

How Common are Fungal Diseases?

Oral, oesophageal and vulvovaginal candidiasis (thrush)

- Oral thrush occurs in ~2.5 million people worldwide based on ~90% of HIV/AIDS patients¹ not taking but needing anti-retroviral therapy, estimated by the WHO in 2011².
- Oral thrush also occurs in normal babies, people taking inhaled steroids for asthma, following radiotherapy to the head and neck for cancer, in denture wearers and in some leukaemia and transplant patients.
- Candida infection of the oesophagus (gullet) affects an estimated ~1.4 million people as ~20% of HIV/AIDS patients³ not on anti-retroviral therapy, and ~0.5% if on antiretroviral therapy⁴ develop it.
- Repeated attacks of vulvovaginal candidiasis affect at least 135 million women annually as 5-10% have at least 4 attacks annually^{5,6,7,8}. The impact of on quality of life is substantial⁹. About 70% of all premenopausal women develop thrush at some point in their lives¹⁰.

Invasive and life-threatening fungal infection

Candida infection

- Candidaemia occurs at a population rate of 2-26/100,000^{11,12,13}, so using 5.9 cases/100,000, ~400,000 cases are predicted worldwide, with a mortality of 30-55%¹⁴. The numbers rose in the US by 52% between 2000 and 2005¹⁵. Rates in India and Brazil are much higher, so the overall estimate could be greater.
- Candida peritonitis both those undergoing long term peritoneal dialysis for renal failure (CAPD) and post-surgical patients, usually in intensive care. In a large multicentre study in 101 French intensive care units (ICU), hospital-acquired Candida peritonitis was documented in 73 patients over 8 months, compared with 123 patients with candidaemia without Candida peritonitis; 26 patients had both¹⁶. Assuming this is generalisable to other populations, this suggests a ratio of 1 patient with hospital-acquired (almost all post-operative) Candida peritonitis for every 2 patients with candidaemia, in ICU. As between 30 and 50% of candidaemia cases occur in ICU, and there are about 400,000 episodes of candidaemia globally, this suggests about 60,000 - 100,000 cases of Candida peritonitis each year. The mortality of Candida peritonitis was 38%. In those with end stage renal disease worldwide (~1.7M) CAPD is used in about 50%. Patients get 1 infection per 18 months on average and ~0.05 episodes per patient year are attributable to Candida spp., equivalent to ~42,500 cases annually.
- Around 150,000 of the 7.5 million patients admitted to intensive care (ICU) in Europe, USA and Japan each year grow Candida in their urine (a rate of 2.7% of ICU admissions¹⁷) and is a common finding in

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hospitalised patients¹⁸ and those with catheters (~16%)¹⁹ especially those in ICU.

Invasive aspergillosis

- Over 10 million patients in Europe, USA and Japan are at risk of invasive aspergillosis (IA) each year because of corticosteroid or other therapies. Over 50% of patients with IA die, even with treatment.
- Over 300,000 patients develop IA annually. Key groups include ~10% of acute leukaemia (300,000 new cases annually)²⁰ (30,000 IA cases) and stem cell and other transplants (>75,000 annually in the USA, Europe and Japan) (7,500 IA cases) and 1.3-3.9% of COPD patients admitted to hospital^{21,22} (7% of the global number of moderate and severe COPD = 65M (WHO)) (60,000-180,000 confirmed IA cases). There are 11.9M COPD admissions in China each year and a mean rate in OECD countries of 198/100,000 (range 364 (Ireland) to 71 (Portugal)²³. IA also complicates lung cancer, at a rate of 2.63%²⁴. Worldwide there are 1,242,000 cases annually²⁵, consistent with an additional 32,600 IA cases. A recent large survey of IA in liver failure in China documented a 5% rate, with a 95% mortality²⁶. These patients probably account for 50-65% of patients, with those admitted to intense care (ICU), with lymphoma or chronic leukaemia and various immunological disorders and treatments accounting for the remainder. Under diagnosis is a major problem in this disease.

