

## Burden of serious fungal infections in Spain

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### Abstract

Estimates of the incidence and prevalence of serious fungal infections, based on epidemiological data, are essential in order to inform public health priorities given the lack of resources dedicated to the diagnosis and treatment of these serious fungal diseases. However, epidemiology of these infections is largely unknown, except for candidaemia and cryptococcosis. The aim of this work is to calculate the burden of serious fungal infections in Spain. All published epidemiology papers reporting fungal infection rates from Spain were identified. Where no data existed, we used specific populations at risk and fungal infection frequencies in those populations to estimate national incidence or prevalence, depending on the condition. Around 8.1 million people suffer a fungal infection every year. Most of them are skin or mucosal infections causing no deaths. Candidaemia is more common than in other European countries and has risen by 1.88-fold in frequency in the last decade (8.1 cases × 100 000). Good estimates of invasive aspergillosis (2.75 cases × 100 000) and mucormycosis (0.04 × 100 000) are available. Fungal infections with a high mortality such as invasive aspergillosis, candidaemia, *Pneumocystis pneumonia* and mucormycosis are not numerous in Spain, but they affect those with severe underlying diseases and are therefore linked to poor outcomes. Additional studies are required, especially for high burden diseases such as recurrent thrush in women (~9000 cases × 100 000 women), allergic bronchopulmonary aspergillosis (126 cases × 100 000) and severe asthma with fungal sensitisation (198 cases × 100 000).

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### Introduction

Epidemiology of fungal infections is largely unknown except for candidaemia and cryptococcosis where some population-based

surveillance studies have been published [1,2]. Global estimates of cutaneous fungal infections, invasive fungal infections, chronic pulmonary aspergillosis after pulmonary tuberculosis, and sarcoidosis and allergic bronchopulmonary aspergillosis complicating asthma have recently been published [3–7]. Apart from the mildest cutaneous and mucosal fungal infections, most are serious, causing a high mortality and morbidity that increase if they are not suspected, diagnosed and treated as quickly as possible. Estimates of the incidence and prevalence of serious

fungal infections, based on epidemiological data, are essential in order to inform public health priorities given limited resources to diagnose and treat these diseases.

The aim of this work is to calculate the burden of serious fungal infections in Spain, a country with an estimated population of 47 million. Such an estimate of fungal burden has not previously been attempted in this country.

## Material and methods

All published epidemiology papers reporting fungal infection rates from Spain were identified. Where no data existed, we used specific populations at risk and fungal infection frequencies in those populations to estimate national incidence or prevalence, depending on the condition.

2010 population statistics were derived from the Statistics National Institute (<http://www.ine.es/>).

Prevalence of skin fungal diseases was obtained from Vos *et al.* [3].

The number of women aged between 14 and 55 years was obtained from the National Statistics Institute (<http://www.ine.es>). A 9% rate of recurrent vulvovaginal candidiasis was used and 'recurrent' defined as at least four episodes per year [8].

The number of HIV/AIDS patients in Spain was taken from epidemiologic surveillance of AIDS [9,10]. The proportion of HIV-infected patients receiving antiretroviral therapy (ARV) was estimated from the PISCIS cohort [11,12]. The annual new AIDS cases, the proportion of AIDS patients presenting with *Pneumocystis pneumonia* (PCP) or with cryptococcal meningitis and AIDS-related deaths in 2010 were obtained from the CoRIS cohort [13].

The number of pulmonary tuberculosis (PTB) cases was obtained from the National Registry [14]. Using the approach taken in Denning *et al.* [4], the 5-year point prevalence of chronic pulmonary aspergillosis (CPA) following PTB was estimated, assuming a 12% cavitation rate following therapy [4]. Further, it was assumed that PTB was the underlying diagnosis of CPA in 25% of cases (slightly higher than that of Smith & Denning [15], but lower than in France [16]).

The number of people with chronic obstructive pulmonary disease (COPD) was ascertained nationally [17] and a regional estimate of the number of admissions with COPD obtained from Andalusia [18], recently confirmed by the Organisation for Economic Co-operation and Development statistics [19].

Asthma rates in adults (children were not included for risk estimation) were obtained from multiple sources [20–24] and a mean of 7% of the adult population was used for estimates. The risk of allergic bronchopulmonary aspergillosis (ABPA) complicating asthma was estimated at 2.5% based on five previous studies

[6]. The rate of severe asthma with fungal sensitisation (SAFS) was estimated as the worst 10% of the total asthma population, of whom at least 33% have fungal sensitisation [25].

Cystic fibrosis numbers were obtained from the European registry of the European Cystic Fibrosis Society and the Spanish Scientific Society of Cystic Fibrosis ([https://www.ecfs.eu/files/webfm/webfiles/File/ecfs\\_registry/ECFSPR\\_Report0809\\_v32012.pdf](https://www.ecfs.eu/files/webfm/webfiles/File/ecfs_registry/ECFSPR_Report0809_v32012.pdf)).

Incidence and prevalence of haematological diseases were taken from Globocan 2008 (<http://globocan.iarc.fr>) and the Spanish Registry of Leukaemia and Lymphomas (<http://www.leucemiaylinfoma.com/resources/files/f9412075-9481-479b-a8ef-81c4fd333152.pdf>). Percentages of invasive aspergillosis (IA) in this population were taken from a study performed in Italy in 2004 [26]. Italy is a neighbouring Mediterranean country, and the haematological diseases figures are similar in the Globocan database (<http://globocan.iarc.fr>).

The rate of IA in critical care was assumed to be all attributable to COPD, and the Madrid-based study showed that 1.3% of COPD admissions developed IA in the final year, based on culture with support from serum (but not respiratory) galactomannan in a few patients [27].

The number of transplants was obtained from the Spanish National Organization for Transplantation (<http://www.ont.es/infesp/Paginas/Memorias.aspx>). The incidence of invasive aspergillosis in solid organ-transplanted patients was taken from different studies [28–31]. PCP cases in non-AIDs patients were derived from Calderón *et al.* as a population estimate was provided, 3.4 cases per 100 000 [32]. Cases in AIDs patients were calculated using data obtained in the CoRIS study [13].

Candidaemia cases were estimated from a population-based surveillance study recently performed in Spain [33]. The number of critical care beds in Spain in 2010 was obtained from the intensive care units registry (<http://www.msssi.gob.es/organizacion/sns/planCalidadSNS/docs/UCL.pdf>); 35.1% of candidaemia cases were among patients admitted to the intensive care unit (ICU) [33]. The annual number of cases of *Candida* peritonitis following surgery and ratio to candidaemia was assumed to be the same as in France, as there are no data from Spain, and as it is a neighbouring country we expect the number to be similar to that in Spain [34]. *Candida* peritonitis complicating chronic ambulatory peritoneal dialysis was not estimated.

For mucormycosis, we used a rate of 0.43 cases per 1 million inhabitants, as previously documented [35].

The annual incidence of histoplasmosis was calculated after reviewing the records of the Mycology Reference Laboratory for the last 5 years. Most of the cases identified in Spain are diagnosed or confirmed in this laboratory [36].

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