



Effects of Cigarette Smoking, Tobacco Heating System Use, and Smoking Cessation on Cough

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Background

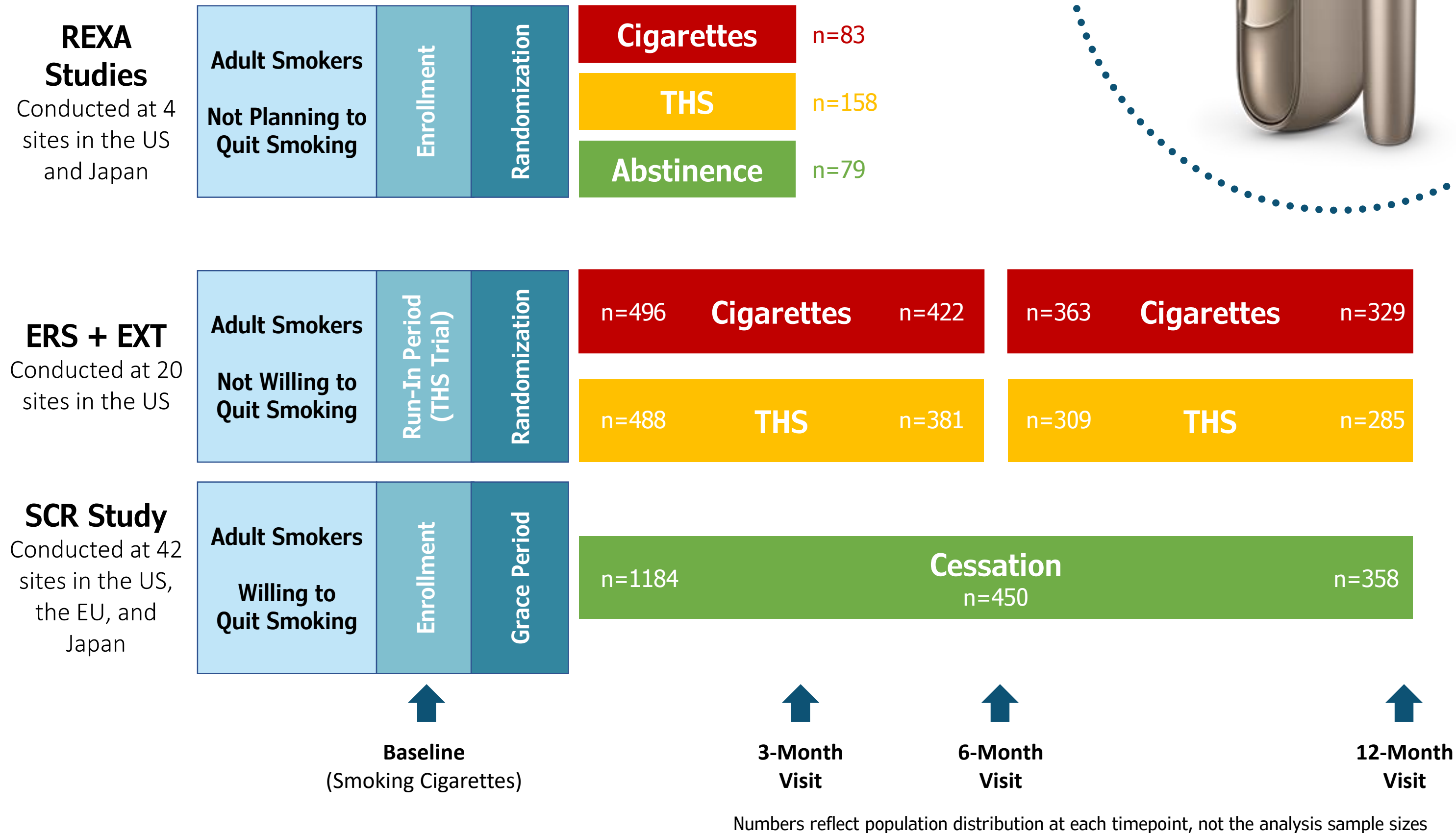
- Philip Morris International has developed and assessed its Tobacco Heating System (THS), which is currently sold in more than 50 markets around the world under the brand name IQOS®.
- THS heats tobacco (<350°C) to deliver a nicotine-containing aerosol to the user. Because the THS does not burn the tobacco, it emits substantially lower levels of toxicants relative to cigarette smoke.
- A causal relationship has been established between smoking and respiratory symptoms, such as coughing, in particular “smoker’s cough”. Smoker’s cough might be an indicator of chronic bronchitis.
- As reported in literature, approximately 40% of smokers develop some form of bronchitis, and almost half of such smokers might further develop chronic obstructive pulmonary disease (COPD).
- Smoking cessation reduces cough. There is also emerging evidence that e-cigarette users experience a decline in the incidence of cough.