Cryptococcal meningitis

- The incidence of cryptococcal meningitis in AIDS has probably been falling as antiretroviral therapy is extended. An initial estimate of a million cases each year, resulting in ~600,000 deaths, of which ~70% are in sub-saharan Africa²⁷ has been replaced with lower estimates. A recent one is 278,250 cases in AIDS²⁸. In addition, cases occur in other immunocompromised groups and in normal people. In Thailand the records are good, and an estimated 108 'normal' and 251 immunocompromised people develop cryptococcal meningitis each year²⁹.

Pneumocystis pneumonia

- About 2.8 million HIV/AIDS infected patients² who should be receiving anti-retroviral therapy are at risk of Pneumocystis pneumonia (PCP), as well as many other immunocompromised patients, unless taking oral antifungal prophylaxis with cotrimoxazole.

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- The rate of PCP as an AIDS indicator disease is very variable. In African children, using reasonably sensitive diagnostic methods prevalence rates were 10% (South Africa, 2000), 49% (South Africa, 2002), 31% (Botswana, 2003) and 5% (Malawi, 2011). In adults from Africa, rates were 9% (Malawi, 2001), 33% (Tunisia, 2002), 37% (Kenya, 2003), 11% (Malawi, 2007), 30% (Ethiopia, 2008), 4% (Uganda, 2010), 5% (Namibia, 2012), 10% (Tanzania, 2012) and 11% (Uganda, 2012). Patient inclusion varied in these studies [<http://www.gaffi.org/media/fact-sheets/>] Pneumocystis pneumonia has a 10-30% mortality in the USA and UK^{30,31}.
- Precise estimates of annual incidence are difficult because of diagnostic deficiencies but case numbers certainly exceed 400,000 globally per year^{28,32}.

Disseminated histoplasmosis

- In AIDS, disseminated histoplasmosis is a devastating infection and difficult to diagnose rapidly enough to save the patients with either antigen or PCR testing. As the rates are highly variable from one locality to another, a global burden estimate is missing. An approximation of ~100,000 is likely²⁸, with Central and parts of South America most affected, and some cases in Africa and SE Asia.

Mucormycosis

- Three population analyses of mucormycosis have been conducted in the USA, France and India. A population estimate from the USA of 2 cases of mucormycosis per million³³ and from France of 0.6 per million³⁴. The high rate of diabetes in India is probably accountable for a much higher rate of mucormycosis there, as well as unique presentations such as renal mucormycosis. The projected annual incidence is as high as 13 per 100,000³⁵.

Allergic fungal disease

Allergic bronchopulmonary aspergillosis (ABPA)

- Approximately 4.8 million people develop ABPA among the 193 million adults with active asthma worldwide³⁶.
- Individual country estimates of asthma for 70 countries are now available³⁷, superseding older estimates²⁴.
- ~ 15% of people with cystic fibrosis develop ABPA, ~9,000 affected³⁸.

Severe Asthma with Fungal Sensitisation (SAFS)

- SAFS is predicted to affect ~6.5 million (range 3.25-13 million) adults worldwide depending on the frequency of severe asthma (5-20% of all asthmatics)^{14,39}. There is some duplication between ABPA and SAFS

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(collectively termed 'fungal asthma') because all ABPA patients are sensitized to fungi, and some have severe asthma.

Allergic fungal rhinosinusitis

- Allergic fungal sinusitis and rhinitis affects ~12 million people at any time. Allergic sinusitis and rhinitis affects ~15% of the world's population or around 900 million people⁴⁰ and ~1.3% is predominantly fungal allergy (assuming a 50% endoscopic examination rate)⁴¹. Two country rates have been ascertained – Israel and India. In Israel, nearly 0.5% of the population (40,000) is thought to be affected⁴². In India, a community survey of allergic fungal rhinosinusitis (FRS) in rural India found a population prevalence of 0.11% of chronic FRS with allergic FRS in 41 (56.1%), chronic granulomatous FRS in 13 (17.8%), eosinophilic FRS in 11 (15.0%), fungal ball in 7 (9.5%) and chronic invasive FRS in one (1.3%)⁴³.

