

Deployment of the Demographic Subgroup Analysis Service

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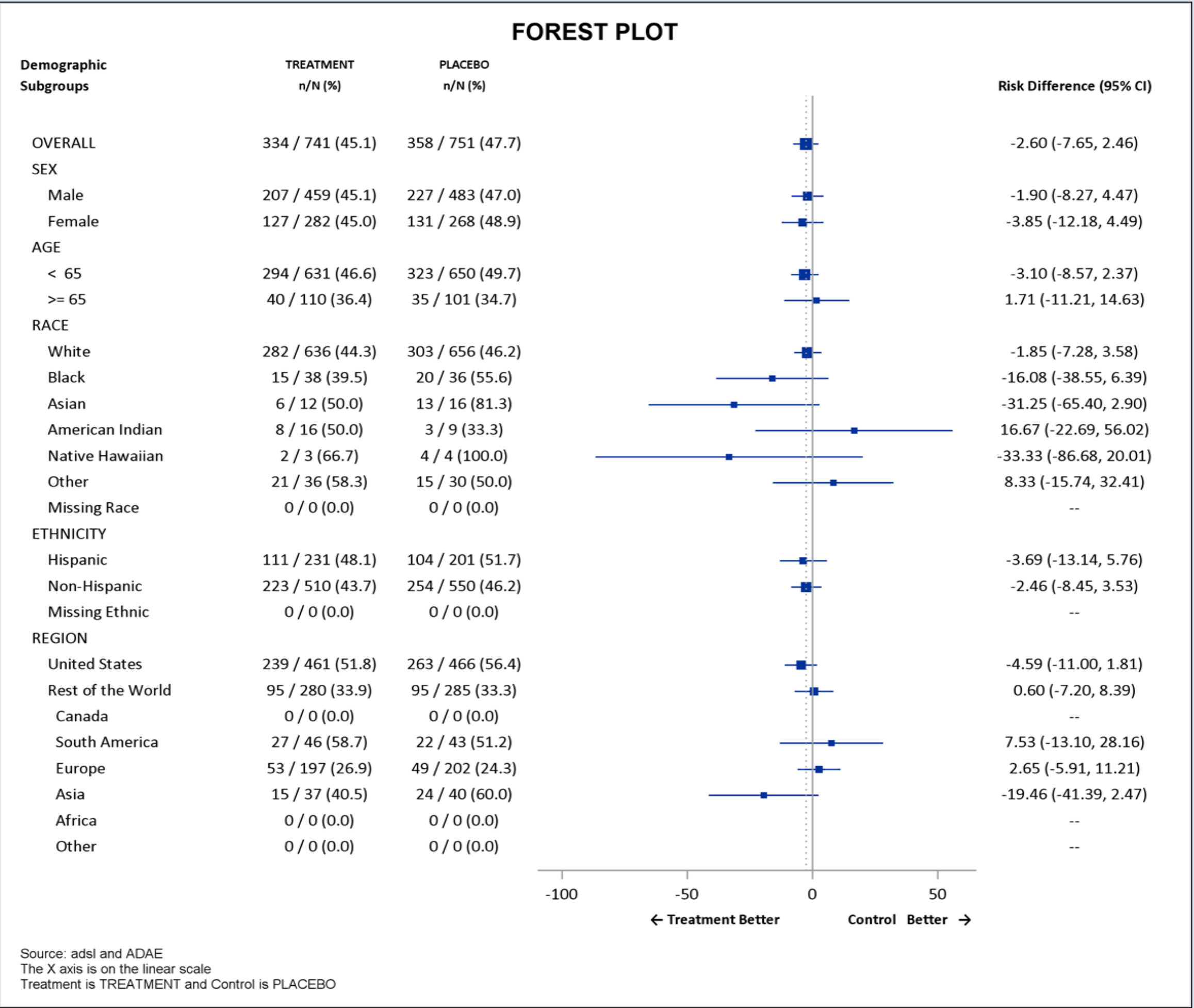
Background

Section 907 of the Food and Drug Administration Safety and Innovation Act of 2012¹ (FDASIA) requires the reporting of safety and effectiveness outcomes by demographic subgroups. To implement this requirement into the FDA 21st Century Review, the Office of Computational Science (OCS), in collaboration with the Office of New Drugs and the Office of Biostatistics, developed the Demographic Subgroup Analysis Program (“Demographic Tool”). With CDISC compliant data (i.e., SDTM/ADaM), the program can assist reviewers and analysts in conducting parameter-driven safety analyses seamlessly without having to spend time with statistical coding.