Hypothesis

Switching to THS reduces self-reported need to cough.

Methods

Apparently healthy smoking adults were asked to continue to smoke cigarettes, switch to THS, or abstain from smoking for different periods of time for up to 12 months.



3-Month Reduced Exposure Studies (REXA)

- REXA-JP (NCT01970995) and REXA-US (NCT01989156)
- Multicenter, randomized, controlled, open-label, 3-arm parallel group study
- 2 days baseline + 5 days confined exposure + 85 days ambulatory exposure

6-Month Exposure Response Study (ERS)

- ERS-US (NCT02396381)
- Multicenter, randomized, controlled, open-label, 2-arm parallel group study
- 6 months ambulatory exposure (with visits at 3 and 6 months)

6-Month Extension ERS

- ERS-EXT-US (NCT02649556)
- 6 months ambulatory exposure following the ERS (with visit at 12 months)

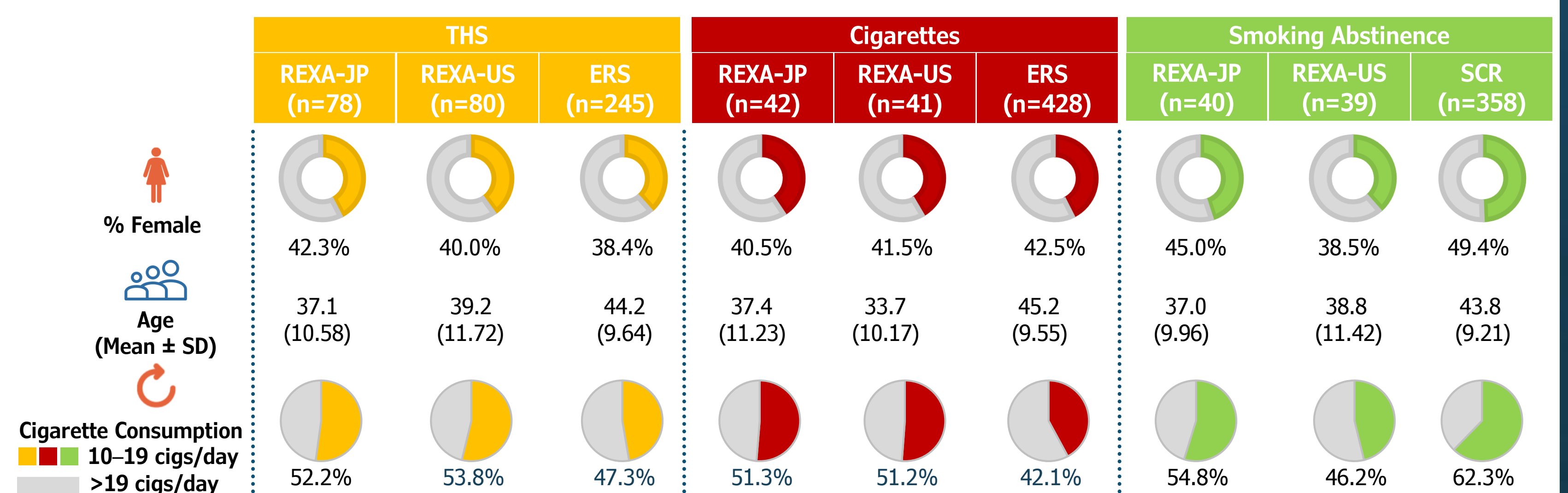
12-Month Smoking Cessation Response Study (SCR)

- SCR-INT (NCT02432729) conducted in US, EU and Japan
- Multicenter, single-arm study
- 12 months ambulatory smoking cessation (with visits at 3, 6 and 12 months)

COUGH ASSESSMENT

- Cough was assessed at each visit by using a self-reported questionnaire in the local language.
- Subjects were asked if they had experienced a regular need to cough within the 24 hours prior to the visit.
- The number and percentage of subjects reporting cough were summarized by arm and visit as well as overall across all post-baseline visits.