Chronic fungal disease

- Prevalence of chronic pulmonary aspergillosis following tuberculosis is estimated at about 1.2 million cases⁴⁴. Chronic pulmonary aspergillosis complicates many respiratory disorders including tuberculosis, ABPA, sarcoidosis and COPD^{22,45,46}, and so the total burden of this debilitating disorder is ~3 million.
- About 25,000 cases of coccidioidomycosis occur in the US each year¹⁰, and many more in Central and South America.
- Up to 50 million people are thought to have been infected with histoplasmosis, with ~500,000 new infections each year, most asymptomatic and based on skin testing⁴⁷. About 25,000 cases of symptomatic histoplasmosis are estimated in the USA annually¹⁰.

Fungal eye infections

- Estimates of the annual incidence of fungal keratitis vary from 1 million to 6 million in SE Asia annually. Rates vary from as low as 6.3/100,000 in Hong Kong⁴⁸ to as high as 799/100,000 in Kathmandu⁴⁹. Rates of keratitis in S. America and Africa are not known. Among causes of avoidable blindness, corneal opacities (caused by fungi or bacteria) accounts for 10% of the 284 million people visually impaired worldwide⁵⁰.

Cutaneous fungal infections

- Fungal infection of the skin, hair or nails affects ~1 billion people⁵¹ and in the US alone accounted for 4M outpatient medical visits⁵².

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- Fungal nail infection (onychomycosis) is common in the general adult population, probably 5-25% rate with an increasing incidence in elderly people^{53,54}.
- Athlete's foot (tinea pedis) is more common than onychomycosis and is more common in younger people and sportsmen.
- Hair infection (tinea capitis) is most common among children, often resulting in bald patches with psychosocial consequences. In a recent US survey, tinea capitis was found in 6.6% with ranges from 0% to 19.4%⁵⁵, is more common in deprived areas and black children (with rates up to 41%)^{56,57,58,59}, suggesting a global prevalence of 200 million cases.

**The Fungal Infection Trust
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References

- ¹ Matee MI, Scheutz F, Moshy J. Occurrence of oral lesions in relation to clinical and immunological status among HIV-infected adult Tanzanians. *Oral Dis* 2000;6:106-11.
- ² <http://www.unaids.org/en/resources/fact-sheet> (assumes that 1 in 7 of those not on antiretroviral therapy has a low CD4 counts and is susceptible to opportunistic infection)
- ³ Smith E, Orholm M. Trends and patterns of opportunistic diseases in Danish AIDS patients 1980-1990. *Scand J Infect Dis.* 1990;22(6):665-72.
- ⁴ Buchacz K, Baker RK, Palella FJ Jr, Chmiel JS, Lichtenstein KA, Novak RM, Wood KC, Brooks JT; HOPS Investigators. AIDS-defining opportunistic illnesses in US patients, 1994-2007: a cohort study. *AIDS.* 2010 Jun 19;24(10):1549-59.
- ⁵ Sobel JD. Vulvovaginal candidosis. *Lancet.* 2007 Jun 9;369(9577):1961-71.
- ⁶ Foxman B, Marsh JV, Gillespie B, Sobel JD. Frequency and response to vaginal symptoms among white and African American women: results of a random digit dialing survey. *J Womens Health* 1998; 7:1167-74.
- ⁷ Corsello S, Spinillo A, Osnengo G, Penna C, Guaschino S, Beltrame A, Blasi N, Festa A. An epidemiological survey of vulvovaginal candidiasis in Italy. *Eur J Obstet Gynecol Reprod Biol* 2003;110:66-72.
- ⁸ Foxman B, Muraglia R, Dietz, JP, Sobel JD, Wagner J. Prevalence of recurrent vulvovaginal candidiasis in 5 european countries and the United States: Results from an internet panel survey. *J Low Genit Tract Dis* 2013;17:340-5.
- ⁹ Aballea S, Guelfucci F, Wagner J, Khemiri A, Dietz JP, Sobel JD, Toumi M. Subjective health status and health-related quality of life among women with recurrent vulvovaginal candidosis (RVVC) in Europe and the USA. *Health Qula Life Outcomes* 2013;11:169.
- ¹⁰ Ferre J. Vaginal candidosis: epidemiological and etiological factors. *Int J Gynaecol Obstet* 2000;71 Suppl 1:S21-7.
- ¹¹ Arendrup MC. Epidemiology of invasive candidiasis. *Curr Opin Crit Care.* 2010 Oct;16(5):445-52.
- ¹² Cleveland AA, Farley MM, Harrison LH, Stein B, Hollick R, Lockhart SR, Magill SS, Derado G, Park BJ, Chiller TM. Changes in incidence and antifungal drug resistance in candidemia: results from population-based laboratory surveillance in Atlanta and Baltimore, 2008-2011. *Clin Infect Dis* 2012;55:1352-61.

