	18417.6	
Iteration 12	Type 3 Wald p-values	AGEGRP1	0.700
		SEX	0.631
		BMIGRP*EBHIS2	0.511
		INCGRP1*TREAT	0.485
		GOLDGR*TREAT	0.473
		AGEGRP1*BMIGRP	0.462
		INCGRP1*SUSMHS	0.450
		RACEGRP2*SEX	0.448
		BMIGRP*SUSMHS	0.414
		SEX*TREAT	0.395
		RACEGRP2*TREAT	0.370
		EBHIS2*SUSMHS	0.354
		EBHIS2*SEX	0.330
		AGEGRP1*RACEGRP2	0.247
		GOLDGR*INCGRP1	0.216
		RACEGRP2	0.212
		BMIGRP*SEX	0.201
		BMIGRP*RACEGRP2	0.186
		EBHIS2*RACEGRP2	0.184
		EBHIS2*TREAT	0.132
		BMIGRP	0.113
		AGEGRP1*EBHIS2	0.055*
		INCGRP1*SEX	0.051*
		EBHIS2*INCGRP1	0.045*
		SUSMHS	0.041*
		AGEGRP1*SEX	0.041*
		RACEGRP2*SUSMHS	0.024*
		INCGRP1*RACEGRP2	0.015*
		BMIGRP*TREAT	0.012*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 12	Type 3 Wald p-values	INCGRP1	0.007*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	0.002*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 12	Removed Effect	BMIGRP*EBHIS2	0.511
Iteration 12	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 13	AIC	18416.0	
Iteration 13	Type 3 Wald p-values	AGEGRP1	0.690
		SEX	0.626
		AGEGRP1*BMIGRP	0.486
		INCGRP1*TREAT	0.481
		GOLDGR*TREAT	0.477
		INCGRP1*SUSMHS	0.452
		RACEGRP2*SEX	0.449
		BMIGRP*SUSMHS	0.422
		EBHIS2*SUSMHS	0.406
		SEX*TREAT	0.395
		RACEGRP2*TREAT	0.373
		EBHIS2*SEX	0.327
		AGEGRP1*RACEGRP2	0.246
		BMIGRP*SEX	0.218
		GOLDGR*INCGRP1	0.214
		RACEGRP2	0.211
		BMIGRP*RACEGRP2	0.194
		EBHIS2*RACEGRP2	0.144
		EBHIS2*TREAT	0.143
		BMIGRP	0.122
		AGEGRP1*EBHIS2	0.059*
		EBHIS2*INCGRP1	0.053*
		INCGRP1*SEX	0.049*
		SUSMHS	0.042*
		AGEGRP1*SEX	0.041*
		RACEGRP2*SUSMHS	0.023*
		INCGRP1*RACEGRP2	0.016*
		BMIGRP*TREAT	0.013*
		INCGRP1	0.006*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 13	Type 3 Wald p-values	BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 13	Removed Effect	AGEGRP1*BMIGRP	0.486
Iteration 13	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 14	AIC	18414.5	
Iteration 14	Type 3 Wald p-values	SEX	0.640
		AGEGRP1	0.571
		BMIGRP*SUSMHS	0.516
		INCGRP1*TREAT	0.484
		GOLDGR*TREAT	0.483
		INCGRP1*SUSMHS	0.460
		RACEGRP2*SEX	0.436
		EBHIS2*SUSMHS	0.408
		SEX*TREAT	0.388
		RACEGRP2*TREAT	0.376
		EBHIS2*SEX	0.326
		AGEGRP1*RACEGRP2	0.298
		GOLDGR*INCGRP1	0.215
		RACEGRP2	0.209
		BMIGRP*RACEGRP2	0.194
		BMIGRP*SEX	0.179
		EBHIS2*RACEGRP2	0.146
		EBHIS2*TREAT	0.143
		BMIGRP	0.119
		AGEGRP1*EBHIS2	0.060*
		EBHIS2*INCGRP1	0.052*
		INCGRP1*SEX	0.048*
		SUSMHS	0.046*
		AGEGRP1*SEX	0.041*
		RACEGRP2*SUSMHS	0.025*
		INCGRP1*RACEGRP2	0.016*
		BMIGRP*TREAT	0.013*
		INCGRP1	0.006*
		BMIGRP*INCGRP1	0.003*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 14	Type 3 Wald p-values	EBHIS2	<0.001*
		TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 14	Removed Effect	BMIGRP*SUSMHS	0.516
Iteration 14	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 15	AIC	18412.9	
Iteration 15	Type 3 Wald p-values	SEX	0.638
		AGEGRP1	0.569
		INCGRP1*SUSMHS	0.518
		GOLDGR*TREAT	0.487
		INCGRP1*TREAT	0.478
		RACEGRP2*SEX	0.431
		EBHIS2*SUSMHS	0.414
		SEX*TREAT	0.388
		RACEGRP2*TREAT	0.371
		EBHIS2*SEX	0.326
		AGEGRP1*RACEGRP2	0.299
		GOLDGR*INCGRP1	0.219
		RACEGRP2	0.200
		BMIGRP*SEX	0.196
		BMIGRP*RACEGRP2	0.169
		EBHIS2*RACEGRP2	0.148
		EBHIS2*TREAT	0.140
		BMIGRP	0.138
		AGEGRP1*EBHIS2	0.061*
		SUSMHS	0.057*
		EBHIS2*INCGRP1	0.052*
		INCGRP1*SEX	0.045*
		AGEGRP1*SEX	0.041*
		RACEGRP2*SUSMHS	0.029*
		INCGRP1*RACEGRP2	0.015*
		BMIGRP*TREAT	0.013*
		INCGRP1	0.007*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Protocol: 207941
Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 15	Type 3 Wald p-values	TREAT	<0.001*
		GOLDGR	<0.001*
Iteration 15	Removed Effect	INCGRP1*SUSMHS	0.518
Iteration 15	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 16	AIC	18411.3	
Iteration 16	Type 3 Wald p-values	SEX	0.643
		AGEGRP1	0.580
		GOLDGR*TREAT	0.490
		INCGRP1*TREAT	0.474
		RACEGRP2*SEX	0.422
		EBHIS2*SUSMHS	0.420
		SEX*TREAT	0.386
		RACEGRP2*TREAT	0.367
		EBHIS2*SEX	0.327
		AGEGRP1*RACEGRP2	0.304
		GOLDGR*INCGRP1	0.205
		BMIGRP*SEX	0.202
		RACEGRP2	0.202
		BMIGRP*RACEGRP2	0.172
		EBHIS2*RACEGRP2	0.150
		BMIGRP	0.141
		EBHIS2*TREAT	0.140
		AGEGRP1*EBHIS2	0.062*
		SUSMHS	0.060*
		EBHIS2*INCGRP1	0.053*
		INCGRP1*SEX	0.041*
		AGEGRP1*SEX	0.039*
		BMIGRP*TREAT	0.013*
		RACEGRP2*SUSMHS	0.011*
		INCGRP1*RACEGRP2	0.011*
		INCGRP1	0.008*
		BMIGRP*INCGRP1	0.004*
		EBHIS2	<0.001*
		TREAT	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 16	Type 3 Wald p-values	GOLDGR	<0.001*
Iteration 16	Removed Effect	GOLDGR*TREAT	0.490
Iteration 16	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 17	AIC	18409.8	
Iteration 17	Type 3 Wald p-values	SEX	0.651
		AGEGRP1	0.575
		INCGRP1*TREAT	0.470
		EBHIS2*SUSMHS	0.425
		RACEGRP2*SEX	0.421
		SEX*TREAT	0.406
		RACEGRP2*TREAT	0.377
		EBHIS2*SEX	0.320
		AGEGRP1*RACEGRP2	0.305
		GOLDGR*INCGRP1	0.208
		RACEGRP2	0.202
		BMIGRP*SEX	0.200
		BMIGRP*RACEGRP2	0.171
		EBHIS2*TREAT	0.154
		EBHIS2*RACEGRP2	0.148
		BMIGRP	0.147
		AGEGRP1*EBHIS2	0.063*
		SUSMHS	0.060*
		EBHIS2*INCGRP1	0.055*
		INCGRP1*SEX	0.041*
		AGEGRP1*SEX	0.039*
		RACEGRP2*SUSMHS	0.011*
		INCGRP1*RACEGRP2	0.011*
		BMIGRP*TREAT	0.010*
		INCGRP1	0.008*
		BMIGRP*INCGRP1	0.004*
		EBHIS2	<0.001*
		TREAT	<0.001*
		GOLDGR	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 17	Removed Effect	INCGRP1*TREAT	0.470
Iteration 17	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 18	AIC	18408.3	
Iteration 18	Type 3 Wald p-values	SEX	0.657
		AGEGRP1	0.582
		RACEGRP2*TREAT	0.509
		SEX*TREAT	0.457
		RACEGRP2*SEX	0.434
		EBHIS2*SUSMHS	0.429
		EBHIS2*SEX	0.320
		AGEGRP1*RACEGRP2	0.302
		RACEGRP2	0.220
		GOLDGR*INCGRP1	0.208
		BMIGRP*SEX	0.202
		BMIGRP*RACEGRP2	0.173
		EBHIS2*TREAT	0.151
		BMIGRP	0.147
		EBHIS2*RACEGRP2	0.144
		AGEGRP1*EBHIS2	0.063*
		SUSMHS	0.061*
		EBHIS2*INCGRP1	0.051*
		INCGRP1*SEX	0.045*
		AGEGRP1*SEX	0.039*
		RACEGRP2*SUSMHS	0.012*
		INCGRP1*RACEGRP2	0.011*
		INCGRP1	0.010*
		BMIGRP*TREAT	0.007*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		TREAT	<0.001*
		GOLDGR	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 18	Removed Effect	RACEGRP2*TREAT	0.509
Iteration 18	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 19	AIC	18406.8	
Iteration 19	Type 3 Wald p-values	SEX	0.641
		AGEGRP1	0.579
		RACEGRP2*SEX	0.441
		EBHIS2*SUSMHS	0.429
		SEX*TREAT	0.393
		EBHIS2*SEX	0.313
		AGEGRP1*RACEGRP2	0.304
		RACEGRP2	0.254
		GOLDGR*INCGRP1	0.206
		BMIGRP*SEX	0.201
		BMIGRP*RACEGRP2	0.168
		BMIGRP	0.143
		EBHIS2*TREAT	0.142
		EBHIS2*RACEGRP2	0.131
		AGEGRP1*EBHIS2	0.064*
		SUSMHS	0.057*
		EBHIS2*INCGRP1	0.051*
		INCGRP1*SEX	0.045*
		AGEGRP1*SEX	0.039*
		RACEGRP2*SUSMHS	0.011*
		INCGRP1*RACEGRP2	0.011*
		INCGRP1	0.010*
		BMIGRP*TREAT	0.008*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 19	Removed Effect	RACEGRP2*SEX	0.441

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description	
Iteration 19	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Population: Intent-to-Treat

Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 20	AIC	18405.3	
Iteration 20	Type 3 Wald p-values	AGEGRP1	0.605
		EBHIS2*SUSMHS	0.435
		RACEGRP2	0.406
		SEX*TREAT	0.400
		EBHIS2*SEX	0.315
		AGEGRP1*RACEGRP2	0.272
		BMIGRP*SEX	0.227
		GOLDGR*INCGRP1	0.200
		BMIGRP*RACEGRP2	0.169
		EBHIS2*TREAT	0.137
		BMIGRP	0.135
		EBHIS2*RACEGRP2	0.129
		SEX	0.090*
		AGEGRP1*EBHIS2	0.066*
		INCGRP1*SEX	0.061*
		SUSMHS	0.057*
		EBHIS2*INCGRP1	0.048*
		AGEGRP1*SEX	0.042*
		INCGRP1	0.014*
		RACEGRP2*SUSMHS	0.011*
		BMIGRP*TREAT	0.008*
		INCGRP1*RACEGRP2	0.008*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 20	Removed Effect	EBHIS2*SUSMHS	0.435

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description	
Iteration 20	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 21	AIC	18404.0	
Iteration 21	Type 3 Wald p-values	AGEGRP1	0.595
		RACEGRP2	0.405
		SEX*TREAT	0.400
		EBHIS2*SEX	0.333
		AGEGRP1*RACEGRP2	0.271
		BMIGRP*SEX	0.222
		GOLDGR*INCGRP1	0.202
		BMIGRP*RACEGRP2	0.171
		BMIGRP	0.135
		EBHIS2*TREAT	0.134
		EBHIS2*RACEGRP2	0.101
		AGEGRP1*EBHIS2	0.089*
		SEX	0.089*
		SUSMHS	0.067*
		INCGRP1*SEX	0.061*
		EBHIS2*INCGRP1	0.047*
		AGEGRP1*SEX	0.041*
		INCGRP1	0.014*
		RACEGRP2*SUSMHS	0.010*
		INCGRP1*RACEGRP2	0.008*
		BMIGRP*TREAT	0.008*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 21	Removed Effect	SEX*TREAT	0.400
Iteration 21	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 22	AIC	18402.7	
Iteration 22	Type 3 Wald p-values	AGEGRP1	0.589
		RACEGRP2	0.406
		EBHIS2*SEX	0.349
		AGEGRP1*RACEGRP2	0.272
		BMIGRP*SEX	0.238
		GOLDGR*INCGRP1	0.204
		BMIGRP*RACEGRP2	0.173
		EBHIS2*TREAT	0.151
		BMIGRP	0.130
		SEX	0.124
		EBHIS2*RACEGRP2	0.102
		AGEGRP1*EBHIS2	0.086*
		SUSMHS	0.068*
		INCGRP1*SEX	0.059*
		EBHIS2*INCGRP1	0.047*
		AGEGRP1*SEX	0.042*
		INCGRP1	0.014*
		RACEGRP2*SUSMHS	0.010*
		BMIGRP*TREAT	0.009*
		INCGRP1*RACEGRP2	0.008*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 22	Removed Effect	EBHIS2*SEX	0.349
Iteration 22	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 23	AIC	18401.5	
Iteration 23	Type 3 Wald p-values	AGEGRP1	0.619
		RACEGRP2	0.425
		AGEGRP1*RACEGRP2	0.274
		BMIGRP*SEX	0.243
		GOLDGR*INCGRP1	0.207
		BMIGRP*RACEGRP2	0.173
		EBHIS2*TREAT	0.160
		BMIGRP	0.129
		EBHIS2*RACEGRP2	0.122
		SEX	0.088*
		SUSMHS	0.069*
		AGEGRP1*EBHIS2	0.059*
		INCGRP1*SEX	0.056*
		AGEGRP1*SEX	0.036*
		EBHIS2*INCGRP1	0.032*
		INCGRP1	0.013*
		RACEGRP2*SUSMHS	0.010*
		BMIGRP*TREAT	0.009*
		INCGRP1*RACEGRP2	0.008*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 23	Removed Effect	AGEGRP1*RACEGRP2	0.274
Iteration 23	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 24	AIC	18400.7	
Iteration 24	Type 3 Wald p-values	RACEGRP2	0.557
		BMIGRP*SEX	0.249
		GOLDGR*INCGRP1	0.201
		EBHIS2*TREAT	0.164
		BMIGRP*RACEGRP2	0.161
		BMIGRP	0.134
		EBHIS2*RACEGRP2	0.111
		SEX	0.088*
		SUSMHS	0.081*
		AGEGRP1	0.066*
		INCGRP1*SEX	0.062*
		AGEGRP1*EBHIS2	0.054*
		AGEGRP1*SEX	0.051*
		EBHIS2*INCGRP1	0.031*
		INCGRP1	0.017*
		RACEGRP2*SUSMHS	0.014*
		BMIGRP*TREAT	0.009*
		INCGRP1*RACEGRP2	0.005*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 24	Removed Effect	BMIGRP*SEX	0.249
Iteration 24	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 25	AIC	18400.0	
Iteration 25	Type 3 Wald p-values	RACEGRP2	0.555
		GOLDGR*INCGRP1	0.205
		BMIGRP*RACEGRP2	0.193
		EBHIS2*TREAT	0.163
		EBHIS2*RACEGRP2	0.111
		SUSMHS	0.079*
		AGEGRP1	0.067*
		SEX	0.057*
		AGEGRP1*EBHIS2	0.055*
		AGEGRP1*SEX	0.051*
		BMIGRP	0.041*
		INCGRP1*SEX	0.041*
		EBHIS2*INCGRP1	0.032*
		RACEGRP2*SUSMHS	0.014*
		INCGRP1	0.013*
		BMIGRP*TREAT	0.010*
		INCGRP1*RACEGRP2	0.006*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 25	Removed Effect	GOLDGR*INCGRP1	0.205
Iteration 25	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 26	AIC	18399.7	
Iteration 26	Type 3 Wald p-values	RACEGRP2	0.574
		BMIGRP*RACEGRP2	0.209
		EBHIS2*TREAT	0.172
		EBHIS2*RACEGRP2	0.117
		SUSMHS	0.074*
		AGEGRP1	0.068*
		SEX	0.056*
		AGEGRP1*EBHIS2	0.052*
		AGEGRP1*SEX	0.050*
		EBHIS2*INCGRP1	0.040*
		INCGRP1*SEX	0.036*
		BMIGRP	0.033*
		INCGRP1	0.026*
		RACEGRP2*SUSMHS	0.013*
		BMIGRP*TREAT	0.009*
		INCGRP1*RACEGRP2	0.006*
		BMIGRP*INCGRP1	<0.001*
		EBHIS2	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 26	Removed Effect	BMIGRP*RACEGRP2	0.209
Iteration 26	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 27	AIC	18399.2	
Iteration 27	Type 3 Wald p-values	RACEGRP2	0.867
		EBHIS2*TREAT	0.167
		EBHIS2*RACEGRP2	0.119
		SUSMHS	0.078*
		AGEGRP1	0.069*
		AGEGRP1*EBHIS2	0.054*
		SEX	0.053*
		AGEGRP1*SEX	0.050*
		EBHIS2*INCGRP1	0.042*
		INCGRP1*SEX	0.034*
		INCGRP1	0.033*
		RACEGRP2*SUSMHS	0.013*
		BMIGRP*TREAT	0.009*
		INCGRP1*RACEGRP2	0.006*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	<0.001*
		BMIGRP	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 27	Removed Effect	EBHIS2*TREAT	0.167
Iteration 27	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 28	AIC	18399.1	
Iteration 28	Type 3 Wald p-values	RACEGRP2	0.884
		EBHIS2*RACEGRP2	0.115
		SUSMHS	0.074*
		AGEGRP1	0.069*
		AGEGRP1*EBHIS2	0.054*
		AGEGRP1*SEX	0.053*
		SEX	0.053*
		EBHIS2*INCGRP1	0.044*
		INCGRP1*SEX	0.034*
		INCGRP1	0.034*
		RACEGRP2*SUSMHS	0.012*
		BMIGRP*TREAT	0.010*
		INCGRP1*RACEGRP2	0.006*
		BMIGRP*INCGRP1	0.002*
		EBHIS2	0.001*
		BMIGRP	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 28	Removed Effect	EBHIS2*RACEGRP2	0.115
Iteration 28	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 29	AIC	18399.6	
Iteration 29	Type 3 Wald p-values	RACEGRP2	0.751
		EBHIS2*INCGRP1	0.132
		AGEGRP1*EBHIS2	0.078*
		SUSMHS	0.076*
		AGEGRP1	0.062*
		AGEGRP1*SEX	0.055*
		SEX	0.049*
		INCGRP1*SEX	0.031*
		INCGRP1	0.028*
		RACEGRP2*SUSMHS	0.013*
		BMIGRP*TREAT	0.010*
		INCGRP1*RACEGRP2	0.009*
		EBHIS2	0.004*
		BMIGRP*INCGRP1	0.003*
		BMIGRP	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*
Iteration 29	Removed Effect	EBHIS2*INCGRP1	0.132
Iteration 29	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.1
Summary of Pneumonia Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 30	AIC	18399.9	
Iteration 30	Type 3 Wald p-values	RACEGRP2	0.789
		AGEGRP1*EBHIS2	0.083*
		SUSMHS	0.071*
		AGEGRP1	0.063*
		AGEGRP1*SEX	0.053*
		SEX	0.049*
		INCGRP1	0.039*
		INCGRP1*SEX	0.028*
		RACEGRP2*SUSMHS	0.012*
		BMIGRP*TREAT	0.011*
		INCGRP1*RACEGRP2	0.009*
		BMIGRP*INCGRP1	0.003*
		EBHIS2	<0.001*
		BMIGRP	<0.001*
		GOLDGR	<0.001*
		TREAT	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.04 (0.02,0.05)	0.02 (0.01,0.03)		
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.05 (0.03,0.08)	0.03 (0.01,0.04)		
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.06 (0.03,0.08)	0.03 (0.02,0.04)		0.00 (0/ 1)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.08 (0.04,0.11)	0.04 (0.02,0.06)		
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.01,0.04)	0.02 (0.01,0.03)		
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.06)	0.03 (0.01,0.04)		
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.04 (0.02,0.06)	0.03 (0.02,0.05)		
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.06 (0.03,0.08)	0.04 (0.02,0.07)		

