Supplementary material

The final PubMed search used was: Mucorales[MeSH Terms] NOT (plants[MeSH Terms] OR plant diseases[MeSH Terms]))combined, using AND term, with criteria terms including (mortality[MeSH Terms]) OR (morbidity[MeSH Terms]) OR (hospitalisation[MeSH Terms]) OR (disability[All Fields])) OR (drug resistance, fungal[MeSH Terms]) OR (prevention and control[MeSH Subheading]) OR (disease transmission, infectious[MeSH Terms]) OR (diagnostic[Title/Abstract]) OR (antifungal agents[MeSH Terms]) OR (epidemiology[MeSH Terms]) OR (surveillance [Title/Abstract]).

The final Web of Science search used was: [(TI=(“Mucorales”) OR AB=(“Mucorales”)) NOT (TS=(plant) OR TS=(wilt) OR TS=(rot) OR TS=(fruit) OR TS=(vegetable) OR TS=(crop))], combined, using AND term, with criteria terms each as topic search, including (mortality) OR (case fatality) OR (morbidity) OR (hospitali\*ation) OR (disability) OR (drug resistance) OR (prevention and control) OR (disease transmission) OR (diagnostic) OR (antifungal agents) OR (epidemiology) OR (surveillance). The symbol \* allows a truncation search for variations of the term (e.g. hospitalisation or hospitalization).

All searchers were limited to 1 January to 23 February 2021.

**Table S1. Risk of Bias Assessment by Domain.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Overall risk** | **Domains assessed** | | | | | |
| **Selection of participants** | **Confounding variables** | **Measurement of exposure** | **Blinding of outcome assessments** | **Incomplete outcome data** | **Selective outcome reporting** |
| Alastruey-Izquierdo *et al*.[91] | 2018 | High | High | High | High | Unclear | High | High |
| Arendrup *et al*.[92] | 2015 | High | High | High | High | High | Unclear | Unclear |
| Bonifaz *et al*.[23] | 2014 | High | Unclear | High | Unclear | Unclear | High | Unclear |
| Bonifaz *et al*.[32] | 2021 | High | High | High | Low | Unclear | Low | Low |
| Bonifaz *et al*.[35] | 2021 | High | Unclear | High | Low | High | High | High |
| Caramalho *et al*.[30] | 2015 | High | High | High | High | High | High | High |
| Chakrabarti *et al*.[24] | 2019 | High | Unclear | High | Low | Low | Unclear | Low |
| Chowdhary *et al*.[29] | 2014 | High | High | High | High | NA | High | Unclear |
| Dolatabadi *et al*.[33] | 2018 | High | High | High | Low | NA | High | High |
| Espinel-Ingroff e*t al.*[49] | 2015 | High | Low | High | Low | Unclear | Unclear | Low |
| Kontoyiannis *et al*.[14] | 2016 | High | Low | High | High | Low | Unclear | Low |
| Lee *et al*.[22] | 2020 | High | Low | High | Low | Unclear | Unclear | Low |
| Legrand *et al*. [20] | 2016 | High | Low | High | Low | Low | Unclear | Unclear |
| Manesh *et al*.[21] | 2019 | High | Low | Low | High | Unclear | Low | Low |
| Marty *et al*.[36] | 2016 | Low | Low | Low | Low | Low | Low | Low |
| Millon *et al*.[34] | 2016 | High | Unclear | High | Unclear | Low | High | Low |
| Ozenci *et al*.[93] | 2019 | High | Low | High | Unclear | Low | High | Low |
| Pana *et al*.[31] | 2016 | High | High | Low | Low | Low | Low | Low |
|  |  |  |  |  |  |  |  |  |
| Patel *et al*.[26] | 2020 | High | High | Low | Low | Low | Unclear | Low |
| Pfaller *et al*.[27] | 2018 | High | High | High | High | High | High | Unclear |
| Prakash *et al*.[6] | 2019 | High | High | Low | Low | Low | Low | Low |
| Salmanton-Garcia *et al*.[25] | 2020 | High | High | High | Unclear | Unclear | Unclear | High |
| Van den Nest *et al*.[15] | 2021 | High | High | High | Low | Unclear | Unclear | Low |
| Wagner *et al*.[28] | 2019 | High | High | High | High | Unclear | Unclear | Low |

NA: not applicable.

