

1 **Online Supplement:**

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3 **Guideline adherence predicts Survival of Candidemia in Europe: Results from**
4 **the ECMM *Candida* III multinational European Observational Cohort Study**

5
6 Martin Hoenigl, Prof, ^{1,2,3#}, Jon Salmanton-García, PhD,^{4,5}, Matthias Egger, MD,^{1,3}, Jean-Pierre Gangneux,
7 Prof, ⁶, Tihana Bicanic, MD,⁷, Sevtap Arikan-Akdagli, Prof, ⁸, Ana Alastruey-Izquierdo, PhD, ⁹, Nikolai
8 Klimko, Prof, ¹⁰, Aleksandra Barac, MD,¹¹, Volkan Özenci, Prof, ^{12,13}, Eelco F. J. Meijer, MD,^{14,15,1}, Nina
9 Khanna, MD,¹⁷, Matteo Bassetti, Prof, ^{18,19}, Riina Rautemaa-Richardson, MD,^{20,21}, Katrien Lagrou, Prof,
10 ^{22,23}, Kai-Manuel Adam, MD,¹⁶, Emin Halis Akalin, Prof, ²⁴, Murat Akova, Prof, ²⁵, Valentina Arsic
11 Arsenijevic, MD, ²⁶, Avinash Aujayeb, MD, ²⁷, Ola Blennow, MD, ²⁸, Stéphane Bretagne, Prof, ²⁹, François
12 Danion, MD,³⁰, Blandine Denis, MD, ³¹, Nick Alexander de Jonge, MD,³², Guillaume Desoubeaux, Prof, ³³,
13 Lubos Drgona, MD,³⁴, Nurettin Erben, MD,³⁵, Andrea Gori, MD, ^{36,37}, Julio García Rodríguez, PhD ³⁸,
14 Carolina Garcia-Vidal, MD, ³⁹, Daniele Roberto Giacobbe, MD, ^{18,19}, Anna L. Goodman, MD, ⁴⁰, Petr
15 Hamal, MD,⁴¹, Helena Hammarström, MD,⁴², Christina Toscano, MD, ⁴³, Fanny Lanternier, Prof,⁴⁴,
16 Cornelia Lass-Flörl, Prof, ⁴⁵, Deborah E. A. Lockhart, PhD, ^{46,47}, Thomas Longval, MD, ⁴⁸, Laura Loughlin,
17 MD, ⁴⁹, Tadeja Matos, MD, ⁵⁰, Malgorzata Mikulska, Prof, ^{18,19}, Manjusha Narayanan, FRCPath ⁵¹, Sonia
18 Martín-Pérez, MD, ⁵², Juergen Prattes, MD,^{1,2,3,4}, Benedict Rogers, MBChB ⁵³, Laman Rahimli, MD, ^{4,5},
19 Maite Ruiz, PhD,^{54,55}, Emmanuel Roilides, Prof,⁵⁶, Michael Samarkos, Prof, ⁵⁷, Ulrike Scharmann, MD, ⁵⁸,
20 Uluhan Sili, Prof, ⁵⁹, Ogun Resat Sipahi, Prof, ⁶⁰, Alena Sivakova, MD,⁶¹, Joerg Steinmann, Prof, ^{58,62}, Janina
21 Trauth, MD, ⁶³, Ozge Turhan ⁶⁴, Jens Van Praet, MD, ⁶⁵, Antonio Vena, PhD, ^{18,19}, P. Lewis White, Prof, ⁶⁶,
22 Birgit Willinger, Prof, ⁶⁷, Anna Maria Tortorano, PhD, ⁶⁸, Maiken C. Arendrup, Prof,^{69,70,71}, Philipp Koehler,
23 MD,^{4,5,72*}, Oliver A. Cornely, Prof, ^{4,5,72,73**} - on behalf of the ECMM *Candida* III Study Group\$