The OCS also created the Demographic Subgroup Analysis Service (“Demographic Service”) to incorporate the program into the review process and to provide reviewers with additional support in conducting their safety analysis. The service presents the demographic subgroup safety analysis results, produced by the Demographic Tool, to reviewers as well as provides instructions in using the Demographic Tool on their own.

The piloted Demographic Tool requires users to have access to SAS and Microsoft Excel via a local machine or scientific workstation. The user opens an Excel form to provide specific information related to the study data of a particular New Drug Application (NDA) or Biologics License Application (BLA). When finished, the user saves the form and launches the program. The program will autonomously run and generate a custom table and forest plot of the safety analysis. The service was piloted in 2016 to test a standardized delivery mode.

Table 8.6 Subgroup Analysis for Primary Endpoint (SAFFL= "Y")					
Subgroup	TREATMENT N=741		PLACEBO N=751		Risk Difference (95% CI)
	n(%)	Total,N	n(%)	Total,N	
Safety Subgroup (TREATMFL= "Y")					
SEX					
Male	207 (45.1)	459	227 (47.0)	483	-1.90 (-8.27, 4.47)
Female	127 (45.0)	282	131 (48.9)	268	-3.85 (-12.18, 4.49)
AGE					
< 65	294 (46.6)	631	323 (49.7)	650	-3.10 (-8.57, 2.37)
>= 65	40 (36.4)	110	35 (34.7)	101	1.71 (-11.21, 14.63)
RACE					
White	282 (44.3)	636	303 (46.2)	656	-1.85 (-7.28, 3.58)
Black	15 (39.5)	38	20 (55.6)	36	-16.08 (-38.55, 6.39)
Asian	6 (50.0)	12	13 (81.3)	16	-31.25 (-65.40, 2.90)
American Indian	8 (50.0)	16	3 (33.3)	9	16.67 (-22.69, 56.02)
Native Hawaiian	2 (66.7)	3	4 (100.0)	4	-33.33 (-86.68, 20.01)
Other	21 (58.3)	36	15 (50.0)	30	8.33 (-15.74, 32.41)
Missing Race	0 (0.0)	0	0 (0.0)	0	--
ETHNICITY					
Hispanic	111 (48.1)	231	104 (51.7)	201	-3.69 (-13.14, 5.76)
Non-Hispanic	223 (43.7)	510	254 (46.2)	550	-2.46 (-8.45, 3.53)
Missing Ethnic	0 (0.0)	0	0 (0.0)	0	--
REGION					
United States	239 (51.8)	461	263 (56.4)	466	-4.59 (-11.00, 1.81)
Rest of the World	35 (33.3)	280	35 (33.3)	285	0.60 (-7.20, 8.39)
Canada	0 (0.0)	0	0 (0.0)	0	--
South America	27 (58.7)	46	22 (51.2)	43	7.53 (-13.10, 28.16)
Europe	53 (26.9)	197	49 (24.3)	202	2.65 (-5.91, 11.21)
Asia	15 (40.5)	37	24 (60.0)	40	-19.46 (-41.39, 2.47)
Africa	0 (0.0)	0	0 (0.0)	0	--
Other	0 (0.0)	0	0 (0.0)	0	--



Results of Pilot

Eight clinical reviewers requested the Demographic Subgroup Analysis Service and participated in the pilot. The first two Demographic Service sessions ran over the allotted meeting time of 1.5 hours. When the sessions were relocated to a room with larger dual screens that allowed multiple analysts as well as reviewers display their laptops, the sessions ran close to the allotted time.

Follow-up surveys were collected from all of these reviewers, and each reviewer responded indicating the service and the program were helpful. The reviewers also said they would request the service again in their future reviews. One clinical reviewer indicated in the survey that the results from the Demographic Service detected novel findings, and they planned to discuss these findings with their statistical reviewer.

The Office of Computational Science demonstrated that both the Demographic Service and the Demographic Tool are feasible and useful to reviewers. The success of the pilot prompted the Office to move the service into production and 40 Demographic Services are being delivered this fiscal year.

