

<https://helda.helsinki.fi>

---

## Management of anaphylaxis due to COVID-19 vaccines in the elderly

Bousquet, Jean

2021-10

---

Bousquet, J, Agache, I, Blain, H, Jutel, M, Ventura, M T, Worm, M, Del Giacco, S, Benetos, A, Bilo, B M, Czarlewski, W, Abdul Latiff, A H, Al-Ahmad, M, Angier, E, Annesi-Maesano, I, Atanaskovic-Markovic, M, Bachert, C, Barbaud, A, Bedbrook, A, Bennoor, K S, Berghea, E C, Bindslev-Jensen, C, Bonini, S, Bosnic-Anticevich, S, Brockow, K, Brussino, L, Camargos, P, Canonica, G W, Cardona, V, Carreiro-Martins, P, Carriazo, A, Casale, T, Caubet, J-C, Cecchi, L, Cherubini, A, Christoff, G, Chu, D K, Cruz, A A, Dokic, D, El-Gamal, Y, Ebisawa, M, Eberlein, B, Farrell, J, Fernandez-Rivas, M, Fokkens, W J, Fonseca, J A, Gao, Y, Gavazzi, G, Gawlik, R, Gelincik, A, Gemiciglu, B, Gotua, M, Guerin, O, Haahtela, T, Hoffmann-Sommergruber, K, Hoffmann, H J, Hofmann, M, Hrubisko, M, Illario, M, Irani, C, Ispayeva, Z, Ivancevich, J C, Julge, K, Kaidashev, I, Khaitov, M, Knol, E, Kraxner, H, Kuna, P, Kvedariene, V, Lauerma, A, Le, L T T, Le Moing, V, Levin, M, Louis, R, Lourenco, O, Mahler, V, Martin, F C, Matucci, A, Milenkovic, B, Miot, S, Montella, E, Morais-Almeida, M, Mortz, C G, Mullol, J, Namazova-Baranova, L, Neffen, H, Nekam, K, Niedozytko, M, Odemyr, M, O'Hehir, R E, Okamoto, Y, Ollert, M, Palomares, O, Papadopoulos, N G, Panzner, P, Passalacqua, G, Patella, V, Petrovic, M, Pfaar, O, Pham-Thi, N, Plavec, D, Popov, T A, Recto, M T, Regateiro, F S, Reynes, J, Roller-Winsberger, R E, Rolland, Y, Romano, A, Rondon, C, Rottem, M, Rouadi, P W, Salles, N, Samolinski, B, Santos, A F, Sarquis, F, Sastre, J, M. G. A. Schols, J, Scichilone, N, Sediva, A, Shamji, M H, Sheikh, A, Skypala, I, Smolinska, S, Sokolowska, M, Sousa-Pinto, B, Sova, M, Stelmach, R, Sturm, G, Suppli Ulrik, C, Todo-Bom, A M, Toppila-Salmi, S, Tsiligianni, I, Torres, M, Untersmayr, E, Urrutia Pereira, M, Valiulis, A, Vitte, J, Vultaggio, A, Wallace, D, Walusiak-Skorupa, J, Wang, D-Y, Wasserman, S, Yorgancioglu, A, Yusuf, O M, Zernotti, M, Zidarn, M, Chivato, T, Akdis, C A, Zuberbier, T & Klimek, L 2021, ' Management of anaphylaxis due to COVID-19 vaccines in the elderly ', *Allergy : European journal of allergy and clinical immunology*, vol. 76, no. 10, pp. 2952-2964. <https://doi.org/10.1111/all.14838>