24 * Shared Senior authorship

25

26

27

28

29 **Affiliations**

30 ¹Division of Infectious Diseases, Medical University of Graz, Graz, Austria

31 ²Biotech Med, Graz

32 ³Translational Medical Mycology Research Unit, ECMM Excellence Center for Medical Mycology, Medical
33 University of Graz, Graz, Austria

34 ⁴University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine,
35 Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical
36 Mycology (ECMM), Cologne, Germany

37 ⁵University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Excellence Cluster on
38 Cellular Stress Responses in Aging-Associated Diseases (CECAD),Cologne, Germany

39 ⁶Univ Rennes, CHU Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail), UMR_S
40 1085, F-35000 Rennes, France

41 ⁷Institute of Infection and Immunity, St George's University of London, London, UK

42 ⁸Hacettepe University Medical School, Department of Medical Microbiology, Ankara, Turkey

43 ⁹Mycology Reference Laboratory, National Centre for Microbiology, Instituto de Salud Carlos III, Madrid, Spain.

44 ¹⁰Department of Clinical Mycology, Allergy and Immunology, North Western State Medical University, St Petersburg,
45 Russia

46 ¹¹ Clinic for Infectious and tropical diseases, University Clinical Center of Serbia, Faculty of Medicine, University of
47 Belgrade, Belgrade, Serbia

48 ¹²Division of Clinical Microbiology, Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden

49 ¹³ Department of Clinical Microbiology, Karolinska University Hospital, Sweden

50 ¹⁴ Canisius Wilhelmina Hospital (CWZ), Medical Microbiology and Infectious Diseases, Nijmegen, the Netherlands

51 ¹⁵ Center of Expertise in Mycology Radboudumc/CWZ, Nijmegen, the Netherlands.

52 ¹⁶ Department of Medical Microbiology, Radboud University Medical Center, Nijmegen, the Netherlands

53 ¹⁷ Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Basel, Basel, Switzerland

54 ¹⁸ Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy

55 ¹⁹ IRCCS Ospedale Policlinico San Martino, Infectious Diseases Unit, Genoa, Italy²⁰ Mycology Reference Centre
56 Manchester and Department of Infectious Diseases, Wythenshawe Hospital, Manchester University NHS Foundation
57 Trust, Manchester, UK

58 ²¹ Division of Evolution, Infection and Genomics, Faculty of Biology, Medicine and Health, University of Manchester,
59 UK

60 ²² Laboratory of Clinical Microbiology, Department of Microbiology, Immunology and Transplantation, KU Leuven,
61 Leuven, Belgium

62 ²³ Department of Laboratory Medicine and National Reference Center for Mycosis,, UZ Leuven, Leuven, Belgium

63 ²⁴ Bursa Uludag University, Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Bursa,
64 Turkey

65 ²⁵ Hacettepe University Medical School Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey

66 ²⁶ Faculty of Medicine University of Belgrade, Institute of Microbiology and Immunology, Medical Mycology
67 Reference Laboratory (MMRL), Belgrade, Institute of Public Health of Vojvodina, Centre for Microbiology - Novi
68 Sad, Serbia

69 ²⁷ Northumbria Healthcare NHS Foundation Trust, Northshields, UK

70 ²⁸ Department of Infectious Diseases, Karolinska University Hospital, Stockholm, Sweden

71 ²⁹ Laboratory of Parasitology and Mycology, Saint Louis University Hospital, Assistance Publique-Hôpitaux de Paris
72 (AP-HP), Paris, France

73 ³⁰ Department of Infectious Diseases, CHU de Strasbourg; Université de Strasbourg, Strasbourg, France

74 ³¹ Department of Infectious Diseases, Hôpital Saint-Louis, Fernand Widal, Lariboisière, Assistance Publique-Hôpitaux
75 de Paris (AP-HP), Paris, France

76 ³² Department of Hematology, Amsterdam University Medical Centers, Amsterdam, the Netherlands

77 ³³ Department of Parasitology-Mycology-Tropical medicine, CHRU de Tours, Tours, France

78 ³⁴Department of Oncohematology, Comenius University and National Cancer Institute, Bratislava, Slovakia

79 ³⁵Eskisehir Osmangazi University, Faculty of Medicine, Department of Infectious Disease and Clinical Microbiology,
80 Eskisehir, Turkey

81 ³⁶Department of Internal Medicine, Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore
82 Policlinico, 20122 Milan, Italy.