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.04 (0.02,0.06)	0.02 (0.01,0.03)	0.00 (0 / 2)	0.00 (0/ 1)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.05 (0.03,0.08)	0.03 (0.01,0.04)	0.00 (0 / 1)	
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.06 (0.04,0.08)	0.03 (0.02,0.05)	0.00 (0 / 1)	0.00 (0/ 1)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.08 (0.05,0.11)	0.05 (0.03,0.06)		0.00 (0/ 1)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.01 (0.01,0.02)		
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.01,0.04)	0.02 (0.01,0.03)		
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.01,0.03)	0.00 (0 / 2)	
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.06)	0.03 (0.02,0.04)		

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Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
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Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.06 (0.05,0.08)	0.04 (0.03,0.04)	0.03 (2 / 63)	0.00 (0/ 37)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.09 (0.07,0.11)	0.05 (0.04,0.06)	0.00 (0 / 31)	0.05 (1/ 22)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.06 (0.04,0.07)	0.03 (0.02,0.04)	0.00 (0 / 15)	0.00 (0/ 15)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.08 (0.06,0.10)	0.05 (0.03,0.06)	0.00 (0 / 11)	0.00 (0/ 7)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.05 (4 / 78)	0.06 (3/ 49)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.07 (0.05,0.08)	0.05 (0.04,0.06)	0.07 (3 / 44)	0.17 (5/ 30)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.04 (0.03,0.05)	0.03 (0.02,0.04)	0.02 (1 / 54)	0.11 (3/ 27)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.06 (0.05,0.08)	0.05 (0.03,0.06)	0.11 (2 / 18)	0.00 (0/ 13)

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Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
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Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.04 (0.02,0.05)	0.02 (0.01,0.03)	0.00 (0 / 18)	0.00 (0/ 10)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.05 (0.03,0.07)	0.03 (0.02,0.04)	0.25 (3 / 12)	0.00 (0/ 5)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.04 (0.02,0.05)	0.02 (0.01,0.03)	0.00 (0 / 7)	0.00 (0/ 3)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.05 (0.03,0.07)	0.03 (0.02,0.04)	0.00 (0 / 4)	0.00 (0/ 4)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.02 (0.01,0.02)	0.01 (0.01,0.02)	0.04 (1 / 23)	0.00 (0/ 12)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.01,0.03)	0.00 (0 / 21)	0.08 (1/ 13)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.02 (0.01,0.02)	0.01 (0.01,0.02)	0.05 (1 / 21)	0.00 (0/ 13)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.03)	0.00 (0 / 16)	0.00 (0/ 12)

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.03 (0.02,0.05)	0.02 (0.01,0.03)	0.00 (0 / 3)	
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.04 (0.02,0.06)	0.02 (0.01,0.04)		
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.05 (0.03,0.07)	0.03 (0.02,0.04)	0.00 (0 / 1)	
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.05)		
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.03)	0.00 (0 / 2)	
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.02 (0.01,0.04)		1.00 (1/ 1)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.04 (0.02,0.05)	0.03 (0.02,0.04)	0.00 (0 / 1)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.06)		

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Probability of Pneumonia During Year on Study Treatment from Cox Model
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<=64/I & II/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.05 (0.03,0.07)	0.03 (0.02,0.04)	0.11 (1 / 9)	0.00 (0/ 9)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.07 (0.04,0.09)	0.04 (0.02,0.05)		
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.05,0.09)	0.04 (0.03,0.05)	0.00 (0 / 17)	0.00 (0/ 5)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.10 (0.07,0.13)	0.06 (0.04,0.08)	0.00 (0 / 5)	0.00 (0/ 3)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.03)	0.00 (0 / 3)	0.00 (0/ 3)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.02 (0.01,0.04)	0.00 (0 / 1)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.04 (0.02,0.05)	0.03 (0.02,0.04)	0.00 (0 / 10)	0.00 (0/ 4)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.05)	0.00 (0 / 1)	0.00 (0/ 3)

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Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
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<=64/I & II/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.05 (0.04,0.07)	0.03 (0.02,0.04)	0.04 (2 / 53)	0.07 (3/ 46)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.08 (0.06,0.09)	0.04 (0.03,0.05)	0.03 (1 / 30)	0.00 (0/ 13)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.05 (0.04,0.06)	0.03 (0.02,0.04)	0.06 (1 / 17)	0.00 (0/ 17)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.05,0.09)	0.04 (0.03,0.05)	0.08 (1 / 12)	0.00 (0/ 6)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.04 (0.03,0.05)	0.03 (0.02,0.04)	0.02 (2 / 104)	0.03 (2/ 73)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.06 (0.04,0.07)	0.04 (0.03,0.05)	0.00 (0 / 39)	0.08 (2/ 26)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.04 (0.03,0.05)	0.03 (0.02,0.04)	0.02 (2 / 96)	0.02 (1/ 50)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.05 (0.04,0.07)	0.04 (0.03,0.05)	0.07 (2 / 28)	0.04 (1/ 27)

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<=64/I & II/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.05 (0.04,0.06)	0.03 (0.02,0.03)	0.05 (2 / 37)	0.00 (0/ 30)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.07 (0.05,0.08)	0.04 (0.03,0.05)	0.00 (0 / 15)	0.00 (0/ 12)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.04 (0.03,0.06)	0.02 (0.02,0.03)	0.09 (1 / 11)	0.00 (0/ 7)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.06 (0.05,0.08)	0.03 (0.02,0.04)	0.00 (0 / 3)	0.00 (0/ 6)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.02 (0.02,0.03)	0.02 (0.01,0.02)	0.02 (1 / 49)	0.00 (0/ 19)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.02,0.03)	0.00 (0 / 12)	0.00 (0/ 20)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.02)	0.00 (0 / 37)	0.00 (0/ 24)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.02,0.03)	0.06 (1 / 16)	0.00 (0/ 11)

Table 2.2
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Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- of First Event-------- ICS	non-ICS	----Observed Probability----- of First Event-------- ICS	non-ICS
<=64/III & IV/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.05 (0.03,0.08)	0.03 (0.01,0.04)	0.00 (0 / 1)	
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.07 (0.04,0.11)	0.04 (0.02,0.06)		
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.08 (0.05,0.12)	0.05 (0.03,0.06)		
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.12 (0.07,0.16)	0.06 (0.04,0.09)	0.00 (0 / 1)	
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.04 (0.02,0.06)	0.03 (0.01,0.05)		
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.06 (0.03,0.08)	0.04 (0.02,0.06)	0.00 (0 / 1)	
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.06 (0.03,0.09)	0.05 (0.03,0.07)		
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.09 (0.05,0.12)	0.07 (0.04,0.09)	0.00 (0 / 1)	

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<=64/III & IV/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.06 (0.03,0.08)	0.03 (0.02,0.05)	0.33 (1 / 3)	0.00 (0/ 1)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.08 (0.04,0.11)	0.04 (0.02,0.06)	0.00 (0 / 2)	0.00 (0/ 2)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.09 (0.05,0.12)	0.05 (0.03,0.07)	0.25 (3 / 12)	0.00 (0/ 4)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.12 (0.08,0.16)	0.07 (0.04,0.09)	0.50 (1 / 2)	0.00 (0/ 4)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.01,0.04)	0.02 (0.01,0.03)		0.00 (0/ 1)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.06)	0.03 (0.01,0.04)		
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.04 (0.02,0.06)	0.03 (0.02,0.05)	0.00 (0 / 3)	0.00 (0/ 2)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.06 (0.03,0.08)	0.04 (0.02,0.06)		0.00 (0/ 1)

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<=64/III & IV/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.09 (0.07,0.11)	0.05 (0.04,0.06)	0.10 (11/ 109)	0.04 (3/ 85)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.13 (0.10,0.16)	0.07 (0.06,0.09)	0.10 (7 / 69)	0.06 (4/ 63)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.09 (0.07,0.11)	0.05 (0.04,0.06)	0.03 (1 / 32)	0.04 (2/ 52)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.12 (0.09,0.15)	0.07 (0.05,0.09)	0.03 (1 / 37)	0.04 (1/ 24)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.07 (0.05,0.08)	0.05 (0.04,0.07)	0.05 (4 / 84)	0.05 (3/ 55)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.10 (0.08,0.12)	0.07 (0.06,0.09)	0.09 (6 / 70)	0.00 (0/ 35)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.06 (0.05,0.08)	0.05 (0.04,0.06)	0.08 (6 / 72)	0.07 (3/ 44)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.09 (0.07,0.11)	0.07 (0.05,0.09)	0.09 (5 / 56)	0.00 (0/ 36)

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
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<=64/III & IV/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.06 (0.04,0.07)	0.03 (0.02,0.04)	0.10 (2 / 21)	0.00 (0/ 16)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.08 (0.05,0.10)	0.04 (0.03,0.06)	0.05 (1 / 20)	0.17 (1/ 6)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.05 (0.03,0.07)	0.03 (0.02,0.04)	0.00 (0 / 19)	0.00 (0/ 14)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.05,0.10)	0.04 (0.03,0.06)	0.06 (1 / 16)	0.08 (1/ 13)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.01,0.03)	0.05 (1 / 21)	0.00 (0/ 12)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.05)	0.03 (0.02,0.04)	0.05 (1 / 22)	0.00 (0/ 11)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.02 (0.02,0.03)	0.02 (0.01,0.03)	0.07 (1 / 15)	0.00 (0/ 7)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.05)	0.03 (0.02,0.04)	0.00 (0 / 29)	0.00 (0/ 7)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- of First Event-------- ICS	non-ICS	----Observed Probability----- of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.05 (0.02,0.07)	0.03 (0.01,0.04)	0.13 (1 / 8)	0.00 (0/ 2)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.06 (0.03,0.09)	0.04 (0.02,0.05)	0.00 (0 / 2)	0.00 (0/ 5)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.05)	0.00 (0 / 3)	0.00 (0/ 5)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.10 (0.06,0.14)	0.06 (0.03,0.08)	0.33 (1 / 3)	0.11 (1/ 9)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.03 (0.01,0.04)	0.33 (1 / 3)	
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.05 (0.02,0.07)	0.04 (0.02,0.05)	0.25 (1 / 4)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.06)	0.00 (0 / 5)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.07 (0.04,0.10)	0.06 (0.03,0.08)	0.00 (0 / 1)	0.00 (0/ 1)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.05)	0.07 (1 / 14)	0.00 (0/ 14)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.10 (0.06,0.13)	0.05 (0.03,0.08)	0.08 (1 / 12)	0.00 (0/ 5)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.11 (0.08,0.13)	0.06 (0.04,0.08)	0.10 (2 / 21)	0.06 (2/ 34)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.15 (0.11,0.19)	0.08 (0.06,0.11)	0.14 (3 / 21)	0.31 (5/ 16)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.03 (0.01,0.04)	0.00 (0 / 4)	0.00 (0/ 1)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.05)	0.00 (0 / 2)	
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.03,0.05)	0.50 (3 / 6)	0.00 (0/ 4)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.07 (0.05,0.10)	0.06 (0.04,0.08)	0.00 (0 / 4)	0.00 (0/ 2)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.08 (0.07,0.10)	0.04 (0.03,0.05)	0.09 (14/ 153)	0.05 (5/ 110)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.11 (0.09,0.13)	0.06 (0.05,0.08)	0.09 (6 / 66)	0.03 (2/ 67)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.06,0.09)	0.04 (0.03,0.05)	0.06 (4 / 72)	0.07 (3/ 44)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.11 (0.08,0.13)	0.06 (0.04,0.07)	0.23 (11/ 48)	0.04 (1/ 26)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.06 (0.05,0.07)	0.05 (0.04,0.06)	0.04 (5 / 131)	0.03 (3/ 106)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.08 (0.07,0.10)	0.06 (0.05,0.08)	0.04 (3 / 75)	0.05 (3/ 59)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.06 (0.04,0.07)	0.04 (0.03,0.05)	0.06 (7 / 122)	0.03 (3/ 99)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.08 (0.06,0.09)	0.06 (0.05,0.07)	0.06 (5 / 86)	0.01 (1/ 74)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.07 (0.05,0.09)	0.04 (0.03,0.05)	0.04 (2 / 55)	0.00 (0/ 39)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.10 (0.08,0.12)	0.06 (0.04,0.07)	0.11 (4 / 36)	0.08 (3/ 40)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.05,0.08)	0.04 (0.03,0.05)	0.07 (3 / 41)	0.00 (0/ 23)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.09 (0.07,0.11)	0.05 (0.04,0.06)	0.07 (2 / 30)	0.05 (1/ 20)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.03 (0.02,0.03)	0.06 (2 / 33)	0.06 (2/ 32)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.05 (0.03,0.06)	0.04 (0.03,0.05)	0.00 (0 / 23)	0.05 (1/ 21)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.02,0.03)	0.02 (1 / 47)	0.00 (0/ 34)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.04 (0.03,0.06)	0.03 (0.02,0.04)	0.00 (0 / 29)	0.12 (3/ 25)

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.04 (0.02,0.06)	0.02 (0.01,0.03)	0.00 (0 / 1)	
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.05 (0.02,0.07)	0.03 (0.01,0.04)		
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.06 (0.04,0.09)	0.03 (0.02,0.05)		
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.06)	1.00 (1 / 1)	
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.01,0.04)	0.02 (0.01,0.03)		
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.03 (0.01,0.04)		
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.05)		0.00 (0/ 1)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.05 (0.03,0.08)	0.04 (0.02,0.06)		

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- of First Event-------- ICS	non-ICS	----Observed Probability----- of First Event-------- ICS	non-ICS
>=65/I & II/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.04 (0.02,0.06)	0.02 (0.01,0.03)	0.00 (0 / 3)	0.00 (0/ 2)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.05 (0.02,0.07)	0.03 (0.01,0.04)	0.00 (0 / 1)	
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.04,0.09)	0.04 (0.02,0.05)	0.00 (0 / 2)	0.00 (0/ 3)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.06)	0.00 (0 / 1)	0.50 (1/ 2)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.02)		
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.03)		
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.01,0.03)		
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.05)	0.03 (0.01,0.04)	0.00 (0 / 1)	

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- of First Event-------- ICS	non-ICS	----Observed Probability----- of First Event-------- ICS	non-ICS
>=65/I & II/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.07 (0.05,0.09)	0.04 (0.03,0.05)	0.00 (0 / 34)	0.00 (0/ 24)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.08 (0.06,0.10)	0.04 (0.03,0.06)	0.24 (5 / 21)	0.00 (0/ 14)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.05,0.08)	0.04 (0.03,0.05)	0.04 (2 / 52)	0.04 (1/ 28)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.06,0.09)	0.04 (0.03,0.05)	0.12 (3 / 26)	0.00 (0/ 11)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.05 (0.04,0.07)	0.04 (0.03,0.05)	0.03 (1 / 35)	0.00 (0/ 21)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.06 (0.04,0.07)	0.05 (0.03,0.06)	0.05 (1 / 19)	0.00 (0/ 15)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.04 (4 / 90)	0.05 (3/ 55)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.06 (0.04,0.07)	0.04 (0.03,0.05)	0.05 (2 / 37)	0.00 (0/ 38)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.04 (0.03,0.06)	0.02 (0.01,0.03)	0.00 (0 / 7)	0.00 (0/ 4)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.05 (0.03,0.07)	0.03 (0.02,0.04)	0.00 (0 / 5)	0.00 (0/ 2)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.04 (0.02,0.05)	0.02 (0.01,0.03)	0.00 (0 / 10)	0.00 (0/ 2)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.04 (0.03,0.06)	0.02 (0.01,0.03)	0.00 (0 / 4)	
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.02)	0.00 (0 / 12)	0.00 (0/ 6)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.02)	0.00 (0 / 9)	0.00 (0/ 6)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.01 (0.01,0.02)	0.00 (0 / 17)	0.00 (0/ 13)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.02 (0.01,0.03)	0.02 (0.01,0.02)	0.00 (0 / 11)	0.00 (0/ 3)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.04 (0.02,0.07)	0.02 (0.01,0.04)	0.00 (0 / 7)	0.00 (0/ 4)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.05 (0.03,0.07)	0.03 (0.01,0.04)	0.00 (0 / 3)	
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.05)	0.11 (1 / 9)	0.11 (1/ 9)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.08 (0.05,0.11)	0.04 (0.03,0.06)	0.00 (0 / 3)	0.00 (0/ 3)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.03 (0.01,0.04)	0.00 (0 / 3)	0.00 (0/ 3)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.06)	0.03 (0.01,0.04)	0.00 (0 / 1)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.06)	0.00 (0 / 1)	0.00 (0/ 4)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.06 (0.03,0.08)	0.04 (0.03,0.06)		

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.05)	0.14 (2 / 14)	0.00 (0/ 6)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.08 (0.05,0.11)	0.04 (0.03,0.06)	0.00 (0 / 3)	0.00 (0/ 2)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.11 (0.08,0.13)	0.06 (0.04,0.08)	0.18 (3 / 17)	0.08 (1/ 13)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.12 (0.09,0.15)	0.07 (0.05,0.09)	0.14 (1 / 7)	0.10 (1/ 10)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.03 (0.01,0.04)	0.00 (0 / 3)	0.00 (0/ 1)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.04 (0.02,0.05)	0.03 (0.02,0.04)		0.00 (0/ 2)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.03,0.05)	0.17 (2 / 12)	0.00 (0/ 6)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.06 (0.04,0.08)	0.04 (0.03,0.06)	0.00 (0 / 5)	0.00 (0/ 5)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.08 (0.06,0.09)	0.04 (0.03,0.05)	0.14 (6 / 44)	0.00 (0/ 21)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.09 (0.07,0.11)	0.05 (0.04,0.06)	0.00 (0 / 19)	0.08 (1/ 13)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.07 (0.06,0.09)	0.04 (0.03,0.05)	0.03 (2 / 75)	0.00 (0/ 60)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.08 (0.07,0.10)	0.05 (0.03,0.06)	0.03 (1 / 30)	0.11 (2/ 18)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.06 (0.05,0.07)	0.04 (0.03,0.05)	0.07 (4 / 60)	0.02 (1/ 54)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.07 (0.05,0.08)	0.05 (0.04,0.06)	0.00 (0 / 15)	0.05 (1/ 22)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.05 (10/ 190)	0.05 (8/ 164)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.06 (0.05,0.08)	0.05 (0.04,0.06)	0.07 (6 / 91)	0.05 (2/ 42)