---

<http://hdl.handle.net/10138/342322>

<https://doi.org/10.1111/all.14838>

---

acceptedVersion

---

PROF. JEAN BOUSQUET (Orcid ID : 0000-0002-4061-4766)  
PROF. IOANA AGACHE (Orcid ID : 0000-0001-7994-364X)  
PROF. MARGITTA WORM (Orcid ID : 0000-0002-3449-1245)  
DR. MONA AL-AHMAD (Orcid ID : 0000-0003-3720-7032)  
DR. ISABELLA ANNESI-MAESANO (Orcid ID : 0000-0002-6340-9300)  
PROF. MARINA ATANASKOVIĆ-MARKOVIĆ (Orcid ID : 0000-0003-1354-6072)  
PROF. CLAUS BACHERT (Orcid ID : 0000-0003-4742-1665)  
PROF. SERGIO BONINI (Orcid ID : 0000-0003-0079-3031)  
PROF. KNUT BROCKOW (Orcid ID : 0000-0002-2775-3681)  
PROF. GIORGIO WALTER CANONICA (Orcid ID : 0000-0001-8467-2557)  
DR. VICTORIA CARDONA (Orcid ID : 0000-0003-2197-9767)  
PROF. PEDRO MARTINS (Orcid ID : 0000-0002-4129-133X)  
DR. JEAN-CHRISTOPH CAUBET (Orcid ID : 0000-0001-5006-5724)  
DR. LORENZO CECCHI (Orcid ID : 0000-0002-0658-2449)  
PROF. ALVARO A CRUZ (Orcid ID : 0000-0002-7403-3871)  
PROF. MOTOHIRO EBISAWA (Orcid ID : 0000-0003-4117-558X)  
PROF. ASLI GELINCIK (Orcid ID : 0000-0002-3524-9952)  
PROF. MAIA GOTUA (Orcid ID : 0000-0003-2497-4128)  
DR. TARI HAAHTELA (Orcid ID : 0000-0003-4757-2156)  
DR. MUSA KHAITOV (Orcid ID : 0000-0003-4961-9640)  
DR. MICHAEL LEVIN (Orcid ID : 0000-0003-2439-7981)  
PROF. OLGA LOURENÇO (Orcid ID : 0000-0002-8401-5976)  
DR. MÁRIO MORAIS-ALMEIDA (Orcid ID : 0000-0003-1837-2980)  
DR. CHARLOTTE G. MORTZ (Orcid ID : 0000-0001-8710-0829)  
PROF. MAREK NIEDOSZYTKO (Orcid ID : 0000-0003-1089-1911)  
PROF. ROBYN O'HEHIR (Orcid ID : 0000-0002-3489-7595)  
DR. OSCAR PALOMARES (Orcid ID : 0000-0003-4516-0369)  
DR. NIKOLAOS G PAPADOPOULOS (Orcid ID : 0000-0002-4448-3468)  
PROF. PETR PANZNER (Orcid ID : 0000-0002-1291-450X)

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/all.14838](https://doi.org/10.1111/all.14838)

This article is protected by copyright. All rights reserved

PROF. GIOVANNI PASSALACQUA (Orcid ID : 0000-0002-5139-3604)

DR. VINCENZO PATELLA (Orcid ID : 0000-0001-5640-6446)

PROF. OLIVER PFAAR (Orcid ID : 0000-0003-4374-9639)

DR. CARMEN RONDON (Orcid ID : 0000-0003-0976-3402)

DR. PHILIP ROUADI (Orcid ID : 0000-0002-5365-9568)

DR. ALEXANDRA SANTOS (Orcid ID : 0000-0002-7805-1436)

PROF. JOAQUIN SASTRE (Orcid ID : 0000-0003-4689-6837)

DR. MOHAMED H SHAMJI (Orcid ID : 0000-0003-3425-3463)

DR. ISABEL SKYPALA (Orcid ID : 0000-0003-3629-4293)

DR. SANNA TOPPILA-SALMI (Orcid ID : 0000-0003-0890-6686)

PROF. MARÍA JOSÉ TORRES (Orcid ID : 0000-0001-5228-471X)

DR. EVA UNTERSMAJR (Orcid ID : 0000-0002-1963-499X)

DR. JOANA VITTE (Orcid ID : 0000-0002-3344-9408)

DR. ALESSANDRA VULTAGGIO (Orcid ID : 0000-0002-8775-9217)

PROF. CEZMI AKDIS (Orcid ID : 0000-0001-8020-019X)

PROF. TORSTEN ZUBERBIER (Orcid ID : 0000-0002-1466-8875)

DR. MILENA SOKOLOWSKA (Orcid ID : 0000-0001-9710-6685)