83 ³⁷Department of Pathophysiology and Transplantation and Centre for Multidisciplinary Research in Health Science
84 (MACH), University of Milan, 20122 Milan, Italy.

85 ³⁸Microbiology Department, La Paz University Hospital, Madrid, Spain

86 ³⁹ Department of Infectious Diseases, Hospital Clinic de Barcelona, Barcelona, Spain.

87 ⁴⁰Department of Infection, Guy's and St Thomas' NHS Foundation Trust) but if space/capacity please add a secondary
88 one- which is MRC Clinical Trials Unit at University College London

89 ⁴¹ Department of Microbiology, Faculty of Medicine and Dentistry, Palacky University Olomouc, Olomouc, Czech
90 Republic

91 ⁴² Department of Infectious Diseases, Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg,
92 Gothenburg, Sweden

93 ⁴³ Laboratory of Clinical Microbiology and Molecular Biology, Centro Hospitalar de Lisboa Ocidental, Lisboa,
94 Portugal

95 ⁴⁴ Paris Cité Université, Necker Hospital, APHP, Paris, France

96 ⁴⁵Institute of Hygiene and Medical Microbiology Innsbruck Medical University, Innsbruck Medical University,
97 Excellence Center for Medical Mycology (ECMM), Innsbruck, Austria

98 ⁴⁶ Department of Medical Microbiology, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN,, United
99 Kingdom

100 ⁴⁷Institute of Medical Sciences, School of Medicine Medical Sciences & Nutrition, University of Aberdeen, Aberdeen
101 AB25 2ZD, United Kingdom

102 ⁴⁸ Centre Hospitalier de Versailles, Hématologie, Le Chesnay, France

103 ⁴⁹Belfast Health and Social Care Trust, Belfast, United Kingdom

104 ⁵⁰Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

105 ⁵¹Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom

- 106 ⁵² Hospital Nuestra Señora de Sonsoles, Ávila, Spain
- 107 ⁵³ University Hospitals of Leicester NHS Trust, Department of Clinical Microbiology, Leicester, United Kingdom
- 108 ⁵⁴ Unit of Infectious Diseases and Microbiology, Institute of Biomedicine of Seville, University Hospital Virgen del
109 Rocio, Seville, Spain
- 110 ⁵⁵ Centro de Investigación Biomédica en Red de Enfermedades Infecciosas, Madrid, Spain.
- 111 ⁵⁶ Hippokration General Hospital, Infectious Diseases Department, Medical School, Aristotle University of
112 Thessaloniki, Thessaloniki, Greece
- 113 ⁵⁷ 1st Department of Medicine, Laikon General Hospital, Medical School, National & Kapodistrian University of
114 Athens, Greece
- 115 ⁵⁸ Institute of Medical Microbiology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany
- 116 ⁵⁹ Department of Infectious Diseases and Clinical Microbiology, School of Medicine, Marmara University, Istanbul,
117 Turkey
- 118 ⁶⁰ Ege University Medical School Department of Infectious Diseases and Clinical Microbiology, Izmir, Turkey
- 119 ⁶¹ Department of Microbiology of St. Anne's Faculty Hospital and Faculty of Medicine, Masaryk University, Brno,
120 Czech Republic⁶² Institute for Clinical Hygiene, Medical Microbiology and Infectiology, Paracelsus Medical
121 University, Klinikum Nürnberg, Nuremberg, Germany
- 122 ⁶³ Department of Medicine II, Section of Infectious Diseases, Justus-Liebig-University Giessen, Giessen, Germany
- 123 ⁶⁴ Akdeniz University, Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Antalya,
124 Turkey
- 125 ⁶⁵ AZ Sint-Jan Brugge Oostende AV, Nephrology and Infectious Diseases, Brugge, Belgium
- 126 ⁶⁶ Public Health Wales, Microbiology Cardiff and Cardiff University, School of Medicine, Cardiff, United Kingdom
- 127 ⁶⁷ Division of Clinical Microbiology, Department of Laboratory Medicine, Medical University of Vienna, Vienna,
128 Austria
- 129 ⁶⁸ Università degli Studi di Milano, Milano, Italy
- 130 ⁶⁹ Unit of Mycology, Statens Serum Institut, Copenhagen, Denmark
- 131 ⁷⁰ Department of Clinical Microbiology, Rigshospitalet, Copenhagen, Denmark
- 132 ⁷¹ Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

