COPD as a COVID-19 risk group
Is genetic background the reason?

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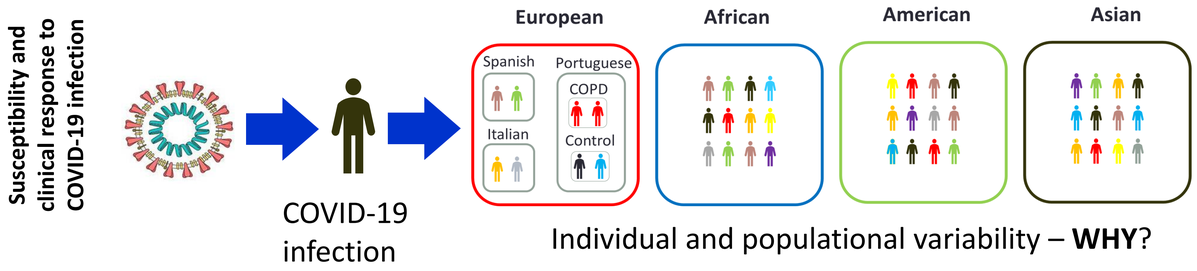
Background

- Chronic obstructive pulmonary disease (COPD) is associated with a poor prognosis upon COVID-19 infection[1].
- High populational variability observed in COVID-19 related outcomes[2].



Aim

- To explore the genetic background as a possible answer to COVID-19 infection response heterogeneity, either for the poor prognosis in people with COPD or across healthy worldwide populations.

Methods

1. Identification of genetic variants associated with COVID-19 susceptibility (rs286914 and rs12329760) and severity (rs657152 and rs11385942)[3-5].
2. Assessment of effect allele frequencies
   1. COPD cohort and control group;
   2. Worldwide populations (Spanish, Italian, European, African, American and Asian).
3. Computation of bi-allelic and polygenic (our cohort only) risk scores.
4. Comparison of effect allele frequencies/proportions of cumulative number of risk alleles – Chi-Square test.
5. Polygenic risk scores comparisons between COPD and control groups – student's t test.
6. Statistical significance was set at 0.01.

Results

- No differences in genetic risk for COVID-19 susceptibility or severity were found between people with COPD and the control group (all p-values > 0.01) (figure 1);
- All populations showed significant differences from the European population in genetic risk for COVID-19 susceptibility and severity (all p-values < 0.0001) (figure 2).

Table 1. Sociodemographic, anthropometric and clinical characteristics of participants.

Characteristics	Baixo Vouga cohort		Portuguese cohort
	COPD (n=255)	Control (n=243)	Baixo Vouga (only control) + Minho (n=623)
Age (years)	68 [61, 74]	67 [60, 72]	66 [58, 72]
Gender (Male), n (%)	203 (79.61%)	176 (72.43%)	359 (57.62%)
Body mass Index (Kg/m²)	25.97 [23.44, 29.73]	27.32 [24.91, 29.75]	27.53 [25.08, 30.22]
FEV_1 (Litres)	1.32 [0.94, 1.81]	2.58 [2.11, 3.06]	n.d.
FEV_1/FVC	53.02 [41.24, 61.94]	83.90 [78.01, 89.02]	n.d.

N (%) - number of individuals and corresponding percentage; remaining data is presented as medians with interquartile range in square brackets. FEV1 - Forced Expiratory Volume in 1-sec in litres; FVC - Forced Vital Capacity in litres; n.d. - no data available.