Article type : EAACI Position Paper

Manuscript Acceptance Date: 29-Mar-2021

## **Management of anaphylaxis due to COVID-19 vaccines in the elderly**

Jean Bousquet,<sup>12,3</sup>Ioana Agache,<sup>4</sup> Hubert Blain,<sup>5</sup> Marek Jutel<sup>6</sup>, Maria Teresa Ventura,<sup>7</sup> Margitta Worm,<sup>1</sup> Stefano Del Giacco,<sup>8</sup> Athanasios Benetos,<sup>9</sup> M. Beatrice Bilo,<sup>10</sup> Wienczyslawa Czarlewski<sup>11</sup>, Amir Hamzah Abdul Latiff<sup>12</sup>, Mona Al-Ahmad,<sup>13</sup> Elizabeth Angier,<sup>14</sup> Isabella Annesi-Maesano,<sup>15</sup> Marina Atanaskovic-Markovic,<sup>16</sup> Claus Bachert,<sup>17</sup> Annick Barbaud,<sup>18</sup> Anna Bedbrook,<sup>12</sup> Kazi S Bennoor,<sup>19</sup> Elena Camelia Berghea,<sup>20</sup> Carsten Bindselev-Jensen,<sup>21</sup> Sergio Bonini,<sup>22</sup> Sinthia Bosnic-Anticevich,<sup>23</sup> Knut Brockow,<sup>24</sup> Luisa Brussino,<sup>25</sup> Paulo

Camargos,<sup>26</sup>G Walter Canonica,<sup>27</sup> Victoria Cardona,<sup>28</sup>Pedro Carreiro-Martins,<sup>29</sup>Ana Carriazo,<sup>30</sup>Thomas Casale,<sup>31</sup>Jean-Christoph Caubet,<sup>32</sup>Lorenzo Cecchi,<sup>33</sup>Antonio Cherubini,<sup>34</sup> George Christoff,<sup>35</sup> Derek K Chu<sup>36</sup> Alvaro A Cruz,<sup>37</sup> DejanDokic,<sup>38</sup>Yehia El-Gamal,<sup>39</sup>MotohiroEbisawa,<sup>40</sup> Bernadette Eberlein,<sup>24</sup> John Farrell,<sup>41</sup> Montserrat Fernandez-Rivas,<sup>42</sup>Wytske J Fokkens,<sup>43</sup>Joao A Fonseca,<sup>44</sup>Yadong Gao,<sup>45</sup>GaëtanGavazzi,<sup>46</sup> RadolslawGawlik,<sup>47</sup>AsliGelincik,<sup>48</sup>BilunGemicioğlu,<sup>49</sup> Maia Gotua,<sup>50</sup>Olivier Guérin,<sup>51</sup>TariHaahtela,<sup>52</sup>Karin Hoffmann-Sommergruber,<sup>53</sup> Hans Jürgen Hoffmann,<sup>54</sup>MajaHofmann,<sup>1</sup> Martin Hrubisko,<sup>55</sup>Maddalenallario,<sup>56</sup> Carla Irani,<sup>57</sup>ZhanatIspayeva,<sup>58</sup>Juan Carlos Ivancevich,<sup>59</sup> Kaja Julge,<sup>60</sup>Igor Kaidashev,<sup>61</sup>Musa Khaitov,<sup>62</sup> Edward Knol,<sup>63</sup> Helga Kraxner,<sup>64</sup> Piotr Kuna,<sup>65</sup>Violeta Kvedariene,<sup>66</sup>Antti Lauerma,<sup>67</sup>Lan TT Le,<sup>68</sup>Vincent Le Moing,<sup>69</sup>Michael Levin,<sup>70</sup> Renaud Louis,<sup>71</sup> Olga