133 ⁷² German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Cologne, Germany

134 ⁷³ University of Cologne, Faculty of Medicine and University Hospital Cologne, Clinical Trials Centre Cologne (ZKS
135 Köln), Cologne, Germany

136

137 **§ ECMM *Candida* III Study Group contributors:**

138 Mario Tumbarello¹, Alida Fe Talento², Alba C Ruiz³, Zdenek Racil⁴, Igor Stoma⁵, María Calbacho⁶, Eric

139 Van Wijngaerden⁷, Júlia Henriques⁸, Harriett Jordan⁹, Valentina Ferroni¹⁰, Ozlem Koyuncu Ozyurt¹¹,

140 Christopher Milacek¹², Robert Krause¹³, Christoph Zurl¹³, Matthijs Backx¹⁴, Ang Li¹⁵, Raphael Seufert¹⁶,

141 Rok Tomazin¹⁷, Yael Blankenheim^{18,19}, Julio Dávila-Valls²⁰, Paloma García-Clemente²¹, Tomas

142 Freiburger²², Jochem Buil²³, Jacques F. Meis²⁴, Deniz Akyol²⁵, Hélène Guegan²⁶, Clare Logan²⁷

143 Affiliations

144 ¹Fondazione Policlinico A. Gemelli IRCCS, Rome, Italy

145 ²Beaumont Hospital Dublin – Dublin, Ireland

146 ³University and Polytechnic La Fe Hospital, Valencia, Spain⁴ Institut of Hematology and Blood Transfuzion, Prague,
147 Czech Republic

148 ⁵Minsk Scintifical and Practical Center of Surgery, Transplantology and Hematology; Gome State University, Minsk,
149 Belarus

150 ⁶Hospital 12 Octubre, Hematology, Madrid, Spain

151 ⁷Department of General Internal Medicine, UZ Leuven, Leuven, Belgium

152 ⁸Laboratory of Clinical Microbiology and Molecular Biology, Centro Hospitalar de Lisboa Ocidental, Lisboa, Portugal

153 ⁹Department of Infection, Guy's and St Thomas' NHS Foundation Trust, St Thomas Hospital, Westminster Bridge,
154 London, United Kingdom

155 ¹⁰Department of Internal Medicine Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

156 ¹¹Akdeniz University, Faculty of Medicine, Department of Medical Microbiology, Antalya, Turkey

157 ¹²Department of Internal Medicine II, Division of Pulmonology, Medical University of Vienna, Vienna, Austria