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.07 (0.05,0.09)	0.04 (0.03,0.05)	0.00 (0 / 17)	0.05 (1/ 20)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.08 (0.06,0.10)	0.04 (0.03,0.06)	0.00 (0 / 10)	0.07 (1/ 14)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.06 (0.05,0.08)	0.04 (0.03,0.05)	0.00 (0 / 30)	0.00 (0/ 23)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.06,0.09)	0.04 (0.03,0.05)	0.18 (2 / 11)	0.00 (0/ 6)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.03 (0.02,0.03)	0.00 (0 / 13)	0.00 (0/ 12)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.04 (0.03,0.05)	0.03 (0.02,0.04)	0.00 (0 / 10)	0.00 (0/ 4)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.02,0.03)	0.02 (1 / 58)	0.06 (2/ 36)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.04 (0.03,0.05)	0.03 (0.02,0.03)	0.00 (0 / 21)	0.00 (0/ 21)

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.06 (0.03,0.09)	0.03 (0.02,0.05)		
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.07 (0.03,0.10)	0.04 (0.02,0.06)	0.00 (0 / 1)	
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.09 (0.05,0.13)	0.05 (0.03,0.07)	0.00 (0 / 1)	0.00 (0/ 1)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.10 (0.06,0.14)	0.06 (0.03,0.08)		0.00 (0/ 1)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.04 (0.02,0.07)	0.03 (0.02,0.05)		
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.05 (0.02,0.07)	0.04 (0.02,0.06)		
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.07 (0.04,0.10)	0.05 (0.03,0.08)		
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.08 (0.04,0.11)	0.06 (0.03,0.09)		

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.06 (0.03,0.09)	0.03 (0.02,0.05)	0.00 (0 / 2)	
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.07 (0.04,0.10)	0.04 (0.02,0.06)	0.00 (0 / 2)	0.00 (0/ 1)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.10 (0.06,0.13)	0.05 (0.03,0.07)	0.00 (0 / 7)	0.00 (0/ 8)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.11 (0.07,0.15)	0.06 (0.04,0.08)	0.50 (2 / 4)	0.00 (0/ 2)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.01,0.05)	0.02 (0.01,0.03)		
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.03 (0.01,0.04)		
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.05)	0.00 (0 / 3)	
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.05 (0.03,0.08)	0.04 (0.02,0.06)		0.00 (0/ 1)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.10 (0.08,0.13)	0.06 (0.04,0.07)	0.11 (6 / 54)	0.05 (2/ 37)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.12 (0.09,0.14)	0.07 (0.05,0.08)	0.10 (5 / 52)	0.04 (1/ 28)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.10 (0.08,0.12)	0.05 (0.04,0.07)	0.07 (6 / 87)	0.02 (1/ 66)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.11 (0.09,0.13)	0.06 (0.05,0.08)	0.09 (5 / 58)	0.05 (2/ 40)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.08 (0.06,0.10)	0.06 (0.04,0.07)	0.03 (1 / 40)	0.11 (2/ 19)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.09 (0.07,0.11)	0.07 (0.05,0.08)	0.19 (5 / 26)	0.00 (0/ 12)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.07 (0.06,0.09)	0.06 (0.04,0.07)	0.05 (6 / 112)	0.05 (3/ 64)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.08 (0.06,0.10)	0.06 (0.05,0.08)	0.06 (4 / 62)	0.08 (5/ 62)

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.06 (0.04,0.08)	0.03 (0.02,0.05)	0.20 (1 / 5)	0.00 (0/ 7)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.07 (0.05,0.10)	0.04 (0.02,0.05)	0.13 (1 / 8)	0.00 (0/ 6)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.06 (0.04,0.08)	0.03 (0.02,0.04)	0.06 (1 / 16)	0.00 (0/ 8)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.07 (0.04,0.09)	0.04 (0.02,0.05)	0.20 (2 / 10)	0.00 (0/ 8)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.01,0.03)	0.00 (0 / 10)	0.00 (0/ 7)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.05)	0.03 (0.02,0.04)	0.00 (0 / 4)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.01,0.03)	0.00 (0 / 14)	0.00 (0/ 10)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.03 (0.02,0.04)	0.02 (0.01,0.03)	0.00 (0 / 8)	0.00 (0/ 7)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.07 (0.04,0.09)	0.04 (0.02,0.05)	0.00 (0 / 8)	0.00 (0/ 23)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.08 (0.04,0.11)	0.04 (0.02,0.06)	0.20 (1 / 5)	0.09 (1/ 11)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.10 (0.06,0.14)	0.06 (0.03,0.08)	0.13 (3 / 23)	0.00 (0/ 12)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.12 (0.07,0.16)	0.06 (0.04,0.09)	0.05 (1 / 20)	0.05 (1/ 21)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.06)	0.33 (1 / 3)	
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.06 (0.03,0.08)	0.04 (0.02,0.06)	0.00 (0 / 2)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.08 (0.05,0.10)	0.06 (0.03,0.08)	0.20 (1 / 5)	0.00 (0/ 4)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.09 (0.05,0.12)	0.07 (0.04,0.09)	0.00 (0 / 3)	

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.10 (0.06,0.14)	0.06 (0.03,0.08)	0.08 (1 / 12)	0.10 (1/ 10)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.11 (0.07,0.16)	0.06 (0.04,0.09)	0.13 (1 / 8)	0.00 (0/ 9)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.15 (0.12,0.19)	0.09 (0.07,0.11)	0.21 (12/ 58)	0.09 (5/ 54)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.17 (0.13,0.21)	0.10 (0.07,0.12)	0.11 (4 / 35)	0.12 (3/ 25)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.05 (0.03,0.07)	0.04 (0.02,0.05)	0.00 (0 / 3)	0.33 (1/ 3)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.06 (0.03,0.08)	0.04 (0.02,0.06)	0.00 (0 / 2)	0.00 (0/ 1)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.08 (0.05,0.10)	0.06 (0.04,0.08)	0.00 (0 / 11)	0.00 (0/ 6)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.09 (0.06,0.11)	0.07 (0.04,0.09)	0.00 (0 / 4)	0.00 (0/ 8)

Protocol: 207941
Population: Intent-to-Treat

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.12 (0.10,0.14)	0.06 (0.05,0.08)	0.07 (5 / 76)	0.05 (4/ 81)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.13 (0.11,0.16)	0.07 (0.06,0.09)	0.14 (8 / 56)	0.05 (2/ 44)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.11 (0.09,0.13)	0.06 (0.05,0.07)	0.08 (13/ 168)	0.03 (5/ 154)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.12 (0.10,0.14)	0.07 (0.05,0.08)	0.11 (12/ 105)	0.10 (9/ 91)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.09 (0.07,0.10)	0.07 (0.05,0.08)	0.04 (4 / 97)	0.01 (1/ 70)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.10 (0.08,0.12)	0.08 (0.06,0.09)	0.10 (5 / 50)	0.06 (2/ 32)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.08 (0.07,0.09)	0.06 (0.05,0.07)	0.07 (21/ 297)	0.04 (9/ 237)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.09 (0.07,0.11)	0.07 (0.06,0.08)	0.06 (10/ 164)	0.07 (9/ 133)

Table 2.2
Probability of Pneumonia During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	1.84 (1.55,2.19)	0.10 (0.08,0.12)	0.06 (0.04,0.07)	0.13 (6 / 48)	0.05 (2/ 37)
	<25 kg/m^2/ Current/>=2	1.84 (1.55,2.19)	0.12 (0.09,0.14)	0.06 (0.05,0.08)	0.07 (2 / 28)	0.00 (0/ 16)
	<25 kg/m^2/ Former/<2	1.84 (1.55,2.19)	0.10 (0.07,0.11)	0.05 (0.04,0.07)	0.14 (9 / 63)	0.04 (2/ 48)
	<25 kg/m^2/ Former/>=2	1.84 (1.55,2.19)	0.11 (0.08,0.13)	0.06 (0.05,0.07)	0.12 (5 / 42)	0.02 (1/ 45)
	>=25 kg/m^2/ Current/<2	1.32 (1.09,1.59)	0.05 (0.04,0.06)	0.04 (0.03,0.05)	0.00 (0 / 25)	0.00 (0/ 21)
	>=25 kg/m^2/ Current/>=2	1.32 (1.09,1.59)	0.06 (0.04,0.07)	0.04 (0.03,0.06)	0.06 (1 / 16)	0.00 (0/ 11)
	>=25 kg/m^2/ Former/<2	1.32 (1.09,1.59)	0.05 (0.03,0.06)	0.03 (0.03,0.04)	0.08 (6 / 80)	0.06 (3/ 48)
	>=25 kg/m^2/ Former/>=2	1.32 (1.09,1.59)	0.05 (0.04,0.07)	0.04 (0.03,0.05)	0.07 (3 / 45)	0.00 (0/ 29)

Protocol: 207941
Population: Intent-to-Treat

Table 2.3
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)

Statistic	Level	
Type 3 Wald p-values	Race	0.789
	Exacerbation History by Age	0.083
	Smoking Status	0.071
	Age	0.063
	Sex by Age	0.053
	Sex	0.049
	Country Income	0.039
	Sex by Country Income	0.028
	Smoking Status by Race	0.012
	Treatment by BMI	0.011
	Country Income by Race	0.009
	BMI by Country Income	0.003
	Exacerbation History	<0.001
	BMI	<0.001
	GOLD	<0.001
	Treatment	<0.001

Protocol: 207941
Population: Intent-to-Treat

Table 2.3
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio	Age >=65 vs <=64	
95% CI		
	At Exacerbation History:<2 Sex:F	1.12 (0.86, 1.45)
	At Exacerbation History:<2 Sex:M	1.47 (1.23, 1.75)
	At Exacerbation History:>=2 Sex:F	0.90 (0.68, 1.18)
	At Exacerbation History:>=2 Sex:M	1.18 (0.95, 1.46)
	BMI >=25 kg/m^2 vs <25 kg/m^2	
	At Treatment:ICS Country Income:High income	0.73 (0.62, 0.87)
	At Treatment:ICS Country Income:Non-high income	0.47 (0.36, 0.61)
	At Treatment:non-ICS Country Income:High income	1.02 (0.82, 1.28)
	At Treatment:non-ICS Country Income:Non-high income	0.65 (0.48, 0.88)
	Country Income Non-high income vs High income	
	At BMI:<25 kg/m^2 Sex:F Race:Asian	1.05 (0.63, 1.75)
	At BMI:<25 kg/m^2 Sex:F Race:Non-Asian	0.59 (0.42, 0.83)
	At BMI:<25 kg/m^2 Sex:M Race:Asian	1.56 (1.05, 2.31)
	At BMI:<25 kg/m^2 Sex:M Race:Non-Asian	0.87 (0.71, 1.08)
	At BMI:>=25 kg/m^2 Sex:F Race:Asian	0.67 (0.38, 1.18)
	At BMI:>=25 kg/m^2 Sex:F Race:Non-Asian	0.38 (0.26, 0.54)
	At BMI:>=25 kg/m^2 Sex:M Race:Asian	0.99 (0.62, 1.59)
	At BMI:>=25 kg/m^2 Sex:M Race:Non-Asian	0.56 (0.43, 0.72)
	Exacerbation History >=2 vs <2	
	At Age:<=64	1.42 (1.18, 1.72)
	At Age:>=65	1.14 (0.97, 1.34)
	GOLD III & IV: FEV1<50% predicted vs I & II: FEV1>=50% predicted	
		1.49 (1.30, 1.71)
	Race Asian vs Non-Asian	
	At Smoking Status:Current smoker Country Income:High income	0.56 (0.35, 0.88)
	At Smoking Status:Current smoker Country Income:Non-high income	0.99 (0.67, 1.48)
	At Smoking Status:Former smoker Country Income:High income	0.94 (0.64, 1.38)
	At Smoking Status:Former smoker Country Income:Non-high income	1.68 (1.30, 2.18)
	Sex M vs F	
	At Age:<=64 Country Income:High income	0.86 (0.69, 1.06)
	At Age:<=64 Country Income:Non-high income	1.27 (0.91, 1.78)

PPD

Protocol: 207941
Population: Intent-to-Treat

Table 2.3
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Age:>=65 Country Income:High income	1.12 (0.92, 1.38)
	At Age:>=65 Country Income:Non-high income	1.67 (1.17, 2.37)
	Smoking Status Current smoker vs Former smoker	
	At Race:Asian	0.63 (0.43, 0.94)
	At Race:Non-Asian	1.08 (0.94, 1.23)
	Treatment ICS vs non-ICS	
	At BMI:<25 kg/m^2	1.84 (1.55, 2.19)
	At BMI:>=25 kg/m^2	1.32 (1.09, 1.59)

Protocol: 207941
Population: Intent-to-Treat

Table 2.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)
Expanded BMI Category

Statistic	Level	
Type 3 Wald p-values	Race	0.222
	BMI by Country Income	0.209
	Exacerbation History by Age	0.087
	Age	0.066
	Country Income	0.047
	Smoking Status	0.044
	Sex by Age	0.033
	Sex by Country Income	0.025
	Treatment by BMI	0.023
	Sex	0.019
	Smoking Status by Race	0.016
	Country Income by Race	0.009
	Exacerbation History	<0.001
	GOLD	<0.001
	BMI	<0.001
	Treatment	<0.001

Protocol: 207941
Population: Intent-to-Treat

Table 2.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)
Expanded BMI Category

Statistic	Level	
Hazard Ratio	Age >=65 vs <=64	
95% CI		
	At Exacerbation History:<2 Sex:F	1.10 (0.85, 1.43)
	At Exacerbation History:<2 Sex:M	1.48 (1.24, 1.78)
	At Exacerbation History:>=2 Sex:F	0.88 (0.67, 1.16)
	At Exacerbation History:>=2 Sex:M	1.19 (0.96, 1.48)
	BMI >=20 - <22 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.75 (0.54, 1.04)
	At Treatment:ICS Country Income:Non-high income	0.72 (0.49, 1.06)
	At Treatment:non-ICS Country Income:High income	0.70 (0.46, 1.06)
	At Treatment:non-ICS Country Income:Non-high income	0.67 (0.43, 1.06)
	BMI >=22 - <23 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.74 (0.52, 1.05)
	At Treatment:ICS Country Income:Non-high income	0.92 (0.60, 1.40)
	At Treatment:non-ICS Country Income:High income	0.51 (0.30, 0.86)
	At Treatment:non-ICS Country Income:Non-high income	0.63 (0.36, 1.10)
	BMI >=23 - <24 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.80 (0.57, 1.14)
	At Treatment:ICS Country Income:Non-high income	0.60 (0.36, 0.98)
	At Treatment:non-ICS Country Income:High income	0.56 (0.34, 0.93)
	At Treatment:non-ICS Country Income:Non-high income	0.42 (0.23, 0.76)
	BMI >=24 - <25 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.59 (0.40, 0.86)
	At Treatment:ICS Country Income:Non-high income	0.58 (0.37, 0.93)
	At Treatment:non-ICS Country Income:High income	0.56 (0.34, 0.91)
	At Treatment:non-ICS Country Income:Non-high income	0.55 (0.32, 0.94)
	BMI >=25 - <26 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.79 (0.55, 1.11)
	At Treatment:ICS Country Income:Non-high income	0.52 (0.31, 0.88)
	At Treatment:non-ICS Country Income:High income	0.68 (0.42, 1.10)
	At Treatment:non-ICS Country Income:Non-high income	0.45 (0.25, 0.83)
	BMI >=26 - <28 kg/m^2 vs <20 kg/m^2	

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Protocol: 207941
Population: Intent-to-Treat

Table 2.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)
Expanded BMI Category

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:ICS Country Income:High income	0.64 (0.47, 0.88)
	At Treatment:ICS Country Income:Non-high income	0.40 (0.25, 0.64)
	At Treatment:non-ICS Country Income:High income	0.61 (0.40, 0.93)
	At Treatment:non-ICS Country Income:Non-high income	0.38 (0.22, 0.66)
	BMI >=28 - <30 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.44 (0.30, 0.65)
	At Treatment:ICS Country Income:Non-high income	0.25 (0.13, 0.45)
	At Treatment:non-ICS Country Income:High income	0.76 (0.49, 1.17)
	At Treatment:non-ICS Country Income:Non-high income	0.42 (0.22, 0.81)
	BMI >=30 - <33 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.45 (0.31, 0.66)
	At Treatment:ICS Country Income:Non-high income	0.37 (0.21, 0.65)
	At Treatment:non-ICS Country Income:High income	0.54 (0.33, 0.86)
	At Treatment:non-ICS Country Income:Non-high income	0.44 (0.23, 0.82)
	BMI >=33 kg/m^2 vs <20 kg/m^2	
	At Treatment:ICS Country Income:High income	0.53 (0.37, 0.76)
	At Treatment:ICS Country Income:Non-high income	0.28 (0.13, 0.58)
	At Treatment:non-ICS Country Income:High income	0.97 (0.63, 1.48)
	At Treatment:non-ICS Country Income:Non-high income	0.51 (0.24, 1.08)
	Country Income Non-high income vs High income	
	At BMI:<20 kg/m^2 Sex:F Race:Asian	1.07 (0.63, 1.81)
	At BMI:<20 kg/m^2 Sex:F Race:Non-Asian	0.59 (0.39, 0.90)
	At BMI:<20 kg/m^2 Sex:M Race:Asian	1.60 (1.04, 2.46)
	At BMI:<20 kg/m^2 Sex:M Race:Non-Asian	0.89 (0.64, 1.24)
	At BMI:>=20 - <22 kg/m^2 Sex:F Race:Asian	1.03 (0.56, 1.89)
	At BMI:>=20 - <22 kg/m^2 Sex:F Race:Non-Asian	0.57 (0.36, 0.91)
	At BMI:>=20 - <22 kg/m^2 Sex:M Race:Asian	1.54 (0.92, 2.57)
	At BMI:>=20 - <22 kg/m^2 Sex:M Race:Non-Asian	0.86 (0.59, 1.24)
	At BMI:>=22 - <23 kg/m^2 Sex:F Race:Asian	1.33 (0.69, 2.55)
	At BMI:>=22 - <23 kg/m^2 Sex:F Race:Non-Asian	0.74 (0.44, 1.24)
	At BMI:>=22 - <23 kg/m^2 Sex:M Race:Asian	1.99 (1.13, 3.49)

Protocol: 207941
Population: Intent-to-Treat

Table 2.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)
Expanded BMI Category