Lourenco,<sup>72</sup>Vera Mahler,<sup>73</sup>Finbarr C Martin,<sup>74</sup>Andrea Matucci,<sup>75</sup>Branislava Milenkovic,<sup>76</sup>Stéphanie Miot,<sup>5</sup> Emma Montella,<sup>77</sup>Mario Morais-Almeida,<sup>78</sup>Charlotte G Mortz,<sup>79</sup> Joaquim Mulla,<sup>80</sup>Leyla Namazova-Baranova,<sup>81</sup> Hugo Neffen,<sup>82</sup>KristofNekam,<sup>83</sup>Marek Niedozytko,<sup>84</sup>MikaëlaOdemyr<sup>85</sup>, Robyn E O’Hehir,<sup>86</sup>YoshitakaOkamoto,<sup>87</sup>Markus Ollert,<sup>88</sup> Oscar Palomares,<sup>89</sup> Nikolaos G. Papadopoulos,<sup>90</sup>PetrPanzner,<sup>91</sup>Gianni Passalacqua,<sup>92</sup>Vincenzo Patella,<sup>93</sup>Mirko Petrovic,<sup>94</sup> Oliver Pfaar,<sup>95</sup>Nhân Pham-Thi,<sup>96</sup> Davor Plavec,<sup>97</sup>Todor A Popov,<sup>98</sup>Marysia T Recto,<sup>99</sup>Frederico S Regateiro,<sup>100</sup>Jacques Reynes,<sup>69</sup>Regina E Roller-Winsberger,<sup>101</sup> Yves Rolland,<sup>102</sup> Antonino Romano,<sup>103</sup> Carmen Rondon,<sup>104</sup> Menachem Rottem,<sup>105</sup> Philip W Rouadi,<sup>106</sup> Nathalie Salles,<sup>107</sup>Boleslaw Samolinski,<sup>108</sup>Alexandra F Santos,<sup>109</sup>FaradibaSarquisSerpa,<sup>110</sup> Joaquin Sastre,<sup>111</sup>Jos M.G.A. Schols<sup>112</sup>, Nicola Scichilone,<sup>113</sup>Anna Sediva,<sup>114</sup> Mohamed H. Shamji,<sup>115</sup>Aziz Sheikh<sup>116</sup>, Isabel Skypala,<sup>117</sup> Sylwia Smolinska,<sup>118</sup> Milena Sokolowska,<sup>119</sup> Bernardo Sousa-Pinto,<sup>44</sup>,<sup>141</sup> Milan Sova,<sup>120</sup>Rafael Stelmach,<sup>121</sup>Gunter Sturm,<sup>122</sup> Charlotte Suppli Ulrik,<sup>123</sup> Ana Maria Todo-Bom,<sup>124</sup>SannaToppila-Salmi,<sup>52</sup>Ioanna Tsiligianni,<sup>125</sup>Maria Torres,<sup>126</sup> Eva Untersmayr,<sup>127</sup> Marilyn Urrutia Pereira,<sup>128</sup>Arunas Valiulis,<sup>129</sup>Joana Vitte,<sup>130</sup> Alessandra Vultaggio,<sup>75</sup>Dana Wallace,<sup>131</sup>Jolanta Walusiak-Skorupa,<sup>132</sup> De-Yun Wang,<sup>133</sup> Susan Wasserman,<sup>36</sup>ArzuYorgancioglu,<sup>134</sup> Osman M Yusuf,<sup>135</sup> Mario Zernotti,<sup>136</sup>Mihaela Zidarn,<sup>137</sup>Tomas Chivato,<sup>138</sup>CezmiA Akdis,<sup>139</sup>TorstenZuberbier,<sup>1</sup>Ludger Klimek.<sup>140</sup>