- 158 ¹³Division of Infectious Diseases, Medical University of Graz, Graz, Austria
- 159 ¹⁴Public Health Wales, Microbiology, Cardiff, United Kingdom
- 160 ¹⁵Newcastle Hospitals, Newcastle Upon Tyne, United Kingdom
- 161 ¹⁶ Institute for Clinical Hygiene, Medical Microbiology and Infectiology, Paracelsus Medical University, Klinikum
162 Nürnberg, Nuremberg, Germany
- 163 ¹⁷ Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia
- 164 ¹⁸University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne; Excellence Cluster on
165 Cellular Stress Responses in Aging-Associated Diseases (CECAD); Cologne, Germany
- 166 ¹⁹University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine,
167 Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical
168 Mycology (ECMM), Cologne, Germany
- 169 ²⁰Hospital Nuestra Señora de Sonsoles, Ávila Spain
- 170 ²¹La Paz University Hospital, Madrid, Spain
- 171 ²²Centre of Cardiovascular Surgery and Transplantation, Brno, and Faculty of Medicine, Masaryk University, Brno,
172 Czech Republic
- 173 ²³Department of Medical Microbiology, Radboud University Medical Center, Nijmegen, the Netherlands
- 174 ²⁴Canisius Wilhelmina Hospital (CWZ), Medical Microbiology and Infectious Diseases, Nijmegen, the Netherlands;
175 Center of Expertise in Mycology Radboudumc/CWZ, Nijmegen, the Netherlands.
- 176 ²⁵Ege University Medical School Department of Infectious Diseases and Clinical Microbiology, Izmir, Turkey
- 177 ²⁶ Univ Rennes, CHU Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail), UMR_S
178 1085, F-35000 Rennes, France
- 179 ²⁷Institute of Infection and Immunity, St George's University of London, London, UK

180

181 # Corresponding author:

182 Prof. Dr. Martin Hoenigl, MD,

183 Division of Infectious Diseases, Department of Internal Medicine,

184 Medical University of Graz,
185 Auenbruggerplatz 15, 8036-Graz, Austria
186 Email: hoeniglmartin@gmail.com

187 Phone: +4331638531425

188

189 Alternate Corresponding author:

190 Prof. Dr. Oliver A. Cornely

191 University of Cologne, Faculty of Medicine and University Hospital Cologne, Translational Research,
192 Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), and
193 University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal
194 Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and
195 Excellence Center for Medical Mycology (ECMM), Cologne, Germany

196 Herderstraße 52-54

197 50931 Cologne, Germany

198 Phone: +49 221 478 88795| Fax: +49 221 478 1421445

199 E-mail: oliver.cornely@uk-koeln.de

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205 **Supplemental Table 1.** Patient Characteristics and distribution of *Candida* species in the overall study
 206 cohort, as well as for survivors and non-survivors at end of follow up (p-values calculated using chi-square
 207 or Mann Whitney U test as appropriate).

	Study Cohort (N=632) (%)	Survivors (N=331)#	Non-survivors (N=286)#	p-value
Age, median (IQR), y	65 (53-73)	61 (51-71)	65 (55-75)	<0.001
Sex – no. (%)				
Male	368 (58%)	189 (57%)	172 (60%)	n.s.
Country				<0.001
UK	95 (15%)	48 (15%)	47 (16%)	
Germany	73 (12%)	41 (12%)	32 (11%)	
France	73 (12%)	30 (9%)	41 (14%)	
Turkey	66 (10%)	28 (8%)	38 (13%)	
Spain	47 (7%)	23 (7%)	24 (8%)	
Russia	35 (6%)	16 (5%)	19 (7%)	
Austria	30 (5%)	18 (5%)	12 (4%)	
Italy	29 (5%)	18 (5%)	11 (4%)	
Serbia	29 (5%)	18 (5%)	-	
Netherlands	27 (4%)	19 (6%)	8 (3%)	
Czech Republic	23 (4%)	10 (3%)	13 (5%)	
Belgium	20 (3%)	12 (4%)	8 (3%)	
Sweden	20 (3%)	9 (3%)	10 (3%)	
Greece	18 (3%)	11 (3%)	7 (2%)	
Portugal	10 (2%)	6 (2%)	4 (1%)	
Switzerland	10 (2%)	10 (3%)	0	
Slovenia	10 (2%)	6 (2%)	4 (1%)	
Slovakia	10 (2%)	4 (1%)	6 (2%)	