Statistic	Level	
Hazard Ratio	At BMI:>=22 - <23 kg/m^2 Sex:M Race:Non-Asian	1.11 (0.71, 1.71)
95% CI		
	At BMI:>=23 - <24 kg/m^2 Sex:F Race:Asian	0.79 (0.39, 1.59)
	At BMI:>=23 - <24 kg/m^2 Sex:F Race:Non-Asian	0.44 (0.25, 0.77)
	At BMI:>=23 - <24 kg/m^2 Sex:M Race:Asian	1.19 (0.64, 2.19)
	At BMI:>=23 - <24 kg/m^2 Sex:M Race:Non-Asian	0.66 (0.40, 1.08)
	At BMI:>=24 - <25 kg/m^2 Sex:F Race:Asian	1.06 (0.53, 2.12)
	At BMI:>=24 - <25 kg/m^2 Sex:F Race:Non-Asian	0.59 (0.34, 1.01)
	At BMI:>=24 - <25 kg/m^2 Sex:M Race:Asian	1.59 (0.87, 2.88)
	At BMI:>=24 - <25 kg/m^2 Sex:M Race:Non-Asian	0.88 (0.56, 1.39)
	At BMI:>=25 - <26 kg/m^2 Sex:F Race:Asian	0.71 (0.35, 1.47)
	At BMI:>=25 - <26 kg/m^2 Sex:F Race:Non-Asian	0.40 (0.22, 0.71)
	At BMI:>=25 - <26 kg/m^2 Sex:M Race:Asian	1.07 (0.56, 2.02)
	At BMI:>=25 - <26 kg/m^2 Sex:M Race:Non-Asian	0.59 (0.36, 0.99)
	At BMI:>=26 - <28 kg/m^2 Sex:F Race:Asian	0.67 (0.34, 1.32)
	At BMI:>=26 - <28 kg/m^2 Sex:F Race:Non-Asian	0.37 (0.22, 0.62)
	At BMI:>=26 - <28 kg/m^2 Sex:M Race:Asian	1.00 (0.55, 1.81)
	At BMI:>=26 - <28 kg/m^2 Sex:M Race:Non-Asian	0.55 (0.36, 0.86)
	At BMI:>=28 - <30 kg/m^2 Sex:F Race:Asian	0.59 (0.27, 1.31)
	At BMI:>=28 - <30 kg/m^2 Sex:F Race:Non-Asian	0.33 (0.17, 0.63)
	At BMI:>=28 - <30 kg/m^2 Sex:M Race:Asian	0.89 (0.44, 1.81)
	At BMI:>=28 - <30 kg/m^2 Sex:M Race:Non-Asian	0.49 (0.28, 0.88)
	At BMI:>=30 - <33 kg/m^2 Sex:F Race:Asian	0.87 (0.40, 1.86)
	At BMI:>=30 - <33 kg/m^2 Sex:F Race:Non-Asian	0.48 (0.26, 0.89)
	At BMI:>=30 - <33 kg/m^2 Sex:M Race:Asian	1.30 (0.65, 2.59)
	At BMI:>=30 - <33 kg/m^2 Sex:M Race:Non-Asian	0.72 (0.42, 1.25)
	At BMI:>=33 kg/m^2 Sex:F Race:Asian	0.56 (0.24, 1.33)
	At BMI:>=33 kg/m^2 Sex:F Race:Non-Asian	0.31 (0.15, 0.65)
	At BMI:>=33 kg/m^2 Sex:M Race:Asian	0.84 (0.37, 1.89)
	At BMI:>=33 kg/m^2 Sex:M Race:Non-Asian	0.47 (0.23, 0.94)
	Exacerbation History >=2 vs <2	
	At Age:<=64	1.41 (1.16, 1.70)

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Protocol: 207941
Population: Intent-to-Treat

Table 2.5
Type 3 p-values and Hazard Ratios from Selected Pneumonia Cox Model
(Based on Nine Covariates)
Expanded BMI Category

Statistic	Level	
Hazard Ratio 95% CI	At Age:>=65	1.13 (0.96, 1.33)
	GOLD III & IV: FEV1<50% predicted vs I & II: FEV1>=50% predicted	1.45 (1.26, 1.67)
	Race Asian vs Non-Asian	
	At Smoking Status:Current smoker Country Income:High income	0.50 (0.31, 0.79)
	At Smoking Status:Current smoker Country Income:Non-high income	0.90 (0.60, 1.34)
	At Smoking Status:Former smoker Country Income:High income	0.83 (0.56, 1.22)
	At Smoking Status:Former smoker Country Income:Non-high income	1.49 (1.14, 1.95)
	Sex M vs F	
	At Age:<=64 Country Income:High income	0.87 (0.70, 1.08)
	At Age:<=64 Country Income:Non-high income	1.30 (0.93, 1.83)
	At Age:>=65 Country Income:High income	1.17 (0.96, 1.44)
	At Age:>=65 Country Income:Non-high income	1.76 (1.24, 2.50)
	Smoking Status Current smoker vs Former smoker	
	At Race:Asian	0.63 (0.42, 0.93)
	At Race:Non-Asian	1.04 (0.91, 1.20)
	Treatment ICS vs non-ICS	
	At BMI:<20 kg/m^2	1.62 (1.22, 2.16)
	At BMI:>=20 - <22 kg/m^2	1.74 (1.22, 2.49)
	At BMI:>=22 - <23 kg/m^2	2.35 (1.46, 3.80)
	At BMI:>=23 - <24 kg/m^2	2.32 (1.45, 3.71)
	At BMI:>=24 - <25 kg/m^2	1.71 (1.09, 2.68)
	At BMI:>=25 - <26 kg/m^2	1.88 (1.19, 2.97)
	At BMI:>=26 - <28 kg/m^2	1.70 (1.17, 2.46)
	At BMI:>=28 - <30 kg/m^2	0.94 (0.61, 1.46)
	At BMI:>=30 - <33 kg/m^2	1.36 (0.86, 2.17)
	At BMI:>=33 kg/m^2	0.89 (0.59, 1.35)

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 1	AIC	112019.7	
Iteration 1	Type 3 Wald p-values	SUSMHS*TREAT	0.967
		GOLDGR*INCGRP1	0.892
		BMIGRP*TREAT	0.823
		AGEGRP1*BMIGRP	0.789
		GOLDGR*SEX	0.773
		INCGRP1*TREAT	0.718
		EBHIS2*SUSMHS	0.709
		BMIGRP*GOLDGR	0.685
		AGEGRP1*SEX	0.662
		GOLDGR*SUSMHS	0.576
		AGEGRP1*RACEGRP2	0.572
		GOLDGR*TREAT	0.558
		AGEGRP1*TREAT	0.505
		EBHIS2*GOLDGR	0.424
		BMIGRP*SUSMHS	0.419
		AGEGRP1	0.385
		RACEGRP2*SUSMHS	0.351
		SUSMHS	0.343
		AGEGRP1*GOLDGR	0.326
		BMIGRP*SEX	0.279
		INCGRP1*SEX	0.190
		AGEGRP1*SUSMHS	0.127
		INCGRP1*RACEGRP2	0.121
		BMIGRP*INCGRP1	0.109
		RACEGRP2*SEX	0.103
		SEX*TREAT	0.098*
		EBHIS2*TREAT	0.087*
		TREAT	0.071*
		SEX	0.067*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Protocol: 207941
Population: Intent-to-Treat

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 1	Type 3 Wald p-values	BMIGRP*EBHIS2	0.067*
		EBHIS2*SEX	0.064*
		BMIGRP*RACEGRP2	0.058*
		EBHIS2*RACEGRP2	0.056*
		GOLDGR*RACEGRP2	0.055*
		INCGRP1*SUSMHS	0.043*
		RACEGRP2*TREAT	0.037*
		SEX*SUSMHS	0.013*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 1	Removed Effect	SUSMHS*TREAT	0.967
Iteration 1	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 2	AIC	112017.7	
Iteration 2	Type 3 Wald p-values	GOLDGR*INCGRP1	0.892
		BMIGRP*TREAT	0.816
		AGEGRP1*BMIGRP	0.789
		GOLDGR*SEX	0.773
		INCGRP1*TREAT	0.717
		EBHIS2*SUSMHS	0.708
		BMIGRP*GOLDGR	0.685
		AGEGRP1*SEX	0.662
		GOLDGR*SUSMHS	0.575
		AGEGRP1*RACEGRP2	0.571
		GOLDGR*TREAT	0.559
		AGEGRP1*TREAT	0.496
		EBHIS2*GOLDGR	0.423
		BMIGRP*SUSMHS	0.419
		AGEGRP1	0.385
		RACEGRP2*SUSMHS	0.352
		SUSMHS	0.341
		AGEGRP1*GOLDGR	0.325
		BMIGRP*SEX	0.279
		INCGRP1*SEX	0.190
		AGEGRP1*SUSMHS	0.127
		INCGRP1*RACEGRP2	0.121
		BMIGRP*INCGRP1	0.109
		RACEGRP2*SEX	0.103
		SEX*TREAT	0.097*
		EBHIS2*TREAT	0.087*
		TREAT	0.070*
		SEX	0.067*
		BMIGRP*EBHIS2	0.067*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Protocol: 207941
Population: Intent-to-Treat