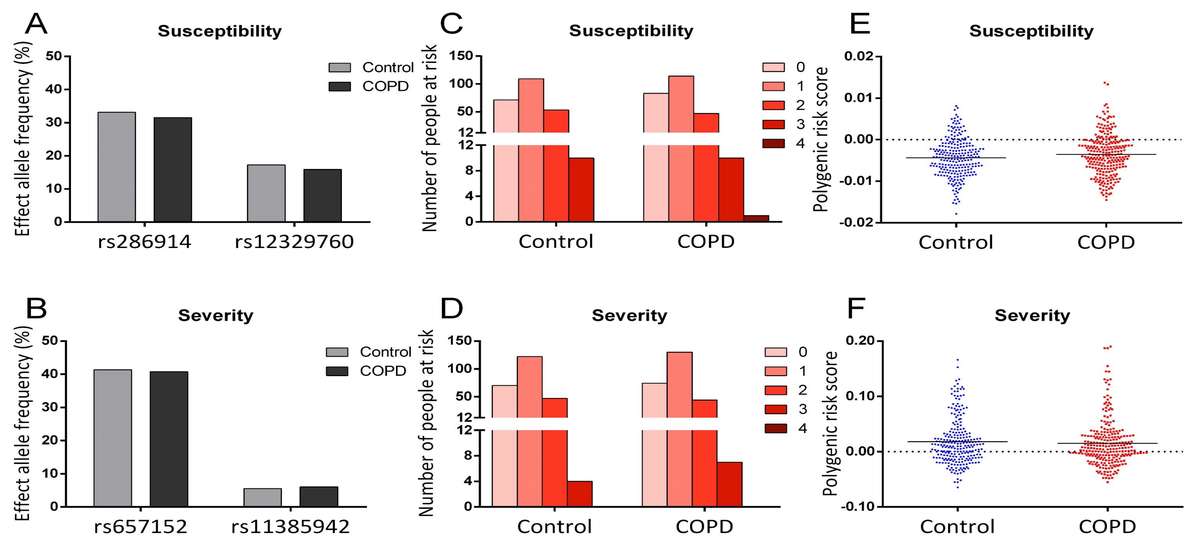


Figure 1. A and B: Allele frequencies for significant SNPs; C and D: Number of people with a cumulative number of risk alleles; E and F: Polygenic risk assessment. Top panel (A/ C/E): genetic risk for COVID-19 susceptibility; bottom panel (B/D/F): genetic risk for severe COVID -19. 0 to 4: sum of effect alleles for each COVID-19 outcome.

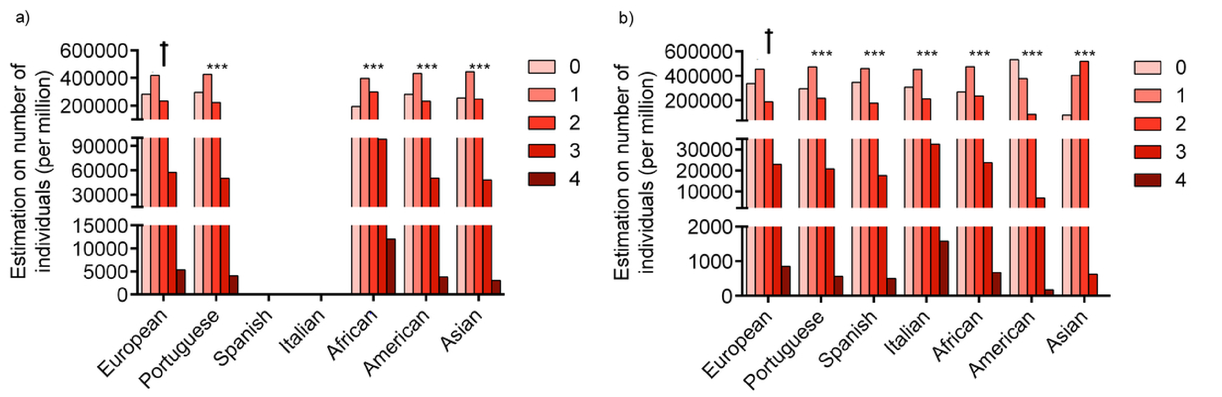


Figure 2. Estimation on the number of people with a cumulative number of risk alleles in the world major populations for A - susceptibility for COVID-19 infection (rs286914 + rs12329760) and B – severe COVID-19 with respiratory failure (rs657152 + rs11385942). 0 to 4 represent the sum of effect alleles for each COVID-19 associated phenotype. ***: p-value<0.0001. Statistical analyses were performed using the European population as reference.

Conclusions

- Low genetic contribution for COVID-19 infection predisposition or worse outcomes in people with COPD.
- High genetic heterogeneity across worldwide populations for the same alleles, even within European subpopulations.

References: [1]Attaway, A., et al. (2020). "SARS-CoV-2 infection in the COPD population is associated with increased healthcare utilization: An analysis of Cleveland clinic's COVID-19 registry". EclinicalMedicine 26:100515; [2]Stawicki, S. et al. (2020). "The 2019-2020 novel coronavirus (severe acute respiratory syndrome coronavirus 2) pandemic: A joint American college of academic international medicine-world academic council of emergency medicine multidisciplinary COVID-19 working group consensus paper". J Global Infect Dis 12(2): 47–93. [3]Kachuri, L. et al. (2020). "The landscape of host genetic factors involved in infection to common viruses and SARS-CoV-2". Genome Medicine 12,93; [4]Hou, Y. et al. (2020). "New insights into genetic susceptibility of COVID-19: An ACE2 and TMPRSS2 polymorphism analysis". BMC Med. 18, 216. [5]Ellinghaus, D. et al. (2020). "Genomewide Association Study of Severe Covid-19 with Respiratory Failure". N. Engl. J. Med. 383:1522-1534.

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