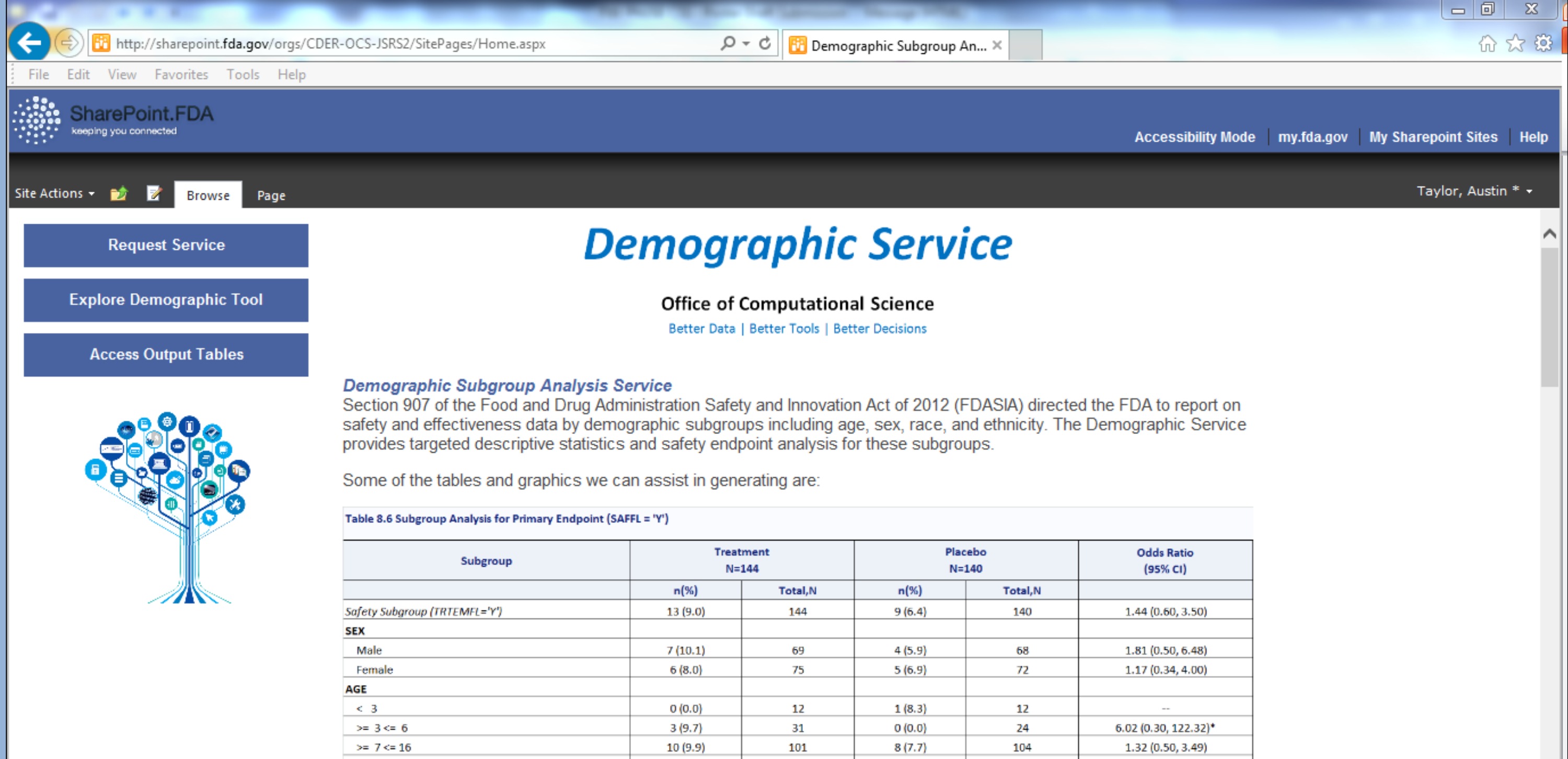
References:

- <https://www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf>

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Disclaimer: The views expressed in this presentation are those of the authors and do not necessarily represent the policy of FDA.

Demographic Service Homepage



Taking to Production

To facilitate a more streamlined service in production, the OCS created a SharePoint site to house the Demographic Tool and to receive requests for the service. The Demographic Tool itself was also enhanced between the pilot and production. The SAS processing was moved to be executed remotely so users were no longer required to access SAS directly. Additionally, the new program includes a comprehensive data checking system, the ability to generate exact confidence intervals, and the ability to analyze additional baseline characteristic subgroups.

Output Table

Demographic Service			
Office of Computational Science			
Demographic Service Output Table for Application # NDA208598			
Presentation and Training Files from the DSAS Team: DSAS Presentation - NDA208598.pdf			
Category	Subcategory	Study	
Descriptive Statistics	Safety Population	DESCRIPTIVE_2002.xlsx	DESCRIPTIVE_2003.xlsx
	Other Population		
Endpoint Analysis	Safety Analysis	SAFETY_2002_TEAS.xlsx	SAFETY_2003_TEAS.xlsx
		SAFETY_2003_TEAS_OI.xlsx	SAFETY_2003_TEAS_OVERALL.xlsx
Data	Data		