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- ¹³ Puig-Asensio M, Padilla B, Garnacho-Montero J, Zaragoza O, Aguado JM, Zaragoza R, Montejo M, Muñoz P, Ruiz-Camps I, Cuenca-Estrella M, Almirante B; CANDIPOP Project; GEIH-GEMICOMED (SEIMC); REIPI. Epidemiology and predictive factors for early and late mortality in *Candida* bloodstream infections: a population-based surveillance in Spain. *Clin Microbiol Infect* 2014;20:O245-54.
- ¹⁴ Brown GD, Denning DW, Gow NAR, Levitz S, Netea M, White T. Human fungal infections: the hidden killers. *Sci Transl Med* 2012;4: 165rv13.
- ¹⁵ Zilberberg MD, Shorr AF, Kollef MH. Secular trends in candidemia-related hospitalization in the United States, 2000-2005. *Infect Control Hosp Epidemiol.* 2008 Oct;29(10):978-80.
- ¹⁶ Montravers P, Mira JP, Gangneux JP, Leroy O, Lortholary O; AmarCand study group. A multicentre study of antifungal strategies and outcome of *Candida* spp. peritonitis in intensive-care units. *Clin Microbiol Infect.* 2011 Jul;17(7):1061-7.
- ¹⁷ Bounoux ME. Candidemia and candiduria in critically ill patients admitted to intensive care units in France: incidence, molecular diversity, management, and outcome. *Intensive Care Med* 2008;34:292-9.
- ¹⁸ Sobel JD, Fisher JF, Kauffman CA, Newman CA. *Candida* urinary tract infections--epidemiology. *Clin Infect Dis.* 2011 May;52 Suppl 6:S433-6.
- ¹⁹ Bouza E, San Juan R, Munoz P, Voss A, Kluytmans J. A European perspective on nosocomial urinary tract infections II. Report on incidence, clinical characteristics, and outcome (ESGNI-004 study). European Study Group on nosocomial infection. *Clin Microbiol Infect* 2001;7:532-42.
- ²⁰ Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin.* 2005 Mar-Apr;55(2):74-108.
- ²¹ Guinea J, Torres-Narbona M, Gijón P, Muñoz P, Pozo F, Peláez T, de Miguel J, Bouza E. Pulmonary aspergillosis in patients with chronic obstructive pulmonary disease: incidence, risk factors, and outcome. *Clin Microbiol Infect.* 2010 Jul;16(7):870-7.
- ²² Xu H, Li L, Huang WJ, Wang LX, Li WF, Yuan WF. Invasive pulmonary aspergillosis in patients with chronic obstructive pulmonary disease: a case control study from China. *Clin Microbiol Infect.* 2012 Apr;18(4):403-8.
- ²³ <http://www.oecd-ilibrary.org/docserver/download/8111101ec040.pdf?expires=1355694700&id=id&accname=guest&checksum=A5D8D12C997E1ABA9EE66C3C4410F4DF>
- ²⁴ Yan X, Li M, Jiang M, Zou LQ, Luo F, Jiang Y. Clinical characteristics of 45 patients with invasive pulmonary aspergillosis: retrospective analysis of 1711 lung cancer cases. *Cancer.* 2009 Nov 1;115(21):5018-25.
- ²⁵ IARC Globocan registry 2012 http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
- ²⁶ Chen J, Yang Q, Huang J, Li L. Risk factors for invasive pulmonary aspergillosis and hospital mortality in acute-on-chronic liver failure patients: A retrospective cohort study. *Int J Med Sci* 2013;10:1625-31.
- ²⁷ Park BJ, Wannemuehler KA, Marston BJ, Govender N, Pappas PG, Chiller TM. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. *AIDS.* 2009 Feb 20;23(4):525-30.
- ²⁸ Denning DW. How the UNAIDS target of reducing annual AIDS deaths below 500,000 by 2020 can be achieved. *Phil Trans Roy Soc B*, In press.
- ²⁹ Chayakulkeeree M, Denning DW. Estimating the burden of serious fungal diseases in Thailand. *Eur J Clin Microbiol Infect Dis* 2017 In press.
- ³⁰ Teshale EH, Hanson DL, Wolfe MI, Brooks JT, Kaplan JE, Bort Z, Sullivan PS; Adult and Adolescent Spectrum of HIV Disease Study Group. Reasons for lack of appropriate receipt of primary *Pneumocystis jirovecii* pneumonia prophylaxis among HIV-infected persons receiving treatment in the United States: 1994-2003. *Clin Infect Dis.* 2007;44:879-83.
- ³¹ Walzer PD, Evans HE, Copas AJ, Edwards SG, Grant AD, Miller RF. Early predictors of mortality from *Pneumocystis jirovecii* pneumonia in HIV-infected patients: 1985-2006. *Clin Infect Dis.* 2008;46:625-33.
- ³² Global Action Fund for Fungal Infections. 95-95 by 2025. Improving outcomes for patients with fungal infections across the world; A roadmap for the next decade. May 2015 <http://www.gaffi.org/roadmap/>