1. Charité, Universitätsmedizin Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Comprehensive Allergy Center, Department of Dermatology and Allergy, Berlin, Germany.
2. University Hospital Montpellier, France.
3. MACVIA-France, Montpellier, France.
4. Faculty of Medicine, Transylvania University, Brasov, Romania.
5. Department of Geriatrics, Montpellier University Hospital, Montpellier, France
6. Department of Clinical Immunology, Wrocław Medical University, Wrocław, and ALL-MED Medical Research Institute, Wrocław, Poland.
7. University of Bari Medical School, Unit of Geriatric Immunoallergology, Bari, Italy.

8. Department of Medical Sciences and Public Health and Unit of Allergy and Clinical Immunology, University Hospital "Duilio Casula", University of Cagliari, Cagliari, Italy.
9. Department of Geriatrics, CHRU de Nancy and Inserm DCAC, Université de Lorraine, Nancy, France.
10. Department of Clinical and Molecular Sciences, Università Politecnica delle Marche – Allergy Unit - Department of Internal Medicine, University Hospital, Ospedali Riuniti di Ancona, Ancona, Italy.
11. Medical Consulting Czarlewski, Levallois, France.
12. Allergy & Immunology Centre, Pantai Hospital, Department of Pediatrics, Universiti Putra Malaysia Teaching Hospital, Kuala Lumpur, Malaysia.
13. Microbiology Department, Faculty of Medicine, Kuwait University and Department of Allergy, Al-Rashed Allergy Center, Kuwait.
14. Primary Care and Population Sciences, University of Southampton, Southampton, UK.
15. Institut Desbrest d'Epidémiologie et Santé Publique (IDESP), INSERM et Université de Montpellier, Montpellier, France.
16. Faculty of Medicine, University Children's Hospital, University of Belgrade, Belgrade, Serbia.
17. Upper Airways Research Laboratory, ENT Dept, Ghent University Hospital, Ghent, Belgium, and Sun Yat-sen University, International Airway Research Center, First Affiliated Hospital Guangzhou, China, and Division of ENT Diseases, CLINTEC, Karolinska Institutet, Stockholm and Department of ENT Diseases, Karolinska University Hospital, Stockholm, Sweden.
18. Division of Service de Dermatologie et Allergologie, Hôpital Tenon, Paris, France & Division of Equipe PEPITES, Sorbonne Université, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France.
19. Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Dhaka, Bangladesh.
20. Allergology and Clinical Immunology, Carol Davila University of Medicine and Pharmacy, Bucharest, and Clinical Emergency Hospital for Children MS Curie, Bucharest, Romania.
21. Department of Dermatology and Allergy Centre, Odense University Hospital, Odense Research Center for Anaphylaxis (ORCA), Odense, Denmark.
22. Institute of Translational Pharmacology, Italian National Research Council, Rome, Italy.
23. Woolcock Institute of Medical Research, University of Sydney and Woolcock Emphysema Centre and Sydney Local Health District, Glebe, NSW, Australia.
24. Department of Dermatology and Allergy Biederstein, School of Medicine, Technical University of Munich, Munich, Germany.
25. Department of Medical Sciences, Allergy and Clinical Immunology Unit, University of Torino & Mauriziano Hospital, Torino, Italy.
26. Federal University of Minas Gerais, Medical School, Department of Pediatrics, Belo Horizonte, Brazil
27. Personalized Medicine Asthma & Allergy Clinic-Humanitas University & Research Hospital, IRCCS-Milano, Italy.

28. Allergy Section, Department of Internal Medicine, Hospital Vall d'Hebron & ARADyAL research network, Barcelona, Spain.
29. Serviço de Imunoalergologia, Hospital de Dona Estefânia, Centro Hospitalar de Lisboa Central, Lisbon, Portugal; CEDOC, Faculdade de Ciências Médicas (FCM), Universidade Nova de Lisboa, Lisbon, Portugal.
30. Regional Ministry of Health of Andalusia, Seville, Spain.
31. Division of Allergy/Immunology, University of South Florida, Tampa, Fla, USA.
32. Pediatric Allergy Unit, Department of Child and Adolescent, Geneva University Hospital, Geneva, Switzerland.
33. SOS Allergology and Clinical Immunology, USL Toscana Centro, Prato, Italy.
34. Geriatria, Accettazione geriatrica e Centro di ricerca per l'invecchiamento, IRCCS INRCA, Ancona, Italy.
35. Medical University, Faculty of Public Health, Sofia.
36. Department of Medicine and Health Research Methods, Evidence & Impact, McMaster University, Hamilton, Ontario, Canada.
37. Fundação ProAR, Federal University of Bahia and GARD/WHO Planning Group, Salvador, Bahia, Brazil.
38. University Clinic of Pulmology and Allergy, Medical Faculty Skopje, Republic of Macedonia.
39. Pediatric Allergy and Immunology Unit, Children's Hospital, Ain Shams University, Cairo, Egypt.
40. Clinical Research Center for Allergy and Rheumatology, NHO Sagamihara National Hospital, Sagamihara, Japan.
41. LANUA International Healthcare Consultancy, Down, UK.
42. Allergy Department Hospital Clínico San Carlos, UCM, IdISSC, Madrid, Spain.
43. Department of Otorhinolaryngology, Academic Medical Centers, AMC, Amsterdam, The Netherland, and EUFOREA, Brussels, Belgium.
44. CINTESIS, Center for Health Technology and Services Research, Faculdade de Medicina, Universidade do Porto, Porto, Portugal ; Allergy Unit, CUF Porto, Porto, Portugal.
45. Department of Allergology, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, China.
46. Service Gériatrie Clinique, Centre Hospitalo-Universitaire Grenoble-Alpes, GREPI (TIMC-IMAG, CNRS 5525), Université Grenoble-Alpes, Grenoble, France.
47. Dept of Internal Medicine, Allergy and Clin Immunology, Silesian University of Medicine, Katowice, Poland.
48. Division of Immunology and Allergic Diseases, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey.
49. Department of Pulmonary Diseases, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey.
50. Center of Allergy and Immunology, Georgian Association of Allergology and Clinical Immunology, Tbilisi, Georgia.
51. Service de Gériatrie, CHRU Nice, France.
52. Skin and Allergy Hospital, Helsinki University Hospital, and University of Helsinki University, Helsinki, Finland.

