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Estimating the burden of invasive and serious fungal disease in the United Kingdom

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Summary *Background:* The burden of fungal disease in the UK is unknown. Only limited data are systematically collected. We have estimated the annual burden of invasive and serious fungal disease.
Methods: We used several estimation approaches. We searched and assessed published estimates of incidence, prevalence or burden of specific conditions in various high risk groups. Studies with adequate internal and external validity allowed extrapolation to estimate current UK burden. For conditions without adequate published estimates, we sought expert advice.
Results: The UK population in 2011 was 63,182,000 with 18% aged under 15 and 16% over 65. The following annual burden estimates were calculated: invasive candidiasis 5142; *Candida* peritonitis complicating chronic ambulatory peritoneal dialysis 88; *Pneumocystis* pneumonia 207—587 cases, invasive aspergillosis (IA), excluding critical care patients 2901—2912, and IA in critical care patients 387—1345 patients, <100 cryptococcal meningitis cases. We estimated 178,000 (50,000—250,000) allergic bronchopulmonary aspergillosis cases in people with asthma, and 873 adults and 278 children with cystic fibrosis. Chronic pulmonary aspergillosis is estimated to affect 3600 patients, based on burden estimates post tuberculosis and in sarcoidosis.
Conclusions: Uncertainty is intrinsic to most burden estimates due to diagnostic limitations, lack of national surveillance systems, few published studies and methodological limitations. The largest uncertainty surrounds IA in critical care patients. Further research is needed to produce a more robust estimate of total burden.
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Background

Invasive fungal disease is thought to be increasing in the United Kingdom (UK) due to a variety of factors including increased survival time from previously fatal illnesses and an increase in immunosuppression from disease treatment. Understanding of the overall burden of invasive fungal disease in the UK is limited as there is no formal systematic or mandatory surveillance programme specific to fungal infections, although active surveillance networks exist for candidaemias (voluntary laboratory reporting[1]) and specifically for candidaemias in neonates (voluntary reporting[2]).

An analysis of laboratory reports of fungal infections was published in 2001,[3] which highlighted the likely underestimate of the total burden due to the challenges involved in laboratory diagnosis and the voluntary nature of the laboratory reporting system. In 2008, the UK Health Protection Agency issued "Fungal Diseases in the UK: The current provision of support for diagnosis and treatment: assessment and proposed network solution".[4] The UK community of medical mycologists has been active in developing best practice standards for the UK and beyond for the diagnosis and clinical management of fungal disease.[5–9] A necessary next step for healthcare and research prioritisation is to quantify these burdens of invasive fungal disease with improved tools and an expanded range of serious fungal infections.

Methods

We used the UK Office for National Statistics 2011 Census data[10] to estimate UK population size. We used this as the 2011 census is the most recent census in the UK.

We estimated the annual incidence of the following invasive fungal infections: cryptococcal disease and meningitis; *Pneumocystis* pneumonia; invasive aspergillosis; candidaemia; *Candida* peritonitis; and oesophageal candidiasis. In addition, we estimated the prevalence of chronic pulmonary aspergillosis, allergic bronchopulmonary aspergillosis (ABPA) and severe asthma with fungal sensitisation (SAFS). Information on incidence, prevalence and total burden of these conditions in the UK is limited. Where such information was available for the UK or countries within the UK (where UK estimates were not available), we included it in the study, for example the data from the voluntary surveillance of candidaemia in England, Wales and Northern Ireland.[1]

Where the information was not available we took a pragmatic approach. For each fungal condition, we considered which populations were most at risk of the condition, sought published estimates for incidence or prevalence measures for the fungal condition in these specific risk populations, and applied these rates to available published estimates of size of these high risk populations in the UK (or certain countries within the UK where UK estimates were not available).

Where multiple estimates of incidence or prevalence were published, we considered both internal and external validity of the studies in deciding on which estimate to use. The methods used for estimating burden of the specific fungal conditions are outlined below.

Selection criteria for published estimates of incidence: for many of the severe fungal infection, there is a paucity of published estimates of incidence, therefore we had to be pragmatic in our approach. Where more than one published estimate was available, we prioritised studies with the best applicability to the UK population (i.e. where UK studies were available we used these, if not we used studies from countries with as comparable a population as possible, where non-UK studies were selected, this is made clear in italics in the fungal infection section of the Methods) and those with the largest sample sizes (where multiple studies were considered, this is made clear in the fungal infection section of the Methods).

Pneumocystis pneumonia

First method

Prior to March 2013, no published estimates of incidence, prevalence or total burden were available for England except for people living with AIDS (PHE HIV in the UK report[16]).

The high risk populations identified and the data source used to estimate their current size included people living with AIDS[16] and people who had received various solid organ transplants (Tx): Heart Kidney Liver and Lung or Heart and Lung.[11]

Using the estimate of total burden amongst people living with AIDS for 2011—2013,[16] we divided this estimate by three to obtain an average yearly estimate.

The incidence rates specific to solid organ transplant patients were found from a variety of studies.[12,13]

Second method

A UK study estimating the incidence of *Pneumocystis* pneumonia over an 11 year period was published in March 2013.[14] This showed that the incidence had increased significantly over the study period. We aimed to estimate the total burden for the most recent year of the study (2010) based on figures reported in the paper for each of the four data sources: Hospital Episode Statistics (HES) data — the paper reported the number of cases in 2010; Routine Laboratory Reporting — the paper reported a range for number of cases in 2008—2010, we used the central point of this range; Death Certificate Data — the paper reported the number of cases in 2010; HIV Surveillance Data — the paper did not report a number or range for total number of cases in the later years of the study, we obtained an estimate by extrapolating from figure 3 of the paper.

Cryptococcal meningitis

No published estimates of incidence, prevalence or total burden were found for the UK. We obtained an estimate based on a simple direct question to the largest mycology referral laboratories in the UK (Bristol, Leeds and Manchester) of the frequency of positive cryptococcal antigen test results. One publication was found which reported on trends in incidence and numbers of fungal meningitis,[15] but this covered all fungal infections and was not specific to cryptococcal infection.

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