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- ³³ Rees J R, Pinner RW, Hajjeh RA, Brandt ME, Reingold AL. The epidemiological features of invasive mycotic infections in the San Francisco Bay area, 1992-1993: results of population-based laboratory active surveillance. *Clin Infect Dis* 1998;27:1138-1147.
- ³⁴ Bitar D, Morizot G, Van Cauteren D, Dannaoui E, Lanternier F, Lortholary O, Dromer F. Estimating the burden of mucormycosis infections in France (2005-2007) through a capture-recapture method on laboratory and administrative data. *Rev Epidemiol Sante Publique* 2012;60:383-7.
- ³⁵ Chakrabarti A, Sood P, Denning DW. Estimating fungal infection burden in India using computational models: Mucromycosis burden as a case study. 23rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID, 23rd) Berlin 2013. P1044.
- ³⁶ Denning DW, Pleuvry A, Cole DC. Global burden of ABPA in adults with asthma and its complication chronic pulmonary aspergillosis. *Med Mycol* 2013;51:361-70.
- ³⁷ To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, Boulet LP. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health* 2012 19;12:204.
- ³⁸ Armstead J, Morris J, Denning DW. Multi-country estimate of different manifestations of aspergillosis in cystic fibrosis. **PLoS One** 2014;9:e98502.
- ³⁹ Denning DW, Pashley C, Hartl D, Wardlaw, A, Godet C, Del Giacco, Delhaes L, Sergejeva S. Fungal allergy in asthma—state of the art and research needs. *Clin Transl Allergy* 2014;4:14.
- ⁴⁰ Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998;351(9111):1225-32.
- ⁴¹ Dall'Igna C, Palombini BC, Anselmi F, Araújo E, Dall'Igna DP. Fungal rhinosinusitis in patients with chronic sinus disease. *Braz J Otorhinolaryngol.* 2005 Nov-Dec;71(6):712-20.
- ⁴² Ben-Ami R, Denning DW. Estimating the burden of fungal diseases in Israel. *Israel Med Assc J* 2015;17:374-9.
- ⁴³ Chakrabarti A, Rudramurthy SM, Panda N, Das A, Singh A. Epidemiology of chronic fungal rhinosinusitis in rural India. *Mycoses.* 2015 May;58(5):294-302.
- ⁴⁴ Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to tuberculosis. *Bull WHO* 2011;89:864-72.
- ⁴⁵ Smith N, Denning DW. Underlying pulmonary disease frequency in patients with chronic pulmonary aspergillosis. *Eur Resp J* 2011;37:865-72.
