March 2021
WORKING GROUP MEETING MINUTES:
COPD

Meeting details		
Meeting location	Teleconference	
Meeting date	Tues 23rd March	
Meeting time	16:00-17:00 CET	
Chair(s)	Marc Miravitlles	
Attendees	Helgo Magnussen Tony D'Urzo Matevz Harlander Bernardino Alcazar Navarrete David Price Nicolas Roche	Alberto Papi Therese Lapperre Carolina Gouder Alexandros Mathioudakis Sarah Lucas
Objectives		
1	Update on active projects	
2	Future projects	
3	New project ideas/AOB	

Items	
Update on current projects	**Real- life WISDOM** (PI Helgo Magnussen) This study is now completed with a manuscript published- Magnussen, H., Lucas, S., Lapperre, T. Quint J.K., Dandurand R.J., Roche N., Papi A., Price D., Miravitlles M. on behalf of the Respiratory Effectiveness Group. Respir Res 22, 25 (2021). The results are in line with the original WISDOM study. In patients with COPD who have infrequent exacerbations and low blood eosinophils on triple therapy withdrawal of ICS appears safe.
	Peak Inspiratory Flow in COPD (CI Omar Usmani) Update on progress - Currently have 17 potential centres. - Ethical approval at 8 centres.

	- 3 centres recruiting, 26 patients enrolled so far. Marc is planning to start in April. Bernardino is planning to start in May once he has moved hospitals. Pawel is putting in for approval in mid-April. Australian centres are delayed by COVID-19 and delays to ethical approval. Miguel Roman may not be able to participate. Pei Yee to start shortly. Sebastian waiting on ethical approval. Matevz has just recruited first 2 patients. We still need further centres, especially as many centres are seeing less patients as the result of the pandemic. There is a 100Euro per patient payment to help cover any additional costs/extra staff time. ACTION POINTS: If anyone has any suggestions of other sites that may be interested, please put them in contact with Sarah. Therese will talk to another potential centre in Denmark. Marc and Bernardino will see if they find any other Spanish centres. Sarah to send final protocol to Nicolas and Tony to see if they may be able to participate. Sarah will ask Omar about other sites, perhaps in UK.
Future projects	**Prevention of severe exacerbations** proposed by Bernardino. Risk prediction tool for patients recently diagnosed with COPD in primary care to determine 5/10 yr risk of a severe exacerbation. Other risk scores for COPD rely on previous exacerbations, but this would look at patients without previous exacerbations. The aim would be for it to be used like the cardiovascular risk scores and be used to help clinicians determine who should be given more intensive treatment. Will need funding and there have been initial discussions with GSK, however, they raised the issue of treatment changes in the 5-10 yr follow up period after COPD diagnosis. Such changes will need to be accounted for as these will likely alter a patient's risk. Discussions ongoing between Marc, Bernardino, Sarah and Mohsen Sadatsafavi to determine the best method to incorporate treatment into the model. Will need on primary care database to develop the model and then another database population for validation.

	David gave some information on potential databases- OPCRD/ SNDS/ Majorca/ SIDIAP. TAIWAN and Canadian, but these are claims databases so may lack variables such as spirometry and blood eosinophils. S. Korean database although it does lack some variables. Tony mentioned that in their data there seems to be an underestimate of prevalence of COPD, and that there may be value in looking at 'at risk' individuals (e.g. smokers over 40) and follow over time to look for diagnosis. Perhaps results of the initial study could be validated in a prospective study, but it may need a long follow up. This risk score could lead to primary prevention studies on how to treat those at the highest risk. Alex suggested looking at a larger range of potential variables rather than just the usual/pre-selected variables, as there may be other variables, especially comorbidities that may have an impact on risk. **Use of low dose macrolides in COPD** proposed by Therese. Therese presented data from studies that have looked the use of azithromycin in COPD. • Evidence from the MACRO trial that azithromycin reduces exacerbation rate and improves health related quality of life, with the greatest responses in ex-smokers, older people and those in GOLD category 2. • The COLOMBUS trial also showed a reduction in exacerbations, along with a decrease in inflammatory markers (CRP and leukocytes), but no change in lung function or quality of life scores. In this study high blood eosinophils and being in GOLD category C were predictors of response to azithromycin. • BACE study looked at azithromycin treatment started during hospitalisation for an exacerbation and used a composite endpoint which did not quite reach significance. In this study, in contrast to the COLOMBUS trial, those with lower blood eosinophils has a better response. In Belgium there are quite a lot of patients taking azithromycin long term, and long-term use has not been studied in the trials. Inflammatory biomarkers could be predictive of the response to azithromycin. There have been no good studies on mortality. Could use a database approach but would need to determine if enough people were being treated.

	Marc suggested that azithromycin is not infrequently prescribed in severe COPD and that in the SIDIAP database there are likely several hundred patients. David said that there are 957 in OPCRD, and that in the UK there is currently a study on withdrawal of the azithromycin, which might make a study such as this more interesting. In the primary care databases GP's might start azithromycin, but it might not be clear why. Suggested that we could approach BI for funding. ICS increases the risk of pneumonia/infections and so there is potential issues with ICS in infective phenotypes. With a link to infection and ICS BI may be interested. Nicolas raised that in those with inflammatory profiles some have a better response to ICS and some to macrolides. Could do a comparison between those on ICS and those not who are taking azithromycin. There was a study in patients with bronchiectasis comparing ICS with azithromycin, there was an increased risk with ICS, and some of the patients in that study had COPD. We could use a similar type of study design and use propensity matching to compare azithromycin with ICS in COPD. Could look at those on dual bronchodilation (ideally with blood/sputum eosinophil counts) and then see what was added to prevent exacerbations, macrolide or ICS. Would need to look at the percentage on different treatment regimes, perhaps would have enough to do a subanalysis comparing triple therapy with macrolide and triple therapy without. Alex suggested that with outcomes it would be worth looking at the type of exacerbation. Although they will not likely be characterised in terms of biomarkers it would be interesting to look at what was prescribed for exacerbations OCS vs antibiotics.
New projects/AOB	Any new project ideas feel free to email Marc/Sarah.