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 2	Type 3 Wald p-values	EBHIS2*SEX	0.064*
		BMIGRP*RACEGRP2	0.058*
		EBHIS2*RACEGRP2	0.056*
		GOLDGR*RACEGRP2	0.055*
		INCGRP1*SUSMHS	0.043*
		RACEGRP2*TREAT	0.036*
		SEX*SUSMHS	0.013*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 2	Removed Effect	GOLDGR*INCGRP1	0.892
Iteration 2	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 3	AIC	112015.7	
Iteration 3	Type 3 Wald p-values	BMIGRP*TREAT	0.814
		AGEGRP1*BMIGRP	0.791
		GOLDGR*SEX	0.783
		INCGRP1*TREAT	0.717
		EBHIS2*SUSMHS	0.709
		BMIGRP*GOLDGR	0.690
		AGEGRP1*SEX	0.659
		GOLDGR*SUSMHS	0.577
		AGEGRP1*RACEGRP2	0.573
		GOLDGR*TREAT	0.561
		AGEGRP1*TREAT	0.496
		EBHIS2*GOLDGR	0.422
		BMIGRP*SUSMHS	0.420
		AGEGRP1	0.387
		RACEGRP2*SUSMHS	0.353
		SUSMHS	0.341
		AGEGRP1*GOLDGR	0.329
		BMIGRP*SEX	0.281
		INCGRP1*SEX	0.193
		AGEGRP1*SUSMHS	0.127
		INCGRP1*RACEGRP2	0.123
		BMIGRP*INCGRP1	0.110
		RACEGRP2*SEX	0.102
		SEX*TREAT	0.098*
		EBHIS2*TREAT	0.086*
		TREAT	0.070*
		SEX	0.067*
		BMIGRP*EBHIS2	0.067*
		EBHIS2*SEX	0.064*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 3	Type 3 Wald p-values	BMIGRP*RACEGRP2	0.058*
		EBHIS2*RACEGRP2	0.055*
		GOLDGR*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.043*
		RACEGRP2*TREAT	0.036*
		SEX*SUSMHS	0.013*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 3	Removed Effect	BMIGRP*TREAT	0.814
Iteration 3	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 4	AIC	112013.8	
Iteration 4	Type 3 Wald p-values	AGEGRP1*BMIGRP	0.790
		GOLDGR*SEX	0.785
		INCGRP1*TREAT	0.727
		EBHIS2*SUSMHS	0.711
		BMIGRP*GOLDGR	0.690
		AGEGRP1*SEX	0.664
		GOLDGR*SUSMHS	0.579
		AGEGRP1*RACEGRP2	0.575
		GOLDGR*TREAT	0.536
		AGEGRP1*TREAT	0.496
		EBHIS2*GOLDGR	0.424
		BMIGRP*SUSMHS	0.421
		AGEGRP1	0.389
		RACEGRP2*SUSMHS	0.353
		SUSMHS	0.341
		AGEGRP1*GOLDGR	0.331
		BMIGRP*SEX	0.284
		INCGRP1*SEX	0.191
		AGEGRP1*SUSMHS	0.126
		INCGRP1*RACEGRP2	0.124
		BMIGRP*INCGRP1	0.109
		RACEGRP2*SEX	0.102
		SEX*TREAT	0.094*
		EBHIS2*TREAT	0.086*
		SEX	0.067*
		BMIGRP*EBHIS2	0.067*
		EBHIS2*SEX	0.063*
		TREAT	0.062*
		BMIGRP*RACEGRP2	0.058*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 4	Type 3 Wald p-values	EBHIS2*RACEGRP2	0.055*
		GOLDGR*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.043*
		RACEGRP2*TREAT	0.036*
		SEX*SUSMHS	0.013*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 4	Removed Effect	AGEGRP1*BMIGRP	0.790
Iteration 4	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 5	AIC	112011.9	
Iteration 5	Type 3 Wald p-values	GOLDGR*SEX	0.790
		INCGRP1*TREAT	0.727
		EBHIS2*SUSMHS	0.712
		BMIGRP*GOLDGR	0.699
		AGEGRP1*SEX	0.652
		GOLDGR*SUSMHS	0.586
		GOLDGR*TREAT	0.532
		AGEGRP1*RACEGRP2	0.531
		AGEGRP1*TREAT	0.494
		EBHIS2*GOLDGR	0.429
		AGEGRP1	0.363
		BMIGRP*SUSMHS	0.355
		SUSMHS	0.346
		AGEGRP1*GOLDGR	0.346
		RACEGRP2*SUSMHS	0.344
		BMIGRP*SEX	0.294
		INCGRP1*SEX	0.191
		AGEGRP1*SUSMHS	0.132
		INCGRP1*RACEGRP2	0.124
		BMIGRP*INCGRP1	0.112
		RACEGRP2*SEX	0.103
		SEX*TREAT	0.095*
		EBHIS2*TREAT	0.086*
		BMIGRP*EBHIS2	0.068*
		SEX	0.066*
		EBHIS2*SEX	0.064*
		TREAT	0.063*
		BMIGRP*RACEGRP2	0.057*
		EBHIS2*RACEGRP2	0.056*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 5	Type 3 Wald p-values	GOLDGR*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.044*
		RACEGRP2*TREAT	0.036*
		SEX*SUSMHS	0.013*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 5	Removed Effect	GOLDGR*SEX	0.790
Iteration 5	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 6	AIC	112009.9	
Iteration 6	Type 3 Wald p-values	INCGRP1*TREAT	0.725
		EBHIS2*SUSMHS	0.713
		BMIGRP*GOLDGR	0.710
		AGEGRP1*SEX	0.642
		GOLDGR*SUSMHS	0.572
		AGEGRP1*RACEGRP2	0.532
		GOLDGR*TREAT	0.526
		AGEGRP1*TREAT	0.494
		EBHIS2*GOLDGR	0.419
		AGEGRP1	0.363
		AGEGRP1*GOLDGR	0.355
		BMIGRP*SUSMHS	0.354
		SUSMHS	0.352
		RACEGRP2*SUSMHS	0.342
		BMIGRP*SEX	0.306
		INCGRP1*SEX	0.195
		AGEGRP1*SUSMHS	0.133
		INCGRP1*RACEGRP2	0.124
		BMIGRP*INCGRP1	0.113
		RACEGRP2*SEX	0.100*
		SEX*TREAT	0.095*
		EBHIS2*TREAT	0.086*
		SEX	0.069*
		BMIGRP*EBHIS2	0.068*
		TREAT	0.064*
		EBHIS2*SEX	0.060*
		BMIGRP*RACEGRP2	0.057*
		EBHIS2*RACEGRP2	0.056*
		GOLDGR*RACEGRP2	0.045*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 6	Type 3 Wald p-values	INCGRP1*SUSMHS	0.044*
		RACEGRP2*TREAT	0.036*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.003*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 6	Removed Effect	INCGRP1*TREAT	0.725
Iteration 6	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 7	AIC	112008.1	
Iteration 7	Type 3 Wald p-values	EBHIS2*SUSMHS	0.716
		BMIGRP*GOLDGR	0.706
		AGEGRP1*SEX	0.644
		GOLDGR*SUSMHS	0.574
		AGEGRP1*RACEGRP2	0.534
		GOLDGR*TREAT	0.520
		AGEGRP1*TREAT	0.480
		EBHIS2*GOLDGR	0.423
		AGEGRP1	0.365
		AGEGRP1*GOLDGR	0.356
		BMIGRP*SUSMHS	0.354
		SUSMHS	0.352
		RACEGRP2*SUSMHS	0.340
		BMIGRP*SEX	0.303
		INCGRP1*SEX	0.200
		AGEGRP1*SUSMHS	0.133
		INCGRP1*RACEGRP2	0.124
		BMIGRP*INCGRP1	0.114
		RACEGRP2*SEX	0.097*
		SEX*TREAT	0.087*
		EBHIS2*TREAT	0.086*
		SEX	0.070*
		BMIGRP*EBHIS2	0.068*
		EBHIS2*SEX	0.061*
		TREAT	0.060*
		BMIGRP*RACEGRP2	0.056*
		EBHIS2*RACEGRP2	0.056*
		GOLDGR*RACEGRP2	0.045*
		INCGRP1*SUSMHS	0.043*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 7	Type 3 Wald p-values	RACEGRP2*TREAT	0.022*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 7	Removed Effect	EBHIS2*SUSMHS	0.716
Iteration 7	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 8	AIC	112006.2	
Iteration 8	Type 3 Wald p-values	BMIGRP*GOLDGR	0.706
		AGEGRP1*SEX	0.651
		GOLDGR*SUSMHS	0.556
		AGEGRP1*RACEGRP2	0.536
		GOLDGR*TREAT	0.516
		AGEGRP1*TREAT	0.477
		EBHIS2*GOLDGR	0.438
		SUSMHS	0.367
		AGEGRP1	0.362
		BMIGRP*SUSMHS	0.353
		AGEGRP1*GOLDGR	0.351
		RACEGRP2*SUSMHS	0.343
		BMIGRP*SEX	0.303
		INCGRP1*SEX	0.202
		AGEGRP1*SUSMHS	0.135
		INCGRP1*RACEGRP2	0.124
		BMIGRP*INCGRP1	0.114
		RACEGRP2*SEX	0.096*
		SEX*TREAT	0.087*
		EBHIS2*TREAT	0.085*
		BMIGRP*EBHIS2	0.073*
		SEX	0.071*
		TREAT	0.060*
		EBHIS2*SEX	0.058*
		BMIGRP*RACEGRP2	0.055*
		EBHIS2*RACEGRP2	0.052*
		GOLDGR*RACEGRP2	0.046*
		INCGRP1*SUSMHS	0.043*
		RACEGRP2*TREAT	0.022*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 8	Type 3 Wald p-values	SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.002*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 8	Removed Effect	BMIGRP*GOLDGR	0.706
Iteration 8	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 9	AIC	112004.3	
Iteration 9	Type 3 Wald p-values	AGEGRP1*SEX	0.648
		GOLDGR*SUSMHS	0.592
		AGEGRP1*RACEGRP2	0.535
		GOLDGR*TREAT	0.518
		AGEGRP1*TREAT	0.472
		EBHIS2*GOLDGR	0.437
		AGEGRP1	0.364
		SUSMHS	0.361
		AGEGRP1*GOLDGR	0.360
		RACEGRP2*SUSMHS	0.341
		BMIGRP*SUSMHS	0.337
		BMIGRP*SEX	0.313
		INCGRP1*SEX	0.204
		AGEGRP1*SUSMHS	0.135
		INCGRP1*RACEGRP2	0.123
		BMIGRP*INCGRP1	0.116
		RACEGRP2*SEX	0.095*
		SEX*TREAT	0.086*
		EBHIS2*TREAT	0.084*
		SEX	0.071*
		BMIGRP*EBHIS2	0.068*
		TREAT	0.059*
		EBHIS2*SEX	0.058*
		BMIGRP*RACEGRP2	0.056*
		EBHIS2*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.042*
		GOLDGR*RACEGRP2	0.035*
		RACEGRP2*TREAT	0.022*
		SEX*SUSMHS	0.012*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 9	Type 3 Wald p-values	AGEGRP1*EBHIS2	0.009*
		AGEGRP1*INCGRP1	0.003*
		BMIGRP	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 9	Removed Effect	AGEGRP1*SEX	0.648
Iteration 9	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 10	AIC	112002.5	
Iteration 10	Type 3 Wald p-values	GOLDGR*SUSMHS	0.584
		AGEGRP1*RACEGRP2	0.564
		GOLDGR*TREAT	0.519
		AGEGRP1*TREAT	0.481
		EBHIS2*GOLDGR	0.438
		AGEGRP1	0.415
		RACEGRP2*SUSMHS	0.350
		AGEGRP1*GOLDGR	0.345
		SUSMHS	0.344
		BMIGRP*SUSMHS	0.337
		BMIGRP*SEX	0.305
		INCGRP1*SEX	0.190
		AGEGRP1*SUSMHS	0.141
		INCGRP1*RACEGRP2	0.121
		BMIGRP*INCGRP1	0.117
		RACEGRP2*SEX	0.097*
		SEX*TREAT	0.086*
		EBHIS2*TREAT	0.082*
		SEX	0.072*
		BMIGRP*EBHIS2	0.068*
		TREAT	0.058*
		EBHIS2*SEX	0.057*
		BMIGRP*RACEGRP2	0.055*
		EBHIS2*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.042*
		GOLDGR*RACEGRP2	0.035*
		RACEGRP2*TREAT	0.023*
		SEX*SUSMHS	0.013*
		AGEGRP1*EBHIS2	0.010*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 10	Type 3 Wald p-values	AGEGRP1*INCGRP1	0.004*
		BMIGRP	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 10	Removed Effect	GOLDGR*SUSMHS	0.584
Iteration 10	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 11	AIC	112000.8	
Iteration 11	Type 3 Wald p-values	AGEGRP1*RACEGRP2	0.565
		GOLDGR*TREAT	0.520
		AGEGRP1*TREAT	0.477
		AGEGRP1	0.436
		EBHIS2*GOLDGR	0.434
		AGEGRP1*GOLDGR	0.410
		RACEGRP2*SUSMHS	0.358
		BMIGRP*SEX	0.308
		BMIGRP*SUSMHS	0.299
		SUSMHS	0.273
		INCGRP1*SEX	0.190
		AGEGRP1*SUSMHS	0.148
		INCGRP1*RACEGRP2	0.121
		BMIGRP*INCGRP1	0.114
		RACEGRP2*SEX	0.098*
		SEX*TREAT	0.086*
		EBHIS2*TREAT	0.081*
		SEX	0.070*
		BMIGRP*EBHIS2	0.070*
		TREAT	0.058*
		EBHIS2*SEX	0.056*
		BMIGRP*RACEGRP2	0.056*
		EBHIS2*RACEGRP2	0.053*
		INCGRP1*SUSMHS	0.043*
		GOLDGR*RACEGRP2	0.033*
		RACEGRP2*TREAT	0.023*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.010*
		AGEGRP1*INCGRP1	0.004*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 11	Type 3 Wald p-values	BMIGRP	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 11	Removed Effect	AGEGRP1*RACEGRP2	0.565
Iteration 11	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 12	AIC	111999.2	
Iteration 12	Type 3 Wald p-values	AGEGRP1	0.598
		GOLDGR*TREAT	0.522
		AGEGRP1*TREAT	0.475
		AGEGRP1*GOLDGR	0.433
		EBHIS2*GOLDGR	0.431
		RACEGRP2*SUSMHS	0.392
		BMIGRP*SEX	0.307
		BMIGRP*SUSMHS	0.304
		SUSMHS	0.252
		INCGRP1*SEX	0.199
		INCGRP1*RACEGRP2	0.138
		AGEGRP1*SUSMHS	0.137
		BMIGRP*INCGRP1	0.117
		RACEGRP2*SEX	0.089*
		SEX*TREAT	0.085*
		EBHIS2*TREAT	0.082*
		SEX	0.074*
		BMIGRP*EBHIS2	0.071*
		TREAT	0.057*
		EBHIS2*SEX	0.057*
		EBHIS2*RACEGRP2	0.055*
		BMIGRP*RACEGRP2	0.051*
		INCGRP1*SUSMHS	0.046*
		GOLDGR*RACEGRP2	0.035*
		RACEGRP2*TREAT	0.023*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.010*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 12	Type 3 Wald p-values	RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 12	Removed Effect	GOLDGR*TREAT	0.522
Iteration 12	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 13	AIC	111997.6	
Iteration 13	Type 3 Wald p-values	AGEGRP1	0.604
		AGEGRP1*TREAT	0.482
		AGEGRP1*GOLDGR	0.437
		EBHIS2*GOLDGR	0.433
		RACEGRP2*SUSMHS	0.391
		BMIGRP*SUSMHS	0.306
		BMIGRP*SEX	0.306
		SUSMHS	0.252
		INCGRP1*SEX	0.202
		INCGRP1*RACEGRP2	0.138
		AGEGRP1*SUSMHS	0.135
		BMIGRP*INCGRP1	0.119
		SEX*TREAT	0.091*
		RACEGRP2*SEX	0.090*
		SEX	0.074*
		EBHIS2*TREAT	0.074*
		BMIGRP*EBHIS2	0.069*
		EBHIS2*RACEGRP2	0.056*
		EBHIS2*SEX	0.055*
		BMIGRP*RACEGRP2	0.051*
		INCGRP1*SUSMHS	0.045*
		GOLDGR*RACEGRP2	0.035*
		TREAT	0.031*
		RACEGRP2*TREAT	0.025*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.010*
		AGEGRP1*INCGRP1	0.001*
		BMIGRP	0.001*
		RACEGRP2	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 13	Type 3 Wald p-values	EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 13	Removed Effect	AGEGRP1*TREAT	0.482
Iteration 13	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 14	AIC	111996.1	
Iteration 14	Type 3 Wald p-values	AGEGRP1	0.635
		EBHIS2*GOLDGR	0.437
		AGEGRP1*GOLDGR	0.435
		RACEGRP2*SUSMHS	0.382
		BMIGRP*SEX	0.316
		BMIGRP*SUSMHS	0.303
		SUSMHS	0.258
		INCGRP1*SEX	0.205
		INCGRP1*RACEGRP2	0.137
		AGEGRP1*SUSMHS	0.135
		BMIGRP*INCGRP1	0.119
		SEX*TREAT	0.105
		RACEGRP2*SEX	0.092*
		EBHIS2*TREAT	0.076*
		SEX	0.072*
		BMIGRP*EBHIS2	0.070*
		EBHIS2*SEX	0.057*
		EBHIS2*RACEGRP2	0.056*
		BMIGRP*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.045*
		GOLDGR*RACEGRP2	0.035*
		TREAT	0.027*
		RACEGRP2*TREAT	0.027*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.010*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 14	Type 3 Wald p-values	INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 14	Removed Effect	EBHIS2*GOLDGR	0.437
Iteration 14	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 15	AIC	111994.7	
Iteration 15	Type 3 Wald p-values	AGEGRP1	0.631
		AGEGRP1*GOLDGR	0.447
		RACEGRP2*SUSMHS	0.389
		BMIGRP*SEX	0.319
		BMIGRP*SUSMHS	0.301
		SUSMHS	0.258
		INCGRP1*SEX	0.204
		AGEGRP1*SUSMHS	0.134
		INCGRP1*RACEGRP2	0.132
		BMIGRP*INCGRP1	0.123
		SEX*TREAT	0.102
		RACEGRP2*SEX	0.092*
		BMIGRP*EBHIS2	0.084*
		EBHIS2*TREAT	0.075*
		SEX	0.071*
		EBHIS2*SEX	0.063*
		EBHIS2*RACEGRP2	0.061*
		BMIGRP*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.046*
		GOLDGR*RACEGRP2	0.034*
		RACEGRP2*TREAT	0.028*
		TREAT	0.027*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.011*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 15	Type 3 Wald p-values	GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 15	Removed Effect	AGEGRP1*GOLDGR	0.447
Iteration 15	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 16	AIC	111993.3	
Iteration 16	Type 3 Wald p-values	AGEGRP1	0.823
		RACEGRP2*SUSMHS	0.385
		BMIGRP*SEX	0.316
		BMIGRP*SUSMHS	0.315
		SUSMHS	0.256
		INCGRP1*SEX	0.207
		AGEGRP1*SUSMHS	0.142
		INCGRP1*RACEGRP2	0.131
		BMIGRP*INCGRP1	0.123
		SEX*TREAT	0.102
		RACEGRP2*SEX	0.093*
		BMIGRP*EBHIS2	0.087*
		EBHIS2*TREAT	0.077*
		SEX	0.070*
		EBHIS2*SEX	0.062*
		EBHIS2*RACEGRP2	0.059*
		BMIGRP*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.044*
		GOLDGR*RACEGRP2	0.038*
		RACEGRP2*TREAT	0.028*
		TREAT	0.026*
		SEX*SUSMHS	0.012*
		AGEGRP1*EBHIS2	0.009*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 16	Type 3 Wald p-values	EBHIS2	<0.001*
Iteration 16	Removed Effect	RACEGRP2*SUSMHS	0.385
Iteration 16	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 17	AIC	111992.0	
Iteration 17	Type 3 Wald p-values	AGEGRP1	0.793
		BMIGRP*SUSMHS	0.390
		BMIGRP*SEX	0.312
		INCGRP1*SEX	0.205
		AGEGRP1*SUSMHS	0.156
		INCGRP1*RACEGRP2	0.149
		BMIGRP*INCGRP1	0.124
		SEX*TREAT	0.104
		RACEGRP2*SEX	0.089*
		BMIGRP*EBHIS2	0.089*
		EBHIS2*TREAT	0.077*
		SEX	0.075*
		EBHIS2*SEX	0.063*
		INCGRP1*SUSMHS	0.061*
		EBHIS2*RACEGRP2	0.061*
		BMIGRP*RACEGRP2	0.049*
		GOLDGR*RACEGRP2	0.043*
		TREAT	0.029*
		RACEGRP2*TREAT	0.025*
		SEX*SUSMHS	0.015*
		AGEGRP1*EBHIS2	0.009*
		SUSMHS	0.003*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 17	Removed Effect	BMIGRP*SUSMHS	0.390
Iteration 17	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 18	AIC	111990.7	
Iteration 18	Type 3 Wald p-values	AGEGRP1	0.797
		BMIGRP*SEX	0.351
		INCGRP1*SEX	0.215
		INCGRP1*RACEGRP2	0.151
		AGEGRP1*SUSMHS	0.144
		BMIGRP*INCGRP1	0.119
		SEX*TREAT	0.105
		RACEGRP2*SEX	0.090*
		BMIGRP*EBHIS2	0.089*
		EBHIS2*TREAT	0.079*
		SEX	0.074*
		EBHIS2*SEX	0.062*
		EBHIS2*RACEGRP2	0.059*
		INCGRP1*SUSMHS	0.048*
		BMIGRP*RACEGRP2	0.043*
		GOLDGR*RACEGRP2	0.042*
		TREAT	0.029*
		RACEGRP2*TREAT	0.026*
		SEX*SUSMHS	0.016*
		AGEGRP1*EBHIS2	0.009*
		SUSMHS	0.003*
		AGEGRP1*INCGRP1	0.001*
		BMIGRP	<0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 18	Removed Effect	BMIGRP*SEX	0.351
Iteration 18	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 19	AIC	111989.6	
Iteration 19	Type 3 Wald p-values	AGEGRP1	0.795
		INCGRP1*SEX	0.218
		AGEGRP1*SUSMHS	0.146
		BMIGRP*INCGRP1	0.142
		INCGRP1*RACEGRP2	0.140
		RACEGRP2*SEX	0.116
		SEX*TREAT	0.102
		EBHIS2*TREAT	0.082*
		BMIGRP*EBHIS2	0.082*
		EBHIS2*SEX	0.062*
		EBHIS2*RACEGRP2	0.059*
		SEX	0.054*
		BMIGRP*RACEGRP2	0.052*
		INCGRP1*SUSMHS	0.047*
		GOLDGR*RACEGRP2	0.043*
		TREAT	0.029*
		RACEGRP2*TREAT	0.026*
		SEX*SUSMHS	0.010*
		AGEGRP1*EBHIS2	0.009*
		SUSMHS	0.003*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 19	Removed Effect	INCGRP1*SEX	0.218

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description	
Iteration 19	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 20	AIC	111989.1	
Iteration 20	Type 3 Wald p-values	AGEGRP1	0.725
		AGEGRP1*SUSMHS	0.144
		BMIGRP*INCGRP1	0.126
		SEX*TREAT	0.103
		INCGRP1*RACEGRP2	0.095*
		BMIGRP*EBHIS2	0.078*
		EBHIS2*TREAT	0.076*
		EBHIS2*SEX	0.062*
		SEX	0.059*
		EBHIS2*RACEGRP2	0.057*
		BMIGRP*RACEGRP2	0.054*
		GOLDGR*RACEGRP2	0.045*
		RACEGRP2*SEX	0.042*
		INCGRP1*SUSMHS	0.041*
		TREAT	0.029*
		RACEGRP2*TREAT	0.025*
		SEX*SUSMHS	0.010*
		AGEGRP1*EBHIS2	0.009*
		SUSMHS	0.003*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	<0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 20	Removed Effect	AGEGRP1*SUSMHS	0.144

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description	
Iteration 20	Replaced Effect(s)	NONE

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 21	AIC	111989.3	
Iteration 21	Type 3 Wald p-values	AGEGRP1	0.593
		BMIGRP*INCGRP1	0.129
		SEX*TREAT	0.104
		INCGRP1*RACEGRP2	0.090*
		BMIGRP*EBHIS2	0.078*
		EBHIS2*TREAT	0.072*
		EBHIS2*SEX	0.060*
		SEX	0.059*
		EBHIS2*RACEGRP2	0.058*
		BMIGRP*RACEGRP2	0.057*
		INCGRP1*SUSMHS	0.046*
		RACEGRP2*SEX	0.043*
		GOLDGR*RACEGRP2	0.042*
		TREAT	0.030*
		RACEGRP2*TREAT	0.024*
		AGEGRP1*EBHIS2	0.009*
		SEX*SUSMHS	0.006*
		SUSMHS	0.003*
		BMIGRP	0.001*
		AGEGRP1*INCGRP1	<0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 21	Removed Effect	BMIGRP*INCGRP1	0.129
Iteration 21	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 22	AIC	111989.6	
Iteration 22	Type 3 Wald p-values	AGEGRP1	0.592
		SEX*TREAT	0.110
		BMIGRP*EBHIS2	0.077*
		EBHIS2*TREAT	0.071*
		INCGRP1*SUSMHS	0.067*
		SEX	0.063*
		EBHIS2*RACEGRP2	0.060*
		EBHIS2*SEX	0.058*
		RACEGRP2*SEX	0.044*
		GOLDGR*RACEGRP2	0.040*
		INCGRP1*RACEGRP2	0.036*
		TREAT	0.032*
		RACEGRP2*TREAT	0.022*
		BMIGRP*RACEGRP2	0.021*
		AGEGRP1*EBHIS2	0.009*
		SEX*SUSMHS	0.007*
		SUSMHS	0.004*
		BMIGRP	0.002*
		AGEGRP1*INCGRP1	<0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*
Iteration 22	Removed Effect	SEX*TREAT	0.110
Iteration 22	Replaced Effect(s)	NONE	

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

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Table 2.10
Summary of Exacerbation Cox Model Backwards Selection
(Based on Nine Covariates)

Iteration	Description		
Iteration 23	AIC	111990.1	
Iteration 23	Type 3 Wald p-values	AGEGRP1	0.585
		TREAT	0.083*
		BMIGRP*EBHIS2	0.082*
		INCGRP1*SUSMHS	0.068*
		SEX	0.067*
		EBHIS2*SEX	0.061*
		EBHIS2*TREAT	0.061*
		EBHIS2*RACEGRP2	0.055*
		RACEGRP2*SEX	0.049*
		GOLDGR*RACEGRP2	0.040*
		INCGRP1*RACEGRP2	0.035*
		BMIGRP*RACEGRP2	0.021*
		RACEGRP2*TREAT	0.010*
		AGEGRP1*EBHIS2	0.010*
		SEX*SUSMHS	0.007*
		SUSMHS	0.004*
		BMIGRP	0.002*
		AGEGRP1*INCGRP1	<0.001*
		RACEGRP2	<0.001*
		EBHIS2*INCGRP1	<0.001*
		INCGRP1	<0.001*
		GOLDGR	<0.001*
		EBHIS2	<0.001*

Note: Model selected using backwards selection with a Wald p-value cut-off of 0.10.
Note: Main effects were not removed from the model if significant interactions were still present.

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.30 (0.20,0.39)	0.28 (0.18,0.36)		
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.51 (0.36,0.63)	0.52 (0.36,0.64)		
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.29 (0.19,0.38)	0.27 (0.18,0.35)		0.00 (0 / 1)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.50 (0.35,0.62)	0.50 (0.35,0.62)		
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.24 (0.15,0.32)	0.22 (0.14,0.30)		
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.39 (0.25,0.51)	0.40 (0.26,0.51)		
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.23 (0.15,0.31)	0.21 (0.13,0.29)		
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.38 (0.25,0.49)	0.39 (0.25,0.50)		

PPD

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.26 (0.18,0.34)	0.24 (0.17,0.31)	0.00 (0 / 2)	1.00 (1 / 1)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.38 (0.26,0.47)	0.38 (0.26,0.48)	0.00 (0 / 1)	
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.28 (0.20,0.35)	0.26 (0.18,0.33)	0.00 (0 / 1)	0.00 (0 / 1)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.40 (0.28,0.50)	0.40 (0.28,0.50)		1.00 (1 / 1)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.21 (0.14,0.27)	0.19 (0.13,0.25)		
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.28 (0.18,0.37)	0.28 (0.18,0.37)		
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.22 (0.15,0.29)	0.20 (0.14,0.27)	0.00 (0 / 2)	
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.30 (0.19,0.39)	0.30 (0.20,0.39)		

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.43,0.49)	0.51 (0.47,0.54)	0.29 (18 / 63)	0.54 (20 / 37)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.65 (0.61,0.69)	0.73 (0.69,0.77)	0.68 (21 / 31)	0.73 (16 / 22)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.45 (0.42,0.49)	0.50 (0.46,0.53)	0.33 (5 / 15)	0.33 (5 / 15)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.64 (0.59,0.68)	0.72 (0.67,0.76)	0.73 (8 / 11)	0.86 (6 / 7)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.43,0.49)	0.51 (0.47,0.54)	0.47 (37 / 78)	0.51 (25 / 49)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.62 (0.57,0.65)	0.70 (0.66,0.74)	0.61 (27 / 44)	0.63 (19 / 30)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.45 (0.42,0.48)	0.50 (0.46,0.53)	0.43 (23 / 54)	0.37 (10 / 27)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.60 (0.56,0.64)	0.69 (0.64,0.73)	0.33 (6 / 18)	0.54 (7 / 13)

PPD

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.35 (0.32,0.39)	0.39 (0.35,0.43)	0.44 (8 / 18)	0.30 (3 / 10)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.43 (0.38,0.47)	0.51 (0.46,0.55)	0.25 (3 / 12)	0.80 (4 / 5)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.37 (0.33,0.41)	0.42 (0.37,0.46)	0.14 (1 / 7)	0.67 (2 / 3)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.45 (0.40,0.50)	0.53 (0.48,0.58)	0.00 (0 / 4)	1.00 (4 / 4)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.35 (0.32,0.39)	0.39 (0.35,0.43)	0.22 (5 / 23)	0.50 (6 / 12)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.40 (0.36,0.44)	0.47 (0.43,0.52)	0.33 (7 / 21)	0.46 (6 / 13)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.37 (0.33,0.41)	0.41 (0.37,0.45)	0.24 (5 / 21)	0.46 (6 / 13)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.42 (0.38,0.46)	0.50 (0.45,0.55)	0.31 (5 / 16)	0.33 (4 / 12)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.27 (0.21,0.33)	0.25 (0.19,0.31)	0.33 (1 / 3)	
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.51 (0.40,0.60)	0.51 (0.40,0.60)		
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.30 (0.23,0.36)	0.28 (0.21,0.34)	0.00 (0 / 1)	
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.55 (0.43,0.64)	0.55 (0.44,0.64)		
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.21 (0.16,0.27)	0.20 (0.14,0.25)	0.00 (0 / 2)	
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.39 (0.29,0.48)	0.39 (0.29,0.48)		1.00 (1 / 1)
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.24 (0.17,0.30)	0.22 (0.16,0.28)	0.00 (0 / 1)	0.00 (0 / 1)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.42 (0.31,0.52)	0.43 (0.31,0.52)		

