Reviewer's report

Title: Epidemiology and long-term survival in patients with pulmonary arterial hypertension in the Czech Republic: a retrospective analysis of a nationwide registry

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Reviewer: Rui Baptista

Reviewer's report:

Jansa and colleagues from Czech Republic report on a small national registry of incident and prevalent patients with PAH. This is a retrospective report of a multicenter registry from four centers in Czech Republic (3 in Prague and 1 in Brno) on patients with pulmonary hypertension. The authors should be acknowledged for their meticulous analysis and their achievement. However, although survival data is presented, no information is given on vasodilator drug treatment at baseline or follow-up, making difficult to interpret the survival findings.

MAJOR COMPULSORY REVISIONS

Page 8: How do you explain that during 7 years (2000 to 2006) only 100 patients were included, whereas in only one year (2007) 91 patients are identified? Was there any change in PAH screening policy to precipitate this very significant increase in patients? Is any possibility to analyze the incidence in other years to understand if this is a one-year phenomenon? This is a major issue. Having in consideration the survival curves that are presented, it seems unlikely that mortality explains such a discrepancy between prevent and incident cases.

Page 9: Incident patients are, in average, 10 years older than prevalent patients, signaling for a very different population. This may signify that prevalent patients (spanning a 7-year period) were diagnosed at much younger ages than incident patients. Interestingly, time from symptom onset to diagnosis is the same. The authors acknowledge that increased awareness may make physicians reconsider the diagnosis in older patients. In the incident cohort there is even a higher proportion of patients with APAH-CHD, a cohort that is usually diagnosed at younger ages and therefore would lower the mean age at inclusion. This finding must be further discussed, taking in consideration that 50% of the population is incident.

Page 10: Survival of the incident cohort of patients is very favorable, but it is difficult to interpret without information on baseline and follow-up drug treatment. Were these patients treated with pulmonary vasodilators? Which proportion of patients was treated with single, double or triple therapy? How many patients were on prostanoids?

The authors, for unstated reasons, choose only to present patients with some forms of pulmonary arterial hypertension; no information is given on
portopulmonary, HIV-related forms of PH. Why there are no patients with these forms of disease in the registry?

MINOR ESSENTIAL REVISIONS

Page 11: Please discuss why the iPAH incidence rate in Czech Republic is much higher than the reported in most other contemporary registries.

Page 6: Please specify if patients under 18 years were included in the registry (data is only in the abstract).

Page 7: Please specify “significant heart disease”.

Page 7: Why to use Mann-Whitney U test in variables with normal distributions? Please provide p values using Student’s T test for variables with normal distribution.

Page 10: By the incidence calculations, it seems that only adult population was included. Please specify the denominator used (number of Czech residents over x years).

Page 9: Please provide more data regarding the patients with congenital heart disease as they make up 1/4 of the incident cohort. Were these patients mostly Eisenmenger Syndrome or with residual PH? Are there barriers to access of congenital heart disease surgery in children? What was the nature of their defects?

Page 11: Pulmonary vasodilator treatments are very expensive and their availability is very different between countries. Please provide a summary of the therapies available in Czech Republic, introduction date and their widespread use.

Page 13, Line 11: Please correct the sentence, as patients with APAH-CHD have the best prognosis.

DISCRETIONARY REVISIONS

Page 10: Please convert CrCl form mL/s to mL/min, the usual unit to express creatinine clearance, in order to make easier for the reader to put in context the values.

The inclusion of a reference to the new 2013 consensus is important, to highlight the clinical relevance of registries and the range of prevalence and incidence calculations.

When enumerating the different etiologies of PAH, all of the causes should be mentioned, as portopulmonary hypertension, HIV-related, etc. A reference to the updated 2013 clinical classification is welcomed.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.