Exclusion criteria

3.3 Study period

Objectives

Lay Summary

Figure 1

Vaccination status in previous season (yes versus no)

Presence

Brand-specific IVE estimates could be obtained for some brands, but not in a sufficiently robust manner to allow their interpretation and understand the driving factors of VE at the type and brand level as suggested that commenced in January 2018.

The results presented here are based on a limited number of sites being available, differing study designs, and the fact that in the pilot season there was no public release data on site-specific prior year VE. This resulted in a lack of a true internal control for this season.

The results should not reflect the true treatment effectiveness of the vaccine.

The manuscript should reflect only the research conducted in the scope of the pilot study.

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We conducted a random effects meta-analysis...

The weighting method should be mentioned. The analyses here use inverse-variance weighting. If this is the best weighting scheme is to be discussed for the next SAP.

The following covariates were used: age group, sex, years, 15-64 years and younger adults?

The text has been modified to capture the aspect of sample size as well.
6. Discussion

### Specific information

Next steps: brands included

#### 5.4.2 IVE by vaccine

- IVE by vaccine antigen (live attenuated, inactivated)
- IVE by vaccine and by vaccine type.
- IVE by any vaccine

#### 5.4.3 IVE by healthcare setting

- IVE by any healthcare setting.

#### 5.4.4 IVE by vaccine antigen (subunit, split, etc.)

Valid comparison.

#### 5.5.4 IVE by vaccine

Too many comparisons, only a few are relevant for our mission.

#### 5.5.5 IVE by vaccine

Relevant: 5.4.2, 5.5.1, 5.5.4.

#### 5.6.1 Comparison of pooling approaches

The results of the comparison of pooling approaches were in line with the statistical analysis described in section 3.1.1 of the report. The purpose of the analysis was to compare the results of different pooling strategies. The results of the comparison were as expected and in line with the statistical analysis. The results of the comparison showed that the results of the different pooling strategies were in line with the statistical analysis.

### Challenges and limitations of the single stratified analysis

There are several challenges and limitations of the single stratified analysis described in section 3.1.1 of the report. The purpose of the analysis was to compare the results of different pooling strategies. The results of the comparison were in line with the statistical analysis. The results of the comparison showed that the results of the different pooling strategies were in line with the statistical analysis.

#### 5.6.2 Time since vaccination

- Should we consider time since vaccination or calendar time?
- Whether or not data from different healthcare settings is included whenever possible.

#### 5.6.3 Influence on study results

- There are several challenges and limitations of the single stratified analysis described in section 3.1.1 of the report. The purpose of the analysis was to compare the results of different pooling strategies. The results of the comparison were in line with the statistical analysis. The results of the comparison showed that the results of the different pooling strategies were in line with the statistical analysis.

#### 5.6.4 Time since vaccination

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### Conclusion

The ISC decides on integration of EFPIA comments or justifies the current process. The ISC recommends that the process of integration of EFPIA comments is justifiable. The ISC recommends that the process of integration of EFPIA comments is justifiable. The ISC recommends that the process of integration of EFPIA comments is justifiable.

The results from this analysis were not interpretable, situation and not fully presented. However, there was evidence for the ISC to perform the analysis. The results from this analysis were not interpretable, situation and not fully presented. However, there was evidence for the ISC to perform the analysis. The results from this analysis were not interpretable, situation and not fully presented. However, there was evidence for the ISC to perform the analysis.

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Several sections, but specifically interested and comments

Throughout

Minimal set for confounder adjustment

The analysis should include the same minimal covariables for all analysis units. Covariables that are only applicable for certain sites should be pre-defined and the number of analyses may need to be pre-defined (if differences are so extensive and VE can be estimated at the individual level - should the data be pooled if that leads to comparing different HCW, pregnant women etc). Several differences between the protocols which is planned in the next season. The next season should be equal attention to how we deal with these differences in sensitivity/ applying restrictions etc. Criteria for pooling data in the analysis - i.e. appropriate analysis by subgroups/applying statistics, pooling hospital and GP data should be further vetted.

We agree that the results are nicely demonstrating statistical theory, and hence, not relevant for this pilot. However, we note that we will be probably able to stratify all analysis by healthcare setting.

(3) Agree.

(2) Not essential for this pilot.

(1) Report's primary and secondary objectives are the problem well defined in this report. The analysis was done to test the method in order to pilot the method. We think such an exercise fits well in a report on a pilot study to test methods. We agree that the results are nicely demonstrating statistical theory, and hence, not relevant for this pilot. However, we note that we will be probably able to stratify all analysis by healthcare setting. We agree that the report has been substantially revised.