Ireland	4 (1%)	2 (1%)	2 (1%)	
Belarus	2 (0.3%)	2 (1%)	0	
Risk factors for IC				
SOT	14 (2%)	8 (2%)	6 (2%)	n.s.
BMI \geq 30	104 (16%)	57 (17%)	47 (16%)	n.s.
Diabetes mellitus	139 (22%)	69 (21%)	68 (24%)	n.s.
Prosthetic valves/ other foreign body	78 (12%)	40 (12%)	38 (13%)	n.s.
Total parenteral nutrition	136 (22%)	76 (23%)	59 (21%)	n.s.
Major surgery	164 (26%)	92 (28%)	72 (25%)	n.s.
ICU	234 (37%)	98 (30%)	135 (47%)	<0.001
Mechanical ventilation	151/517 (29%)	64/271 (24%)	87/246 (35%)	0.003
ECMO	15 (2%)	7 (2%)	8 (3%)	n.s.
Hematological/Oncological malignancy	247 (39%)	124 (37%)	121 (42%)	n.s.
Causative <i>Candida</i> species*				n.s.
<i>C. albicans</i>	287/621 (46%)	156/323 (48%)	123/284 (43%)	
<i>C. glabrata</i>	133/621 (21%)	73/323 (23%)	58/284 (20%)	
<i>C. parapsilosis</i>	83/621 (13%)	42/323 (13%)	41/284 (14%)	
<i>C. tropicalis</i>	46/621 (7%)	15/323 (5%)	29/284 (10%)	
<i>C. krusei</i>	16/621 (3%)	8/323 (2%)	6/284 (2%)	
<i>C. auris</i>	16/621 (3%)	7/323 (2%)	9/284 (3%)	
<i>C. dubliniensis</i>	10/621 (2%)	7/323 (2%)	3/284 (1%)	
<i>C. lusitaniae</i>	6/621(1%)	3/323 (1%)	3/284 (1%)	
<i>C. kefyr</i>	5/621 (1%)	1/323 (0.3%)	4/284 (1%)	
<i>C. guilliermondii</i>	6/621 (1%)	0	6/284 (2%)	

<i>Others</i>	11/621 (2%)	8/323 (2%)	3/284 (1%)	
Not specified	13/621 (6%)	6/323 (6%)	7/284 (6%)	
<i>C. auris</i> and other emerging <i>Candida</i> spp.	49/621 (8%)	22/323 (7%)	27/284 (10%)	n.s.
Clinical course and outcome				
CRBSI	130 (21%)	69 (21%)	60 (21%)	n.s.
Charlson Comorbidity Index, median (IQR)	5 (3-8)	5 (3-7)	6 (4-8)	<0.001
Complications “				
Cardiac involvement	25/224 (11%)	12/147 (8%)	13/76 (17%)	0.045
Eye involvement	19/169 (11%)	13/129 (10%)	6/38 (16%)	n.s.
Mixed fungal infections §	37/621 (6%)	16/323 (5%)	21/284 (7%)	n.s.
ID/Microbiology Treatment Consultation	502/620 (81%)	277/328 (84%)	214/280 (76%)	0.012
ID consultation	317/620 (51%)	177/328 (54%)	144 /280 (51%)	n.s.
Microbiology consultation	185/620 (30%)	100/328 (30%)	74/280 (26%)	n.s.
Start Echinocandin	353 (56%)	205 (62%)	148 (52%)	0.011
Stepdown Fluconazole	186 (29%)	136 (41%)	50 (17%)	<0.001
Hospital Stay prolonged for parenteral antifungal therapy only	100/631 (16%)	72 (22%)	19 (7%)	<0.001
EQUAL <i>Candida</i> scores relative to max (median, IQR)	0.68 (0.50-0.84)	0.77 (0.63-0.89)	0.58 (0.41-0.77)	<0.001
Overall mortality	286/617 (46%)		286/286 (100%)	
Death attributable to IC according to investigators	77/209 (37%)	-	77/209 (37%)	-