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.24 (0.19,0.29)	0.22 (0.17,0.27)	0.22 (2 / 9)	0.00 (0 / 9)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.37 (0.29,0.44)	0.38 (0.29,0.45)		
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.29 (0.23,0.34)	0.27 (0.21,0.32)	0.00 (0 / 17)	0.20 (1 / 5)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.44 (0.35,0.52)	0.44 (0.35,0.52)	0.20 (1 / 5)	0.00 (0 / 3)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.19 (0.14,0.23)	0.17 (0.13,0.22)	0.00 (0 / 3)	0.00 (0 / 3)
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.28 (0.20,0.34)	0.28 (0.20,0.35)	0.00 (0 / 1)	0.00 (0 / 1)
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.23 (0.17,0.28)	0.21 (0.16,0.26)	0.00 (0 / 10)	0.25 (1 / 4)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.33 (0.25,0.41)	0.33 (0.25,0.41)	0.00 (0 / 1)	0.67 (2 / 3)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.34 (0.32,0.37)	0.38 (0.36,0.41)	0.30 (16 / 53)	0.37 (17 / 46)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.55 (0.50,0.58)	0.63 (0.59,0.67)	0.50 (15 / 30)	0.54 (7 / 13)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.38 (0.35,0.41)	0.42 (0.39,0.45)	0.41 (7 / 17)	0.24 (4 / 17)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.59 (0.54,0.63)	0.67 (0.63,0.71)	0.58 (7 / 12)	0.67 (4 / 6)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.34 (0.32,0.37)	0.38 (0.36,0.41)	0.25 (26 / 104)	0.27 (20 / 73)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.51 (0.47,0.55)	0.60 (0.56,0.63)	0.49 (19 / 39)	0.69 (18 / 26)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.37 (0.35,0.40)	0.42 (0.39,0.45)	0.33 (32 / 96)	0.22 (11 / 50)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.55 (0.51,0.59)	0.64 (0.59,0.67)	0.64 (18 / 28)	0.59 (16 / 27)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.26 (0.23,0.28)	0.29 (0.26,0.32)	0.35 (13 / 37)	0.13 (4 / 30)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.34 (0.31,0.38)	0.41 (0.37,0.45)	0.40 (6 / 15)	0.33 (4 / 12)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.31 (0.28,0.34)	0.34 (0.31,0.38)	0.27 (3 / 11)	0.14 (1 / 7)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.41 (0.36,0.45)	0.48 (0.44,0.53)	0.00 (0 / 3)	0.33 (2 / 6)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.26 (0.23,0.28)	0.29 (0.26,0.32)	0.31 (15 / 49)	0.32 (6 / 19)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.32 (0.28,0.35)	0.38 (0.34,0.42)	0.25 (3 / 12)	0.25 (5 / 20)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.31 (0.28,0.34)	0.34 (0.31,0.37)	0.24 (9 / 37)	0.29 (7 / 24)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.38 (0.34,0.42)	0.45 (0.41,0.49)	0.38 (6 / 16)	0.55 (6 / 11)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.48 (0.35,0.58)	0.45 (0.33,0.55)	1.00 (1 / 1)	
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.74 (0.59,0.83)	0.74 (0.59,0.83)		
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.47 (0.35,0.57)	0.44 (0.32,0.54)		
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.72 (0.58,0.82)	0.73 (0.58,0.82)	1.00 (1 / 1)	
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.39 (0.27,0.50)	0.37 (0.25,0.47)		
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.60 (0.43,0.72)	0.61 (0.44,0.73)	1.00 (1 / 1)	
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.38 (0.26,0.49)	0.36 (0.24,0.46)		
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.59 (0.42,0.71)	0.59 (0.43,0.71)	0.00 (0 / 1)	

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.43 (0.33,0.52)	0.41 (0.31,0.49)	0.33 (1 / 3)	0.00 (0 / 1)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.58 (0.45,0.68)	0.59 (0.46,0.68)	1.00 (2 / 2)	1.00 (2 / 2)
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.45 (0.35,0.54)	0.43 (0.33,0.51)	0.50 (6 / 12)	0.25 (1 / 4)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.61 (0.48,0.70)	0.61 (0.49,0.71)	1.00 (2 / 2)	0.00 (0 / 4)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.35 (0.24,0.44)	0.33 (0.22,0.41)		0.00 (0 / 1)
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.45 (0.32,0.56)	0.46 (0.32,0.57)		
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.37 (0.26,0.46)	0.35 (0.24,0.43)	0.00 (0 / 3)	0.00 (0 / 2)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.48 (0.34,0.59)	0.48 (0.34,0.59)		0.00 (0 / 1)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.60 (0.57,0.63)	0.65 (0.62,0.69)	0.58 (63 / 109)	0.62 (53 / 85)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.79 (0.75,0.82)	0.86 (0.83,0.89)	0.67 (46 / 69)	0.76 (48 / 63)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.59 (0.55,0.62)	0.64 (0.60,0.67)	0.47 (15 / 32)	0.67 (35 / 52)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.78 (0.74,0.81)	0.85 (0.81,0.88)	0.76 (28 / 37)	0.79 (19 / 24)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.60 (0.56,0.63)	0.65 (0.61,0.68)	0.49 (41 / 84)	0.67 (37 / 55)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.76 (0.72,0.79)	0.83 (0.80,0.86)	0.74 (52 / 70)	0.80 (28 / 35)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.59 (0.55,0.62)	0.64 (0.60,0.67)	0.43 (31 / 72)	0.52 (23 / 44)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.74 (0.70,0.78)	0.82 (0.78,0.85)	0.70 (39 / 56)	0.69 (25 / 36)

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.47 (0.43,0.51)	0.52 (0.48,0.57)	0.43 (9 / 21)	0.50 (8 / 16)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.56 (0.51,0.61)	0.65 (0.59,0.70)	0.60 (12 / 20)	0.83 (5 / 6)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.50 (0.45,0.54)	0.55 (0.50,0.59)	0.42 (8 / 19)	0.71 (10 / 14)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.59 (0.54,0.64)	0.67 (0.62,0.72)	0.44 (7 / 16)	0.85 (11 / 13)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.47 (0.43,0.51)	0.52 (0.47,0.56)	0.62 (13 / 21)	0.42 (5 / 12)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.53 (0.48,0.57)	0.61 (0.56,0.66)	0.45 (10 / 22)	0.45 (5 / 11)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.50 (0.45,0.54)	0.55 (0.50,0.59)	0.47 (7 / 15)	0.57 (4 / 7)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.55 (0.50,0.60)	0.64 (0.59,0.69)	0.31 (9 / 29)	0.00 (0 / 7)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.44 (0.37,0.51)	0.42 (0.35,0.48)	0.75 (6 / 8)	0.50 (1 / 2)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.73 (0.65,0.80)	0.74 (0.65,0.80)	1.00 (2 / 2)	0.80 (4 / 5)
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.48 (0.40,0.55)	0.45 (0.38,0.52)	0.67 (2 / 3)	0.00 (0 / 5)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.77 (0.69,0.83)	0.77 (0.69,0.83)	1.00 (3 / 3)	0.56 (5 / 9)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.36 (0.27,0.44)	0.34 (0.25,0.41)	0.33 (1 / 3)	
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.60 (0.48,0.69)	0.60 (0.48,0.70)	0.75 (3 / 4)	0.00 (0 / 1)
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.39 (0.30,0.47)	0.37 (0.28,0.45)	0.40 (2 / 5)	0.00 (0 / 1)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.64 (0.52,0.73)	0.64 (0.52,0.74)	1.00 (1 / 1)	1.00 (1 / 1)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.40 (0.34,0.45)	0.37 (0.31,0.42)	0.29 (4 / 14)	0.14 (2 / 14)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.58 (0.50,0.64)	0.58 (0.50,0.65)	0.50 (6 / 12)	0.80 (4 / 5)
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.46 (0.40,0.52)	0.44 (0.38,0.49)	0.43 (9 / 21)	0.44 (15 / 34)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.66 (0.58,0.72)	0.66 (0.58,0.72)	0.67 (14 / 21)	0.63 (10 / 16)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.32 (0.25,0.38)	0.30 (0.23,0.36)	0.50 (2 / 4)	0.00 (0 / 1)
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.45 (0.35,0.53)	0.45 (0.35,0.54)	0.50 (1 / 2)	
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.38 (0.30,0.45)	0.35 (0.27,0.43)	0.50 (3 / 6)	0.50 (2 / 4)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.52 (0.42,0.61)	0.53 (0.42,0.62)	0.75 (3 / 4)	0.50 (1 / 2)

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.43,0.49)	0.51 (0.48,0.54)	0.42 (64 / 153)	0.43 (47 / 110)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.69 (0.65,0.72)	0.77 (0.73,0.80)	0.61 (40 / 66)	0.73 (49 / 67)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.50 (0.47,0.53)	0.55 (0.52,0.58)	0.49 (35 / 72)	0.41 (18 / 44)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.73 (0.69,0.76)	0.81 (0.77,0.84)	0.65 (31 / 48)	0.69 (18 / 26)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.43,0.49)	0.51 (0.48,0.54)	0.49 (64 / 131)	0.47 (50 / 106)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.65 (0.62,0.69)	0.74 (0.70,0.77)	0.52 (39 / 75)	0.63 (37 / 59)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.50 (0.47,0.53)	0.55 (0.52,0.58)	0.50 (61 / 122)	0.44 (44 / 99)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.69 (0.66,0.73)	0.78 (0.74,0.81)	0.64 (55 / 86)	0.69 (51 / 74)

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.35 (0.32,0.39)	0.40 (0.36,0.43)	0.42 (23 / 55)	0.46 (18 / 39)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.46 (0.42,0.50)	0.54 (0.50,0.59)	0.42 (15 / 36)	0.53 (21 / 40)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.42 (0.38,0.45)	0.46 (0.42,0.50)	0.41 (17 / 41)	0.43 (10 / 23)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.54 (0.49,0.58)	0.62 (0.57,0.67)	0.67 (20 / 30)	0.50 (10 / 20)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.35 (0.32,0.38)	0.39 (0.36,0.43)	0.48 (16 / 33)	0.47 (15 / 32)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.43 (0.39,0.47)	0.51 (0.47,0.55)	0.30 (7 / 23)	0.71 (15 / 21)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.42 (0.38,0.45)	0.46 (0.42,0.50)	0.51 (24 / 47)	0.38 (13 / 34)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.50 (0.46,0.55)	0.59 (0.54,0.63)	0.55 (16 / 29)	0.56 (14 / 25)

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.29 (0.20,0.38)	0.27 (0.18,0.36)	1.00 (1 / 1)	
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.46 (0.32,0.58)	0.47 (0.32,0.58)		
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.29 (0.19,0.37)	0.27 (0.18,0.35)		
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.45 (0.31,0.56)	0.45 (0.31,0.57)	1.00 (1 / 1)	
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.23 (0.15,0.31)	0.22 (0.14,0.29)		
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.35 (0.22,0.46)	0.35 (0.22,0.46)		
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.23 (0.14,0.30)	0.21 (0.13,0.28)		0.00 (0 / 1)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.34 (0.22,0.44)	0.34 (0.22,0.45)		

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.31 (0.21,0.39)	0.29 (0.20,0.36)	1.00 (3 / 3)	0.50 (1 / 2)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.39 (0.27,0.49)	0.39 (0.27,0.50)	1.00 (1 / 1)	
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.33 (0.23,0.41)	0.30 (0.22,0.38)	0.50 (1 / 2)	0.33 (1 / 3)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.41 (0.29,0.51)	0.42 (0.29,0.52)	0.00 (0 / 1)	0.50 (1 / 2)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.24 (0.16,0.32)	0.23 (0.15,0.30)		
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.29 (0.19,0.38)	0.29 (0.19,0.39)		
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.26 (0.18,0.33)	0.24 (0.16,0.31)		
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.31 (0.20,0.40)	0.31 (0.21,0.40)	1.00 (1 / 1)	

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.42,0.49)	0.50 (0.47,0.54)	0.38 (13 / 34)	0.42 (10 / 24)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.59 (0.55,0.63)	0.68 (0.63,0.72)	0.57 (12 / 21)	0.79 (11 / 14)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.45 (0.41,0.48)	0.49 (0.45,0.53)	0.38 (20 / 52)	0.57 (16 / 28)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.58 (0.54,0.62)	0.67 (0.62,0.71)	0.38 (10 / 26)	0.64 (7 / 11)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.42,0.49)	0.50 (0.46,0.54)	0.43 (15 / 35)	0.48 (10 / 21)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.56 (0.52,0.60)	0.65 (0.60,0.69)	0.63 (12 / 19)	0.40 (6 / 15)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.44 (0.41,0.47)	0.49 (0.45,0.52)	0.38 (34 / 90)	0.51 (28 / 55)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.55 (0.51,0.58)	0.63 (0.59,0.67)	0.54 (20 / 37)	0.63 (24 / 38)

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.41 (0.36,0.45)	0.45 (0.41,0.49)	0.71 (5 / 7)	0.00 (0 / 4)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.45 (0.39,0.49)	0.53 (0.47,0.58)	0.40 (2 / 5)	0.50 (1 / 2)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.43 (0.39,0.47)	0.48 (0.43,0.52)	0.30 (3 / 10)	0.50 (1 / 2)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.47 (0.42,0.52)	0.55 (0.49,0.60)	0.50 (2 / 4)	
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.41 (0.36,0.45)	0.45 (0.40,0.49)	0.33 (4 / 12)	0.17 (1 / 6)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.42 (0.37,0.46)	0.49 (0.44,0.54)	0.33 (3 / 9)	0.33 (2 / 6)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.43 (0.39,0.47)	0.47 (0.43,0.52)	0.47 (8 / 17)	0.38 (5 / 13)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.44 (0.39,0.48)	0.52 (0.46,0.57)	0.64 (7 / 11)	0.33 (1 / 3)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.27 (0.20,0.32)	0.25 (0.19,0.30)	0.29 (2 / 7)	0.00 (0 / 4)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.46 (0.36,0.54)	0.46 (0.36,0.55)	0.67 (2 / 3)	
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.29 (0.23,0.35)	0.27 (0.21,0.33)	0.44 (4 / 9)	0.11 (1 / 9)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.49 (0.39,0.58)	0.50 (0.39,0.58)	0.33 (1 / 3)	0.67 (2 / 3)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.21 (0.15,0.26)	0.20 (0.14,0.25)	0.33 (1 / 3)	0.00 (0 / 3)
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.35 (0.25,0.43)	0.35 (0.25,0.43)	0.00 (0 / 1)	1.00 (1 / 1)
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.23 (0.17,0.29)	0.22 (0.16,0.27)	0.00 (0 / 1)	0.00 (0 / 4)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.38 (0.28,0.46)	0.38 (0.28,0.47)		

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.28 (0.22,0.33)	0.26 (0.20,0.31)	0.21 (3 / 14)	0.00 (0 / 6)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.39 (0.30,0.46)	0.39 (0.30,0.47)	0.33 (1 / 3)	0.00 (0 / 2)
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.33 (0.27,0.39)	0.31 (0.25,0.37)	0.29 (5 / 17)	0.38 (5 / 13)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.46 (0.37,0.53)	0.46 (0.37,0.54)	0.43 (3 / 7)	0.80 (8 / 10)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.22 (0.17,0.27)	0.20 (0.15,0.26)	0.67 (2 / 3)	0.00 (0 / 1)
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.29 (0.21,0.36)	0.29 (0.21,0.36)		0.00 (0 / 2)
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.27 (0.20,0.32)	0.25 (0.19,0.30)	0.33 (4 / 12)	0.17 (1 / 6)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.34 (0.26,0.42)	0.35 (0.26,0.43)	0.20 (1 / 5)	0.60 (3 / 5)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.34 (0.31,0.37)	0.38 (0.35,0.41)	0.34 (15 / 44)	0.38 (8 / 21)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.49 (0.45,0.53)	0.58 (0.53,0.61)	0.37 (7 / 19)	0.54 (7 / 13)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.37 (0.34,0.40)	0.41 (0.38,0.44)	0.28 (21 / 75)	0.42 (25 / 60)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.53 (0.49,0.57)	0.62 (0.58,0.65)	0.30 (9 / 30)	0.56 (10 / 18)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.34 (0.31,0.36)	0.38 (0.35,0.41)	0.27 (16 / 60)	0.33 (18 / 54)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.46 (0.42,0.50)	0.54 (0.50,0.58)	0.33 (5 / 15)	0.50 (11 / 22)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.37 (0.34,0.39)	0.41 (0.38,0.44)	0.36 (69 / 190)	0.41 (68 / 164)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.50 (0.46,0.53)	0.58 (0.54,0.62)	0.51 (46 / 91)	0.55 (23 / 42)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.30 (0.27,0.33)	0.34 (0.30,0.37)	0.12 (2 / 17)	0.30 (6 / 20)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.36 (0.32,0.40)	0.43 (0.38,0.47)	0.60 (6 / 10)	0.64 (9 / 14)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.36 (0.32,0.39)	0.40 (0.36,0.43)	0.20 (6 / 30)	0.39 (9 / 23)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.42 (0.38,0.46)	0.50 (0.45,0.54)	0.45 (5 / 11)	0.33 (2 / 6)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.30 (0.27,0.33)	0.33 (0.30,0.37)	0.46 (6 / 13)	0.17 (2 / 12)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.33 (0.29,0.37)	0.40 (0.36,0.44)	0.20 (2 / 10)	0.50 (2 / 4)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.36 (0.32,0.38)	0.40 (0.36,0.43)	0.31 (18 / 58)	0.44 (16 / 36)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.39 (0.35,0.43)	0.47 (0.42,0.51)	0.43 (9 / 21)	0.48 (10 / 21)

Protocol: 207941
Population: Intent-to-Treat

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.48 (0.35,0.58)	0.45 (0.33,0.55)		
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.68 (0.53,0.78)	0.69 (0.54,0.79)	1.00 (1 / 1)	
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.46 (0.34,0.56)	0.44 (0.32,0.53)	0.00 (0 / 1)	0.00 (0 / 1)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.67 (0.52,0.77)	0.67 (0.53,0.77)		0.00 (0 / 1)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.39 (0.26,0.49)	0.36 (0.24,0.46)		
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.55 (0.39,0.67)	0.55 (0.39,0.67)		
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.38 (0.26,0.48)	0.35 (0.24,0.45)		
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.54 (0.38,0.65)	0.54 (0.38,0.66)		