Study Populations

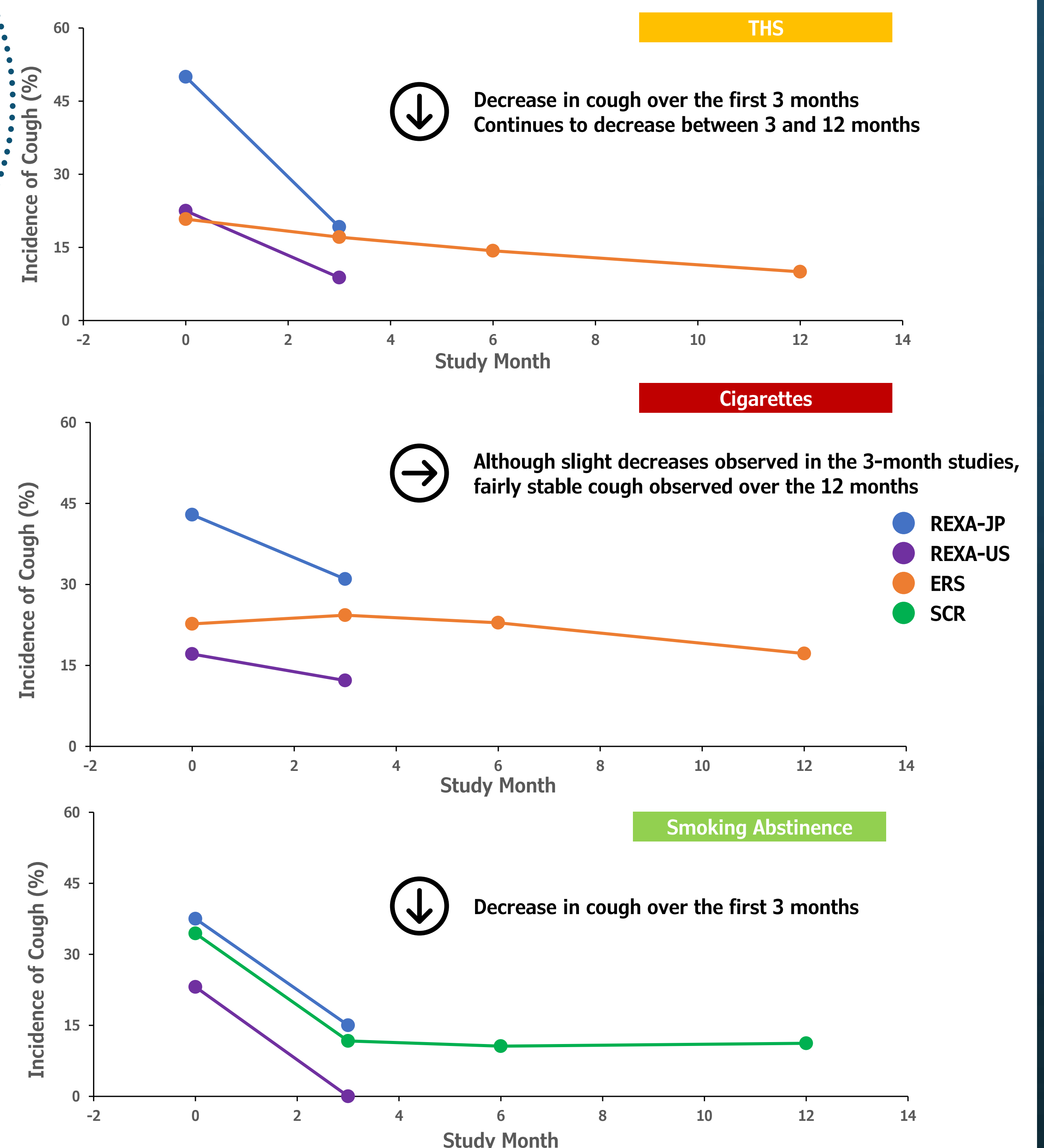


The demographic and baseline characteristics were fairly balanced across the arms in each study. However, there were some differences among the studies.

- The participants were slightly older in the longer response studies (ERS & SCR)
- Participants wanting to quit (SCR study) smoked slightly less cigarettes.

Results

There were some baseline differences among the studies. However, the trends within each study were clear and consistent.



Conclusions

Several reports have shown that smokers with chronic cough had a significant risk of developing COPD and that both chronic cough and the risk of developing COPD decreased overtime when smokers quit smoking altogether.

In our clinical program, we see a consistent decline in the incidence of cough reported after smokers switch to THS relative to those who continue to smoke cigarettes.

This decline in the incidence of cough could be a potential indicator for decreasing the risk of COPD and should, therefore, be studied directly in longer term studies designed to assess the impact of switching to smoke-free products on COPD development and progression.