Abbreviations: *IC* = invasive candidiasis; *SOT* = solid organ transplantation; *BMI* = body mass index; *ICU* = intensive care unit; *ECMO* = extracorporeal membrane oxygenation; *CRBSI* = catheter related bloodstream infection; *ID* = Infectious Diseases; *IQR* = interquartile range; *n.s.* = non-significant

*Species not reported in 11 cases; in 12 cases species identification not done; 10 had mixed *Candida* infections (7 with 2 *Candida* spp., 1 with 3 *Candida* spp.); Others include: *Candida norvegensis* (n=1), *Candida digboensis* (n=1), *Candida rugosa* (n=3), *Candida pelliculosa* (n=2), *Candida inconspicua* (n=2), and *Candida famata* (n=2)

“Echocardiography performed in 224 patients; Ophthalmoscopy performed in 169 patients

Survival status unknown for 15/632

\$ Included 10 mixed *Candida* infections (5 *C. albicans*/*C. glabrata*, each 1 *C. albicans*/*C. parapsilosis*, *C. glabrata*/*C. tropicalis*, *C. guilliermondii*/*C. famata*, *C. inconspicua*/*C. norvegensis*, and *C. auris*/*C. tropicalis*/*C. parapsilosis*)

209 **Supplemental Figure 1.** EQUAL Candida Score Card (left) and EQUAL Candida Scores, EQUAL
 210 Candida Score variables and demographic data in survivors and non-survivors who were diagnosed >7
 211 days after candidemia diagnosis (P-values calculated using chi-square or Mann-Whitney U test).

EQUAL Candida Score 2018^{1,2}

Category	Variable	Points
Diagnosis	Initial blood culture (40mL) ^{3,4}	3
	Species identification ^{3,4}	3
	Susceptibility testing ^{3,4}	2
	Echocardiography ^{3,5}	1
	Ophthalmoscopy ^{5,6}	1
Treatment	Echinocandin treatment ^{3,5}	3
	Step down to fluconazole depending on susceptibility result ^{3,5}	2
	Treatment for 14 days after first negative follow-up culture ^{3,5}	2
	CVC carriers*: CVC removal ^{3,5,7} ≤ 24 hours from diagnosis > 24 < 72 hours from diagnosis	3 2
Follow-Up	Follow-up blood culture (at least one per day until negative) ^{3,5}	2

* CVC carriers receive extra points, total score thus differs in Non-CVC vs. CVC carriers

Variable (%)	Survivors hospitalized > 7 days after candidemia diagnosis (n=315)	Fatalities hospitalized > 7 days after candidemia diagnosis (n=155)	P-value
Age	61 (IQR 50-71)	65 (IQR 53-73)	0.076
Treatment consultation by ID/Microbiology service	266/315 (84)	127/155 (82)	n.s.
CVC	227/315 (72)	125/155 (81)	0.044
EQUAL Candida Score (absolute point value)	17 (IQR 1-19)	15 (IQR 11-18)	<0.001
EQUAL Candida Score (points normalized to max points)	0.76 (95%CI 0.74-0.78) (IQR 0.64-0.91)	0.68 (95%CI 0.65-0.71) (IQR 0.55-0.82)	<0.001
Initial blood culture (40mL)	303/315 (96)	143/155 (92)	0.069
Species identification	309/315 (98)	146/155 (94)	0.046
Susceptibility testing	289/315 (92)	137/155 (88)	n.s.
Echocardiography	176/315 (56)	66/155 (43)	0.007
Ophthalmoscopy	162/315 (51)	53/155 (34)	<0.001
Start with Echinocandin	205/315 (65)	101/155 (65)	n.s.
Stepdown to Fluconazole	135/315 (43)	39/155 (25)	<0.001
Treatment 14 days after first negative blood culture	239/315 (76)	79/155 (51)	<0.001
CVC removal ≤ 24 hours	130/315 (41)	61/155 (39)	n.s.
CVC removal > 24 and < 72 hours	43/315 (14)	27/155 (17)	n.s.
Daily follow-up blood culture until negative	233/315 (74)	104/155 (67)	0.120



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