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.49 (0.38,0.59)	0.46 (0.35,0.56)	0.50 (1 / 2)	
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.60 (0.47,0.70)	0.60 (0.47,0.70)	1.00 (2 / 2)	0.00 (0 / 1)
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.52 (0.41,0.61)	0.49 (0.38,0.58)	0.71 (5 / 7)	0.25 (2 / 8)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.63 (0.50,0.72)	0.63 (0.50,0.72)	1.00 (4 / 4)	0.00 (0 / 2)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.40 (0.28,0.50)	0.38 (0.26,0.47)		
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.47 (0.33,0.58)	0.48 (0.33,0.59)		
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.42 (0.31,0.52)	0.40 (0.28,0.49)	0.00 (0 / 3)	
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.50 (0.36,0.60)	0.50 (0.36,0.61)		0.00 (0 / 1)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.59 (0.56,0.63)	0.64 (0.61,0.68)	0.54 (29 / 54)	0.43 (16 / 37)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.74 (0.70,0.77)	0.81 (0.78,0.85)	0.69 (36 / 52)	0.68 (19 / 28)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.58 (0.55,0.61)	0.63 (0.59,0.67)	0.53 (46 / 87)	0.55 (36 / 66)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.72 (0.68,0.76)	0.80 (0.76,0.84)	0.60 (35 / 58)	0.70 (28 / 40)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.59 (0.55,0.63)	0.64 (0.60,0.68)	0.53 (21 / 40)	0.53 (10 / 19)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.70 (0.66,0.74)	0.78 (0.74,0.82)	0.73 (19 / 26)	0.58 (7 / 12)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.58 (0.54,0.61)	0.63 (0.59,0.66)	0.54 (60 / 112)	0.61 (39 / 64)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.69 (0.65,0.73)	0.77 (0.73,0.81)	0.55 (34 / 62)	0.68 (42 / 62)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.54 (0.49,0.58)	0.59 (0.54,0.63)	0.40 (2 / 5)	0.57 (4 / 7)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.58 (0.52,0.63)	0.67 (0.61,0.72)	0.63 (5 / 8)	0.67 (4 / 6)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.56 (0.52,0.61)	0.61 (0.57,0.66)	0.63 (10 / 16)	0.38 (3 / 8)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.61 (0.55,0.66)	0.69 (0.64,0.74)	0.70 (7 / 10)	0.63 (5 / 8)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.54 (0.49,0.58)	0.59 (0.53,0.63)	0.70 (7 / 10)	0.57 (4 / 7)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.55 (0.49,0.60)	0.63 (0.57,0.68)	0.75 (3 / 4)	0.00 (0 / 1)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.56 (0.52,0.60)	0.61 (0.56,0.66)	0.36 (5 / 14)	0.60 (6 / 10)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.57 (0.52,0.62)	0.66 (0.60,0.71)	0.38 (3 / 8)	0.86 (6 / 7)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Asian/ High	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.44 (0.37,0.50)	0.41 (0.34,0.47)	0.13 (1 / 8)	0.48 (11 / 23)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.68 (0.59,0.74)	0.68 (0.60,0.75)	0.60 (3 / 5)	0.55 (6 / 11)
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.47 (0.40,0.54)	0.45 (0.37,0.51)	0.57 (13 / 23)	0.42 (5 / 12)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.72 (0.64,0.78)	0.72 (0.64,0.78)	0.45 (9 / 20)	0.62 (13 / 21)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.35 (0.27,0.43)	0.33 (0.25,0.40)	0.33 (1 / 3)	
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.54 (0.43,0.63)	0.55 (0.43,0.64)	1.00 (2 / 2)	0.00 (0 / 1)
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.39 (0.30,0.46)	0.36 (0.27,0.44)	0.80 (4 / 5)	0.25 (1 / 4)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.58 (0.47,0.67)	0.59 (0.47,0.68)	0.33 (1 / 3)	

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Asian/ Non-high	<25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.45 (0.39,0.51)	0.43 (0.36,0.48)	0.42 (5 / 12)	0.30 (3 / 10)
	<25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.60 (0.52,0.66)	0.60 (0.52,0.67)	0.25 (2 / 8)	0.67 (6 / 9)
	<25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.53 (0.47,0.58)	0.50 (0.44,0.55)	0.53 (31 / 58)	0.59 (32 / 54)
	<25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.67 (0.60,0.73)	0.68 (0.60,0.74)	0.51 (18 / 35)	0.76 (19 / 25)
	>=25 kg/m^2/ Current/<2	1.09 (0.92,1.28)	0.37 (0.29,0.44)	0.35 (0.26,0.42)	0.33 (1 / 3)	0.67 (2 / 3)
	>=25 kg/m^2/ Current/>=2	0.99 (0.83,1.17)	0.47 (0.37,0.55)	0.47 (0.37,0.56)	1.00 (2 / 2)	1.00 (1 / 1)
	>=25 kg/m^2/ Former/<2	1.09 (0.92,1.28)	0.43 (0.35,0.51)	0.41 (0.32,0.48)	0.27 (3 / 11)	0.33 (2 / 6)
	>=25 kg/m^2/ Former/>=2	0.99 (0.83,1.17)	0.54 (0.44,0.63)	0.55 (0.44,0.63)	0.75 (3 / 4)	0.63 (5 / 8)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Non-Asian/ High	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.43,0.49)	0.51 (0.47,0.54)	0.42 (32 / 76)	0.47 (38 / 81)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.63 (0.59,0.67)	0.72 (0.68,0.75)	0.59 (33 / 56)	0.66 (29 / 44)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.49 (0.47,0.52)	0.54 (0.51,0.57)	0.44 (74 / 168)	0.48 (74 / 154)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.67 (0.64,0.71)	0.76 (0.72,0.79)	0.62 (65 / 105)	0.58 (53 / 91)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.46 (0.43,0.49)	0.50 (0.47,0.53)	0.43 (42 / 97)	0.46 (32 / 70)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.60 (0.56,0.63)	0.68 (0.64,0.72)	0.44 (22 / 50)	0.69 (22 / 32)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.49 (0.47,0.52)	0.54 (0.51,0.57)	0.42 (124/ 297)	0.45 (107/ 237)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.64 (0.60,0.67)	0.72 (0.69,0.75)	0.60 (99 / 164)	0.68 (90 / 133)

Table 2.20
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Nine Covariates)

Age/GOLD/ Sex/Race/ Country Income	BMI/ Smoking/Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M/Non-Asian/ Non-high	<25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.41 (0.37,0.44)	0.45 (0.41,0.49)	0.40 (19 / 48)	0.35 (13 / 37)
	<25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.48 (0.43,0.52)	0.56 (0.51,0.61)	0.39 (11 / 28)	0.56 (9 / 16)
	<25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.48 (0.44,0.51)	0.53 (0.49,0.56)	0.49 (31 / 63)	0.50 (24 / 48)
	<25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.56 (0.51,0.60)	0.64 (0.59,0.68)	0.57 (24 / 42)	0.69 (31 / 45)
	>=25 kg/m^2/ Current/<2	0.87 (0.82,0.93)	0.41 (0.37,0.44)	0.45 (0.41,0.49)	0.04 (1 / 25)	0.33 (7 / 21)
	>=25 kg/m^2/ Current/>=2	0.79 (0.73,0.86)	0.45 (0.40,0.49)	0.53 (0.48,0.57)	0.19 (3 / 16)	0.55 (6 / 11)
	>=25 kg/m^2/ Former/<2	0.87 (0.82,0.93)	0.48 (0.44,0.51)	0.52 (0.49,0.56)	0.49 (39 / 80)	0.42 (20 / 48)
	>=25 kg/m^2/ Former/>=2	0.79 (0.73,0.86)	0.52 (0.48,0.56)	0.61 (0.56,0.65)	0.56 (25 / 45)	0.59 (17 / 29)

Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Type 3 Wald p-values	Age	0.585
	Treatment	0.083
	BMI by Exacerbation History	0.082
	Smoking Status by Country Income	0.068
	Sex	0.067
	Exacerbation History by Sex	0.061
	Treatment by Exacerbation History	0.061
	Exacerbation History by Race	0.055
	Sex by Race	0.049
	GOLD by Race	0.040
	Country Income by Race	0.035
	BMI by Race	0.021
	Treatment by Race	0.010
	Exacerbation History by Age	0.010
	Sex by Smoking Status	0.007
	Smoking Status	0.004
	BMI	0.002
	Age by Country Income	<0.001
	Race	<0.001
	Exacerbation History by Country Income	<0.001
	Country Income	<0.001
	GOLD	<0.001
	Exacerbation History	<0.001

Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio	Age >=65 vs <=64	
95% CI		
	At Exacerbation History:<2 Country Income:High income	0.98 (0.91, 1.06)
	At Exacerbation History:<2 Country Income:Non-high income	1.20 (1.08, 1.33)
	At Exacerbation History:>=2 Country Income:High income	0.86 (0.79, 0.94)
	At Exacerbation History:>=2 Country Income:Non-high income	1.05 (0.94, 1.18)
	BMI >=25 kg/m^2 vs <25 kg/m^2	
	At Exacerbation History:<2 Race:Asian	0.76 (0.61, 0.95)
	At Exacerbation History:<2 Race:Non-Asian	0.99 (0.93, 1.06)
	At Exacerbation History:>=2 Race:Asian	0.70 (0.55, 0.87)
	At Exacerbation History:>=2 Race:Non-Asian	0.91 (0.84, 0.98)
	Country Income Non-high income vs High income	
	At Exacerbation History:<2 Age:<=64 Smoking Status:Current smoker Race:Asian	0.86 (0.70, 1.06)
	At Exacerbation History:<2 Age:<=64 Smoking Status:Current smoker Race:Non-Asian	0.70 (0.63, 0.78)
	At Exacerbation History:<2 Age:<=64 Smoking Status:Former smoker Race:Asian	0.96 (0.78, 1.17)
	At Exacerbation History:<2 Age:<=64 Smoking Status:Former smoker Race:Non-Asian	0.78 (0.69, 0.87)
	At Exacerbation History:<2 Age:>=65 Smoking Status:Current smoker Race:Asian	1.05 (0.85, 1.30)
	At Exacerbation History:<2 Age:>=65 Smoking Status:Current smoker Race:Non-Asian	0.86 (0.76, 0.96)
	At Exacerbation History:<2 Age:>=65 Smoking Status:Former smoker Race:Asian	1.17 (0.97, 1.42)
	At Exacerbation History:<2 Age:>=65 Smoking Status:Former smoker Race:Non-Asian	0.95 (0.86, 1.05)
	At Exacerbation History:>=2 Age:<=64 Smoking Status:Current smoker Race:Asian	0.66 (0.53, 0.81)
	At Exacerbation History:>=2 Age:<=64 Smoking Status:Current smoker Race:Non-Asian	0.53 (0.48, 0.60)

Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio	At Exacerbation History:>=2 Age:<=64 Smoking Status:Former smoker Race:Asian	0.73 (0.59, 0.90)
95% CI	At Exacerbation History:>=2 Age:<=64 Smoking Status:Former smoker Race:Non-Asian	0.59 (0.53, 0.67)
	At Exacerbation History:>=2 Age:>=65 Smoking Status:Current smoker Race:Asian	0.80 (0.65, 0.99)
	At Exacerbation History:>=2 Age:>=65 Smoking Status:Current smoker Race:Non-Asian	0.65 (0.57, 0.75)
	At Exacerbation History:>=2 Age:>=65 Smoking Status:Former smoker Race:Asian	0.89 (0.73, 1.08)
	At Exacerbation History:>=2 Age:>=65 Smoking Status:Former smoker Race:Non-Asian	0.73 (0.65, 0.82)
	Exacerbation History >=2 vs <2	
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Asian	2.02 (1.63, 2.51)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Non-Asian	1.69 (1.50, 1.90)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Asian	1.54 (1.26, 1.90)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Non-Asian	1.29 (1.11, 1.49)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Asian	1.77 (1.44, 2.19)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Non-Asian	1.48 (1.31, 1.67)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Asian	1.35 (1.10, 1.66)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Non-Asian	1.13 (0.97, 1.32)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Asian	2.24 (1.83, 2.75)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Non-Asian	1.87 (1.66, 2.11)

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Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Asian	1.71 (1.42, 2.06)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Non-Asian	1.42 (1.24, 1.64)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Asian	1.96 (1.62, 2.38)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Non-Asian	1.64 (1.46, 1.83)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Asian	1.50 (1.25, 1.79)
	At Treatment:ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Non-Asian	1.25 (1.09, 1.43)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Asian	1.85 (1.47, 2.33)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Non-Asian	1.54 (1.37, 1.73)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Asian	1.41 (1.13, 1.77)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Non-Asian	1.18 (1.02, 1.36)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Asian	1.62 (1.29, 2.04)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Non-Asian	1.35 (1.20, 1.52)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Asian	1.24 (0.99, 1.55)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Non-Asian	1.03 (0.88, 1.20)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Asian	2.05 (1.65, 2.55)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Non-Asian	1.71 (1.53, 1.91)

Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Asian	1.56 (1.27, 1.92)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Non-Asian	1.30 (1.14, 1.49)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Asian	1.80 (1.46, 2.21)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Non-Asian	1.50 (1.35, 1.66)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Asian	1.37 (1.12, 1.67)
	At Treatment:ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Non-Asian	1.14 (1.00, 1.31)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Asian	2.23 (1.79, 2.77)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Non-Asian	1.85 (1.63, 2.10)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Asian	1.70 (1.38, 2.09)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Non-Asian	1.41 (1.22, 1.65)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Asian	1.95 (1.57, 2.42)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Non-Asian	1.63 (1.43, 1.85)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Asian	1.49 (1.21, 1.83)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Non-Asian	1.24 (1.06, 1.45)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Asian	2.46 (2.01, 3.03)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Non-Asian	2.05 (1.82, 2.32)

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Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Asian	1.88 (1.56, 2.27)
95% CI	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Non-Asian	1.57 (1.36, 1.80)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Asian	2.16 (1.78, 2.62)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Non-Asian	1.80 (1.61, 2.02)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Asian	1.65 (1.38, 1.97)
	At Treatment:non-ICS BMI:<25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Non-Asian	1.37 (1.20, 1.58)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Asian	2.03 (1.61, 2.57)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:High income Race:Non-Asian	1.70 (1.50, 1.92)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Asian	1.55 (1.24, 1.95)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:<=64 Country Income:Non-high income Race:Non-Asian	1.29 (1.11, 1.51)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Asian	1.78 (1.41, 2.25)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:High income Race:Non-Asian	1.49 (1.31, 1.69)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Asian	1.36 (1.08, 1.71)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:F Age:>=65 Country Income:Non-high income Race:Non-Asian	1.13 (0.97, 1.33)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Asian	2.25 (1.81, 2.81)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:High income Race:Non-Asian	1.88 (1.67, 2.11)

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Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Asian	1.72 (1.40, 2.11)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:<=64 Country Income:Non-high income Race:Non-Asian	1.43 (1.25, 1.64)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Asian	1.97 (1.60, 2.44)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:High income Race:Non-Asian	1.65 (1.48, 1.83)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Asian	1.51 (1.23, 1.84)
	At Treatment:non-ICS BMI:>=25 kg/m^2 Sex:M Age:>=65 Country Income:Non-high income Race:Non-Asian	1.25 (1.09, 1.44)
	GOLD III & IV: FEV1<50% predicted vs I & II: FEV1>=50% predicted	
	At Race:Asian	1.85 (1.50, 2.28)
	At Race:Non-Asian	1.48 (1.40, 1.56)
	Race Asian vs Non-Asian	
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.57 (0.39, 0.83)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.70 (0.50, 0.98)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.75 (0.57, 0.98)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	0.92 (0.73, 1.16)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.68 (0.47, 1.01)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	0.84 (0.59, 1.20)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	0.90 (0.68, 1.19)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	1.10 (0.85, 1.43)

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Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.72 (0.51, 0.99)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.88 (0.66, 1.17)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.94 (0.76, 1.15)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	1.15 (0.97, 1.37)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.86 (0.62, 1.19)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	1.05 (0.78, 1.42)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	1.13 (0.92, 1.38)
	At Treatment:ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	1.38 (1.14, 1.67)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.44 (0.29, 0.65)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.54 (0.37, 0.77)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.57 (0.43, 0.77)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	0.70 (0.54, 0.92)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.52 (0.35, 0.79)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	0.64 (0.44, 0.94)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	0.69 (0.50, 0.94)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	0.84 (0.63, 1.13)

Protocol: 207941
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Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.55 (0.38, 0.80)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.67 (0.48, 0.94)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.72 (0.54, 0.95)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	0.88 (0.68, 1.13)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.66 (0.45, 0.95)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	0.80 (0.57, 1.14)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	0.86 (0.65, 1.13)
	At Treatment:ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	1.06 (0.81, 1.38)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.46 (0.31, 0.66)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.56 (0.40, 0.78)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.60 (0.46, 0.79)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	0.74 (0.58, 0.94)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.55 (0.37, 0.80)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	0.67 (0.47, 0.96)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	0.72 (0.54, 0.95)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	0.88 (0.68, 1.15)

Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.57 (0.41, 0.79)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.70 (0.53, 0.94)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.75 (0.61, 0.93)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	0.92 (0.77, 1.10)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.69 (0.50, 0.95)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	0.84 (0.63, 1.13)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	0.90 (0.74, 1.10)
	At Treatment:non-ICS BMI:<25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	1.11 (0.91, 1.34)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.35 (0.23, 0.52)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.43 (0.30, 0.62)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.46 (0.34, 0.62)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	0.56 (0.42, 0.75)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.42 (0.28, 0.63)

PPD

Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	0.51 (0.35, 0.76)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	0.55 (0.40, 0.76)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:I & II: FEV1>=50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	0.68 (0.50, 0.92)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:High income	0.44 (0.30, 0.64)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:F Country Income:Non-high income	0.54 (0.38, 0.76)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:High income	0.58 (0.43, 0.77)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:<2 Sex:M Country Income:Non-high income	0.71 (0.54, 0.92)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:High income	0.53 (0.36, 0.77)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:F Country Income:Non-high income	0.64 (0.45, 0.92)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:High income	0.69 (0.52, 0.91)
	At Treatment:non-ICS BMI:>=25 kg/m^2 GOLD:III & IV: FEV1<50% predicted Exacerbation History:>=2 Sex:M Country Income:Non-high income	0.85 (0.64, 1.12)
	Sex M vs F	
	At Exacerbation History:<2 Smoking Status:Current smoker Race:Asian	0.89 (0.68, 1.18)
	At Exacerbation History:<2 Smoking Status:Current smoker Race:Non-Asian	0.68 (0.62, 0.74)
	At Exacerbation History:<2 Smoking Status:Former smoker Race:Asian	1.03 (0.79, 1.35)

PPD

Protocol: 207941
Population: Intent-to-Treat

Table 2.30
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Nine Covariates)