**Table S2. Studies reporting on drug susceptibility for Mucorales.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Study design** | **Study design** | **Study period** | **Country** | **Level of care** | **Fungal pathogen**  **(n of isolates)** | **Population description** | **Number of patients** | **Samples collected from**  **(n of isolates)** |
| Arendrup *et al*.[92] | 2015 | Antifungal susceptibility study | Multi-center | 1998-2014 | Denmark | Not stated | *Lichtheimia corymbifera*:  *n* = 12 *Lichtheimia ramosa*:  *n* = 5 *Mucor circinelloides*: Group 1: *n* = 5 Group 2: *n* = 9 *Rhizomucor pusillus*:  *n* = 9 *Rhizopus microspores*:  *n* = 26 *Rhizopus oryzae*:  *n* = 6 | Not stated | Not stated | Not stated |
| Caramalho *et al*.[30] | 2015 | Antifungal susceptibility study | Multi-center | 2008-2014 | Austria The Netherlands | Tertiary | *Mucorales*:  *n* = 169 | Not stated | Not stated | Not stated |
| Chowdhary *et al*.[29] | 2014 | Antifungal susceptibility study | Multi-center | 2004-2013 | India | Tertiary | *Mucorales* consisting of:  *Rhizopus arrhizus var. delemar*:  *n* = 25 *Rhizopus arrhizus var. arrhizus*: *n* = 15 *Rhizopus microspores*:  *n* = 17 *Syncephalastrum racemosum*:  *n* = 11 Other:  *n* = 12 | Not stated | 71 | Pulmonary  *n* = 39 Rhino-cerebral *n* = 15 Cutaneous  *n* =13 Disseminated  *n* = 4 |
| Espinel-Ingroff *et al*.[49] | 2015 | Antifungal susceptibility study | Multi-center | Not stated | USA India Argentina Canada Mexico Spain Australia Austria The Netherlands Italy | Tertiary | *Apophysomyces variabilis*: *n* = 10 *Cunninghamella bertholletiae*:  *n* = 32 *Lichtheimia corymbifera*:  *n* = 136 *Mucor circinelloides*:  *n* = 123 *Mucor indicus*:  *n* = 10 *Mucor ramosissimus*:  *n* = 19 *Rhizopus arrhizus*:  *n* = 257 *Rhizomucor pusillus*:  *n* = 33 *Rhizopus microspores*:  *n* = 146 *Syncephalastrum racemosum*:  *n* = 35 | Patients with rhinocerebral, pulmonary, skin, bone, cerebral and abdominal mucormycosis | Not stated | Nose Palate Lungs |
| Pfaller *et al*.[27] | 2018 | Antifungal susceptibility surveillance study | Multi-center | 2015-2016 | USA Non-US countries | Not stated | n=292:  *Lichtheimia* spp*. Mucor spp. Rhizomucor pusillus Rhizopus* spp*. Syncephalastrum* spp*.* | Not stated | Not stated | Cerebrospinal fluid Pleural fluid Peritoneal fluid Tissue Abscess Respiratory tract Unspecified |
| Wagner *et al*.[28] | 2019 | Antifungal susceptibility study | Multi-center | Not stated | Germany The Netherlands Spain Belgium | Not stated | *Mucor circinelloides*:  *n* = 14 *Mucor indicus*:  *n* = 10 *Mucor irregularis:*  *n* = 7 *Mucor janssenii:*  *n* = 5 *Mucor lusitanicus:*  *n* = 13 *Mucor velutinosus:*  *n* = 7 *Rhizopus arrhizus:*  *n* = 6 *Rhizopus microsporus*:  *n* = 6 *Lichtheimia corymbifera*:  *n* = 8 Other:  *n* = 17 | Not stated | Not stated | Lungs Deep tissue  Feces Skin and soft tissues Gastric mucosa Muscle Peritoneal dialysis fluid Nails Naso-labial Cornea External auditory meatus Liver Blood  Heart valves |

USA: United States of America; US: United States.

**Table S3. Impact of preventative measures on invasive fungal disease due to Mucorales.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Study design** | **Study design** | **Study period** | **Country** | **Level of care** | **Population description** | **Number of patients** | **Preventative measures** | **Effectiveness** |
| Lee *et al*.[22] | 2020 | Retrospective cohort study | Single-center | Jan 2011- Aug 2018 | South Korea | Tertiary | Adult patients with haematological diseases | 27 | Antifungal prophylaxis Voriconazole (*n* = 3) Posaconazole (*n* = 2) Itraconazole  (*n* = 1) | Break-through infection on antifungal prophylaxis in:  6/26 (23.9%) |
| Chakrabarti *et al*.[24] | 2019 | Prospective cohort study | Multi-center | April 2016-Sept 2017 | India | Tertiary | Adult patients in ICU | 398 | Antifungal prophylaxis  (*n* = 14)  (No details of drugs used) | All (14/14; 100%) developed IMI after a mean of 14.1 days |
| Salmanton-Garcia *et al*.[25] | 2020 | Retrospective review of prospectively collected cases | Multi-center | 1997-2019 | Multiple: Mostly from  India (*n* = 30 [16.1%]), USA  (*n* = 24 [12.9%]), Spain (*n*= 21 [11.3%]), and Germany (*n* = 19 [10.2%]) | Not stated | Adults and children with mucormycosis | 22 | Antifungal prophylaxis  (triazoles *n* = 2), echinocandin *n* = 1) | 3/22 (13.6%) patients had prophylaxis and all 3 had fungal infection whilst on prophylaxis after a median:  109 (IQR: 59–9118) days |

ICU: intensive care unit; IMI: invasive mold infection; USA: United Sates of America; IQR: interquartile ratio.