- ⁴⁶ Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis complicating sarcoidosis. *Eur Resp J* 2013;41:621-6.
- ⁴⁷ Hammerman KJ, Powell KE, Tosh FE. The incidence of hospitalized cases of systemic mycotic infections. *Sabouraudia.* 1974 Mar;12(1):33-45.
- ⁴⁸ Lam DS, Houang E, Fan DS, Lyon D, Seal D, Wong E. Incidence and risk factors for microbial keratitis in Hong Kong: comparison with Europe and North America. *Eye (Lond)* 2002;16:608-18.
- ⁴⁹ Upadhyay MP, Karmacharya PC, Koirala S, Tuladhar NR, Bryan LE, Smolin G, Whitcher JP. Epidemiological characteristics, predisposing factors, and etiologic diagnosis of corneal ulceration in Nepal. *Am J Ophthalmol*, 1991, 111: 92–99.
- ⁵⁰ <http://www.who.int/mediacentre/factsheets/fs282/en/index.html>
- ⁵¹ Vos, T, Flaxman AD, Naghavi M et al, Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990—2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380:2163–2196.
- ⁵² Panackal AA, Halpern EF, Watson AJ. Cutaneous fungal infections in the United States: Analysis of the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS), 1995-2004. *Int J Dermatol.* 2009 Jul;48(7):704-12.
- ⁵³ Pierard G. Onychomycosis and other superficial fungal infections of the foot in the elderly: a pan-European survey. *Dermatology* 2001;202:220-4.
- ⁵⁴ Thomas J, Jacobson GA, Narkowicz CK, Peterson GM, Burnet H, Sharpe C. Toenail onychomycosis: an important global disease burden. *J Clin Pharm Ther.* 2010 Oct;35(5):497-519.
- ⁵⁵ Abdel-Rahman SM, Farrand N, Schuenemann E, Stering TK, Preuett B, Magie R, Campbell A. The prevalence of infections with *Trichophyton tonsurans* in schoolchildren: the CAPITIS study. *Pediatrics.* 2010;125:966-73.

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- ⁵⁶ Ali J, Yifru S, Woldeamanuel Y. Prevalence of tinea capitis and the causative agent among school children in Gondar, North West Ethiopia. *Ethiop Med J* 2009;47:261-9.
- ⁵⁷ Chepchirchir A, Bii C, Ndinya-Achola JO. Dermatophyte infections in primary school children in Kibera slums of Nairobi. *East Afr Med J* 2009;86:59-68.
- ⁵⁸ Nweze EI. Dermatophytosis among children of Fulani/Hausa herdsmen living in southeastern Nigeria. *Rev Iberoam Micol* 2010;27:191-4.
- ⁵⁹ Adefemi SA, Odeigah LO, Alabi KM. Prevalence of dermatophytosis among primary school children in Oke-Oyi community of Kwara state. *Niger J Clin Pract* 2011;14:23-8.