Statistic	Level	
Hazard Ratio 95% CI	At Exacerbation History:<2 Smoking Status:Former smoker Race:Non-Asian	0.78 (0.72, 0.86)
	At Exacerbation History:>=2 Smoking Status:Current smoker Race:Asian	0.99 (0.74, 1.31)
	At Exacerbation History:>=2 Smoking Status:Current smoker Race:Non-Asian	0.75 (0.68, 0.83)
	At Exacerbation History:>=2 Smoking Status:Former smoker Race:Asian	1.14 (0.87, 1.50)
	At Exacerbation History:>=2 Smoking Status:Former smoker Race:Non-Asian	0.87 (0.79, 0.96)
	Smoking Status Current smoker vs Former smoker	
	At Sex:F Country Income:High income	1.04 (0.95, 1.13)
	At Sex:F Country Income:Non-high income	0.93 (0.82, 1.05)
	At Sex:M Country Income:High income	0.90 (0.83, 0.97)
	At Sex:M Country Income:Non-high income	0.81 (0.73, 0.89)
	Treatment ICS vs non-ICS	
	At Exacerbation History:<2 Race:Asian	1.09 (0.92, 1.28)
	At Exacerbation History:<2 Race:Non-Asian	0.87 (0.82, 0.93)
	At Exacerbation History:>=2 Race:Asian	0.99 (0.83, 1.17)
	At Exacerbation History:>=2 Race:Non-Asian	0.79 (0.73, 0.86)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ F	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.42 (0.39,0.44)	0.46 (0.43,0.49)	0.30 (32 / 106)	0.46 (31 / 68)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.58 (0.54,0.61)	0.63 (0.59,0.66)	0.54 (32 / 59)	0.79 (31 / 39)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.41 (0.38,0.43)	0.46 (0.43,0.49)	0.39 (70 / 178)	0.47 (47 / 101)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.57 (0.54,0.60)	0.63 (0.60,0.66)	0.45 (45 / 99)	0.53 (36 / 68)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/I & II/ M	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.33 (0.31,0.35)	0.37 (0.34,0.39)	0.28 (42 / 148)	0.24 (27 / 114)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.47 (0.44,0.50)	0.52 (0.49,0.55)	0.45 (29 / 65)	0.43 (17 / 40)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.32 (0.30,0.34)	0.37 (0.34,0.39)	0.27 (82 / 302)	0.26 (45 / 174)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.46 (0.44,0.49)	0.52 (0.49,0.55)	0.47 (46 / 97)	0.54 (48 / 89)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ F	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.56 (0.53,0.59)	0.61 (0.58,0.64)	0.52 (103/ 197)	0.62 (107/ 172)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.73 (0.70,0.76)	0.78 (0.75,0.81)	0.67 (98 / 147)	0.76 (85 / 112)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.55 (0.52,0.58)	0.61 (0.58,0.64)	0.47 (92 / 195)	0.57 (69 / 121)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.72 (0.69,0.75)	0.78 (0.75,0.81)	0.62 (111/ 179)	0.64 (58 / 90)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
<=64/III & IV/ M	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.45 (0.43,0.48)	0.50 (0.48,0.53)	0.44 (160/ 367)	0.41 (111/ 271)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.62 (0.59,0.65)	0.67 (0.64,0.70)	0.60 (131/ 218)	0.64 (121/ 188)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.45 (0.42,0.47)	0.50 (0.48,0.53)	0.49 (173/ 352)	0.45 (124/ 277)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.61 (0.58,0.64)	0.67 (0.64,0.70)	0.56 (125/ 224)	0.65 (119/ 183)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ F	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.43 (0.40,0.46)	0.48 (0.45,0.51)	0.42 (46 / 109)	0.46 (29 / 63)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.57 (0.53,0.60)	0.62 (0.58,0.65)	0.47 (28 / 59)	0.69 (20 / 29)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.42 (0.40,0.45)	0.48 (0.45,0.51)	0.40 (61 / 154)	0.46 (44 / 96)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.56 (0.52,0.59)	0.62 (0.58,0.65)	0.56 (43 / 77)	0.53 (33 / 62)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/I & II/ M	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.35 (0.33,0.37)	0.39 (0.36,0.41)	0.27 (58 / 213)	0.35 (54 / 156)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.47 (0.44,0.50)	0.52 (0.49,0.55)	0.40 (34 / 86)	0.58 (38 / 66)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.34 (0.32,0.36)	0.39 (0.37,0.41)	0.34 (116/ 340)	0.38 (105/ 280)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.46 (0.43,0.49)	0.52 (0.49,0.55)	0.44 (63 / 143)	0.52 (50 / 97)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ F	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.57 (0.54,0.60)	0.63 (0.59,0.66)	0.54 (93 / 172)	0.48 (61 / 127)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.72 (0.69,0.75)	0.77 (0.74,0.80)	0.67 (90 / 135)	0.65 (56 / 86)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.57 (0.54,0.59)	0.63 (0.59,0.66)	0.52 (93 / 179)	0.59 (59 / 100)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.71 (0.68,0.74)	0.77 (0.74,0.80)	0.59 (59 / 100)	0.66 (55 / 83)

Protocol: 207941
Population: Intent-to-Treat

Table 9.1
Probability of Exacerbation During Year on Study Treatment from Cox Model
(Based on Seven Covariates Pneumonia Model)

Age/GOLD/ Sex	BMI/ Exac.	Modelled Hazard Ratio ICS vs. non-ICS	----Modelled Probability----- -------of First Event-------- ICS	non-ICS	----Observed Probability----- -------of First Event-------- ICS	non-ICS
>=65/III & IV/ M	<25 kg/m^2/ <2	0.87 (0.81,0.93)	0.48 (0.45,0.50)	0.53 (0.50,0.55)	0.45 (206/ 456)	0.48 (200/ 419)
	<25 kg/m^2/ >=2	0.87 (0.81,0.93)	0.62 (0.59,0.64)	0.67 (0.64,0.70)	0.55 (165/ 299)	0.63 (166/ 262)
	>=25 kg/m^2/ <2	0.85 (0.79,0.91)	0.47 (0.45,0.49)	0.53 (0.50,0.55)	0.41 (215/ 522)	0.44 (171/ 389)
	>=25 kg/m^2/ >=2	0.85 (0.79,0.91)	0.61 (0.58,0.64)	0.67 (0.64,0.70)	0.55 (157/ 286)	0.66 (142/ 216)

Protocol: 207941
Population: Intent-to-Treat

Table 9.2
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Seven Covariates Pneumonia Model)

Statistic	Level	
Type 3 Wald p-values	Sex by Age	0.665
	Treatment by BMI	0.650
	BMI	0.613
	Age	0.471
	Exacerbation History by Age	0.131
	Treatment	<0.001
	Sex	<0.001
	GOLD	<0.001
	Exacerbation History	<0.001

Protocol: 207941
Population: Intent-to-Treat

Table 9.2
Type 3 p-values and Hazard Ratios from Selected Exacerbation Cox Model
(Based on Seven Covariates Pneumonia Model)

Statistic	Level	
Hazard Ratio	Age >=65 vs <=64	
95% CI		
	At Exacerbation History:<2 Sex:F	1.05 (0.95, 1.15)
	At Exacerbation History:<2 Sex:M	1.07 (1.00, 1.15)
	At Exacerbation History:>=2 Sex:F	0.97 (0.88, 1.07)
	At Exacerbation History:>=2 Sex:M	0.99 (0.91, 1.08)
	BMI >=25 kg/m^2 vs <25 kg/m^2	
	At Treatment:ICS	0.98 (0.91, 1.04)
	At Treatment:non-ICS	1.00 (0.93, 1.07)
	Exacerbation History >=2 vs <2	
	At Age:<=64	1.61 (1.49, 1.73)
	At Age:>=65	1.49 (1.39, 1.59)
	GOLD III & IV: FEV1<50% predicted vs I & II: FEV1>=50% predicted	1.52 (1.44, 1.60)
	Sex M vs F	
	At Age:<=64	0.74 (0.69, 0.80)
	At Age:>=65	0.76 (0.70, 0.82)
	Treatment ICS vs non-ICS	
	At BMI:<25 kg/m^2	0.87 (0.81, 0.93)
	At BMI:>=25 kg/m^2	0.85 (0.79, 0.91)

PPD

Division: Worldwide Development
Retention Category: GRS019
Information Type: Meta-Analysis Plan

Title:	Meta-Analysis Plan for MID207941: A Study to Evaluate Risk Factors for Pneumonia and Chronic Obstructive Pulmonary Disease (COPD) Exacerbations in a COPD Population of Patients Treated with GW685698 + GW642444 (Fluticasone Furoate + Vilanterol); GW642444 (Vilanterol); CCI18781 (Fluticasone Propionate); GR33343 (Salmeterol); CCI18781+ GR33343 (Fluticasone Propionate + Salmeterol) and Placebo.

Compound Number: GW685698, GW642444, CCI18781, GR33343

Effective Date: 15-MAY-2017

Description:

This document describes the reporting and analysis planned for the MID207941 meta-analysis.

The study is designed to evaluate risk factors for pneumonia and COPD exacerbations in the COPD population of the five contributing studies: HZC102870, HZC102970, SCO100250, SCO40043, and SCO30003.

Subject: COPD, pneumonia, COPD exacerbations, inhaled corticosteroids

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ABBREVIATIONS

BMI	Body Mass Index
COPD	Chronic Obstructive Pulmonary Disease
FF	Fluticasone Furoate
FP	Fluticasone Propionate
GOLD	Global Initiative for Chronic Obstructive Lung Disease
ICS	Inhaled Corticosteroid
ITT	Intent-to-Treat
SAL	Salmeterol
VI	Vilanterol

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1. INTRODUCTION

The purpose of this meta-analysis is to evaluate the most important risk factors, alone and in combination for pneumonia and chronic obstructive pulmonary disease (COPD) exacerbations in patients with COPD.

The analysis will indentify the subgroups of COPD patients which are most at risk for these events and quantify the probability of patients having those events.

Previous analyses of the separate studies [not yet published] have identified some similarities in risk factors for pneumonias and COPD exacerbations in this population and this meta-analysis is intended to provide a more definitive list of risk factors using a larger sample size, and hence additionally more events of interest.

2. OBJECTIVE(S) AND ENDPOINT(S)

2.1. Objective(s)

2.1.1. Primary Objectives

The primary objectives of this study are to evaluate

- Risk factors for pneumonia in the COPD population of the contributing studies
- Risk factors for moderate/severe exacerbations in the COPD patient population of the contributing studies

2.1.2. Exploratory Objective

Based on previous analyses of the separate studies [not yet published] we anticipate that body mass index (BMI) will be an important factor in understanding the risk of pneumonia, both as a main effect and in interaction with treatment (inhaled corticosteroid [ICS] vs. non inhaled-corticosteroid [non-ICS]). In these previous analyses, a single cut-off for BMI subgroups was used: (BMI $< 25 kg/m^2$ vs. BMI $\geq 25 kg/m^2$), this was chosen because the median BMI value in the studies was often close to $25 kg/m^2$. However, there exists literature suggesting that a BMI ≤ 21 kg/m^2 may be an important cut-off for examining the effect of BMI on the risk of a subsequent pneumonia. Therefore the secondary objective for this study is to fully characterise the effect of BMI on risk for pneumonia.

2.2. Endpoint(s)

- Time to first pneumonia
- Time to first moderate/severe exacerbation

3. DATA SOURCES/STUDIES INCLUDED

The following criteria will be used to select studies:

- Randomised, parallel-group, double-blind clinical trials in COPD with FF/VI or FP/SAL as a randomized study drug not in combination with another study drug
- Inclusion of a VI or SAL alone treatment arm
- Constant dose of FP or FF
- At least 52 weeks duration
- Minimum 100 subjects per treatment arm to ensure sufficient events
- Not conducted earlier than TORCH (as this was first study where pneumonia was noted)
- Not solely in moderate COPD patients

The following table lists all studies conducted with FF/VI or FP/SAL of at least 52 weeks duration and the reason for exclusion if excluded.

Study	SFC or FF/VI	Comparators	Duration	Reason for Exclusion
SCO30003 (TORCH)	SFC 50/500	Placebo, Salmeterol, FP	156 weeks	
SCO40043	SFC 50/250	Salmeterol	52 weeks	
SCO100250	SFC 50/250	Salmeterol	52 weeks	
HZC102972	FF/VI 50/25, 100/25, 200/25	Vilanterol	52 weeks	
HZC102871	FF/VI 50/25, 100/25, 200/25	Vilanterol	52 weeks	
SCO40036 (INSPIRE)	50/500	Tiotropium	104 weeks	No VI or SAL arm
SFCB3024 (TRISTAN)	SFC 50/500	Placebo, Salmeterol, FP	52 weeks	Pre TORCH
SCO40002 (COSMIC)	SFC 50/500	Salmeterol	52 weeks	FP withdrawn
SCO40041 (Bone Mineral Density Study)	SFC 50/250	Salmeterol	104 weeks	<100 subjects per arm
SUMMIT	FF/VI 100/25	Placebo, Vilanterol, FP	Mean Treatment Exposure 1.6-1.7 years	Moderate COPD only

This is therefore a meta-analysis of five randomised double blind parallel group studies. Treatment assignments will be pooled into two groups "ICS treated" and "non-ICS treated" based on whether the patient was randomised to an inhaled corticosteroid (ICS) treatment alone or in combination: FF in the HZC studies, or FP in the SCO studies.

All available on-treatment data will be used from each study.

The numbers in the intent-to-treat (ITT) population and assigned treatment arms in each of the contributing studies is given in Table 1.

Table 1

Study	ITT	FF/VI 200/25	FF/VI 100/25	FF/VI 50/25	VI 25	FP/SAL 250/50	SAL 50	FP 500	Placebo	Total ICS	Total non-ICS

										treated	**treated**
HZC102871	1622	402	403	408	409					1213	409
HZC102970	1633	409	403	412	409					1224	409
SCO100250	797					394	403			394	403
SCO40043	782					394	388			394	388
SCO30003	6112					1533	1521	1534	1524	3067	3045
Meta-analysis	10946	811	806	820	818	2321	2312	1534	1524	6392	4654

Further details can be found in the protocols and reporting analysis plans (RAPs) of the contributing studies.

4. PLANNED ANALYSES

4.1. Analysis Methods

The analyses will be based on a backwards selection process for covariates. A starting Cox model will be fitted to the data using all relevant covariates and covariates will be removed iteratively until the selected model is found.

4.2. Statistical Hypotheses

The comparisons of interest will all be tests of significance of the type III Wald statistic of covariates in a Cox model. The hypothesis tested is:

H_0: The estimated beta coefficient of the covariate is equal to zero (i.e. the covariate has no effect on the outcome)

H_1: The estimated beta coefficient of the covariate is non-zero (i.e. the covariate has an effect on the outcome)

5. ANALYSIS POPULATIONS

The intent-to-treat (ITT) population will be used, and will consist of the ITT populations from each of the contributing studies.

6. TREATMENT COMPARISONS

Treatment comparisons will be made by pooling patients into two groups “ICS treated” and “non-ICS treated” based on whether the patient was randomised to an FF/VI arm in the HZC studies, or either FP alone, or in combination with salmeterol: FP/SAL in the SCO studies.

7. GENERAL CONSIDERATIONS FOR DATA ANALYSES

In using the backward selection process to select the most significant model covariates, inevitably concerns about multiple testing will arise. The purpose of this analysis is not confirmatory and so the control of the type I error level is not paramount. Any conclusions drawn from the final model will take into account the nature of the selection process in performing multiple hypothesis tests on model covariates.

In the final publication of results, reference will be made to the previous analyses of risk factors for pneumonia and COPD exacerbation which were performed separately on each study [not yet published]. These "by study" results will be used to assess the heterogeneity of studies used in this meta-analysis.

8. DATA HANDLING CONVENTIONS

8.1. Premature Withdrawal and Missing Data

No imputation of missing data will be performed for the purposes of this study.

8.2. Derived and Transformed Data

No additional derivations will be used.

8.3. Assessment Windows

Not applicable

8.4. Subgroup and Covariate Definitions

The covariates to be used in the primary analyses are all binary categorical variables measured at baseline: treatment assignment (ICS, non-ICS) age ($\leq$64, $\geq$65), sex, BMI ($<25kg/m^2$, $\geq25kg/m^2$), GOLD status (I & II, III & IV), smoking status (current smoker, former smoker), exacerbation history in the previous year (<2, ≥2). Only covariates which are measured in all contributing studies are included.

In additional analyses two more binary covariates will be used: race (Asian, non-Asian), and the World Bank categorisation of country income group from the year in which the contributing study started (2000 for SCO30003, 2004 for the SCO exacerbation studies, and 2009 for the HZC exacerbation studies). The World Bank categorises countries into four groups: high income, upper-middle income, lower-middle income and low income, which for the purposes of this analysis will be regrouped further into high income and non-high income countries to give more reasonable sample sizes in the categories.

Note, that neither study nor region will be used as a covariate in the analyses. Study will not be used because the variable has no predictive value for the wider COPD population and this analysis is intended to provide useful indicators of risk in the wider COPD population. Region will not be used because of colinearity issues with the race covariate.

It is hoped that race and income group will account for some aspects which the study and region covariates would traditionally adjust for, namely differences in the standards of care in different countries.

8.5. Other Data Handling Conventions

Only on-treatment moderate/severe exacerbations and pneumonias will be considered for this analysis, and follow up time will be censored at the end of the on-treatment period (see individual study RAPs for definitions of the on-treatment period in each study).

9. ANALYSES

9.1. Study Population

Disposition, demography, baseline characteristics and exposure tables will be produced.

9.2. Efficacy and Safety Analyses

The analyses of risk factors for i) pneumonia and ii) exacerbations will be based on a) selecting the best fitting Cox models using a backwards selection procedure, and then b) presenting the hazard ratios and probabilities from the selected model.

9.2.1. Analysis of risk of pneumonia event based on seven common covariates

9.2.1.1. Backwards selection

The starting Cox model will contain covariates for treatment, age, BMI, exacerbation history, GOLD, sex, and smoking status and all possible (21) pairwise interactions of those main effects. Covariates will be iteratively removed from the model based on the type III Wald statistics of the covariate. The covariate with the largest statistic will be removed until in the final model all remaining covariates have a p-value > 0.1. However, main effects will not be eligible for removal during the selection procedure if there is an interaction term involving that main effect still remaining in the covariate list. (Thus the finally selected model may contain main effects with associated p-values > 0.1.)

9.2.1.2. Subgroup probabilities and hazard ratios

Once the final model has been selected, the model estimated probability of pneumonia during the first year will be presented together with a figure of the survival function for each subgroup combination of the covariates remaining in the final model. Hazard ratios for each of the covariates in the final model will also be presented. Although data from the full three years of the SCO30003 (TORCH) study will be used in the model, survival estimates from the Cox model will be presented up to one year only.

9.2.2. Analysis of risk of pneumonia event based on nine common covariates

This analysis will be as for the analysis of pneumonia based on seven common covariates, but will additionally include race, and the World Bank country income groups and all their interactions in the starting model for the backwards selection process.

9.2.3. Analysis of risk of exacerbation event based on seven common covariates

This analysis will be as for the analysis of pneumonia based on seven common covariates replacing the analysis variables of time to pneumonia with time to moderate/severe exacerbation

9.2.4. Analysis of risk of exacerbation event based on nine common covariates

This analysis will be as for the analysis of pneumonia based on nine common covariates replacing the analysis variables of time to pneumonia with time to moderate/severe exacerbation

9.3. Exploratory analyses

Examination of BMI effect and BMI by treatment effect in risk of pneumonia

In the primary analysis for risk of pneumonia, the BMI subgroup variable will be "cut" at 25kg/m^2 (<25kg/m^2, >=25kg/m^2), and based on previous analyses of pneumonia risk in the individual studies, it is anticipated that BMI and/or treatment*BMI, will be significant explanatory covariates of the risk of pneumonia. If this is indeed the case, in order to better understand the risk profile for patients with different BMIs, the following two models (or one model if the selected models are identical) will be rerun, using a BMI covariate with more than two modalities.

1. The final pneumonia Cox model selected based on seven common covariates

2. The final pneumonia Cox model selected based on nine common covariates

The BMI covariate will be "cut" as follows into groups which are roughly deciles of the data: (0, 20), [20, 22), [22, 23), [23, 24), [24, 25), [25, 26), [26, 28), [28, 30), [30, 33), 33+

Using these two models the effect (hazard ratios vs. BMI reference level) of BMI on pneumonia, using the lowest (0, 20) kg/m^2 group as the reference level, will be presented and plotted in any subgroups which interact with BMI

Additionally assuming an interaction between BMI and treatment is present, the treatment effect (hazard ratio for ICS vs. non-ICS) at each of the BMI subgroup levels.

10. REFERENCES

11. ATTACHMENTS

11.1. List of Trials

Data from the following trials will be used in this study: HZC102870, HZC102970, SCO100250, SCO40043, and SCO30003.