53. Institute of Pathophysiology and Allergy Research, Center of Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria.
54. Department of Respiratory Diseases and Allergy, Aarhus University Hospital, Aarhus & Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark.
55. Department of Clinical Immunology and Allergy, Oncology Institute of St Elisabeth, Heydukova, Bratislava, Slovakia.
56. Federico II University & Hospital, Department of Public Health and Research and Development Unit Naples, Italy.
57. Department of Internal Medicine and Infectious Diseases, St Joseph University, Hotel Dieu de France Hospital, Beirut, Lebanon.
58. President of Kazakhstan Association of Allergology and Clinical Immunology, Department of Allergology and clinical immunology of the Kazakh National Medical University, Kazakhstan.
59. Servicio de Alergia e Immunologia, Clinica Santa Isabel, Buenos Aires, Argentina.
60. Tartu University Institute of Clinical Medicine, Children's Clinic, Tartu, Estonia.
61. Ukrainina Medical Stomatological Academy, Poltava, Ukraine.
62. National Research Center, Institute of Immunology, Federal Medicobiological Agency, Laboratory of Molecular Immunology, Moscow, Russia.
63. Departments of Immunology and Dermatology/Allergology, University Medical Center Utrecht, The Netherlands.
64. Department of Otorhinolaryngology, Head and Neck Surgery, Semmelweis University, Budapest, Hungary.
65. Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz, Poland.
66. Institute of Biomedical Sciences, Department of Pathology, Faculty of Medicine, Vilnius University and Institute of Clinical Medicine, Clinic of Chest diseases and Allergology, faculty of Medicine, Vilnius University, Vilnius, Lithuania.
67. Department of Dermatology and Allergology, University of Helsinki and Helsinki University, Meilahdentie Helsinki, Finland.
68. University of Medicine and Pharmacy, Hochiminh City, Vietnam.
69. Department of Infectiology, Montpellier University Hospital, France.
70. Division Paediatric Allergology, University of Cape Town, Cape Town, South Africa.
71. Department of Pulmonary Medicine, CHU Sart-Tilman, and GIGA I3 research group, Liege, Belgium.
72. Faculty of Health Sciences and CICS – UBI, Health Sciences Research Centre, University of Beira Interior, Covilhã, Portugal.
73. Paul-Ehrlich-Institut, Langen, Germany.
74. Emeritus Geriatrician and Professor of Medical Gerontology Population Health Sciences I, King's College London, UK.

75. Immunoallergy Unit, Careggi University Hospital, Florence, Italy.
76. Clinic for Pulmonary Diseases, Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, Serbian Association for Asthma and COPD, Belgrade, Serbia
77. Federico II University & Hospital, Department of Public Health and Research and Development Unit, Naples, Italy.
78. Allergy Center, CUF Descobertas Hospital, Lisbon, Portugal
79. Department of Dermatology and Allergy Centre, Odense Research Centre for Anaphylaxis (ORCA), Odense University Hospital, Odense, Denmark.
80. Rhinology Unit & Smell Clinic, ENT Department, Hospital Clínic; Clinical & Experimental Respiratory Immunoallergy, IDIBAPS, CIBERES, University of Barcelona, Spain.
81. Pediatrics and Child Health Research Institute, Central Clinical Hospital of the Russian Academy of Sciences, Russian National Research Medical University, Moscow, Russia.
82. Director of Center of Allergy, Immunology and Respiratory Diseases, Santa Fe, Argentina
83. Hospital of the Hospitaller Brothers in Buda, Budapest, Hungary.
84. Medical University of Gdańsk, Department of Allergology, Gdańsk, Poland
85. EFA European Federation of Allergy and Airways Diseases Patients' Associations, Brussels, Belgium
86. Department of Allergy, Immunology and Respiratory Medicine, Central Clinical School, Monash University, and Alfred Health, Melbourne, Victoria, Australia.
87. Dept of Otorhinolaryngology, Chiba University Hospital, Chiba, Japan.
88. Department of Infection and Immunity, Luxembourg Institute of Health, Esch-sur-Alzette, Luxembourg & Department of Dermatology and Allergy Center, Odense Research Center for Anaphylaxis, Odense University Hospital, University of Southern Denmark, Odense, Denmark.
89. Department of Biochemistry and Molecular Biology, School of Chemistry, Complutense University of Madrid, Madrid, Spain.
90. Allergy Department, 2nd Pediatric Clinic, Athens General Children's Hospital "P&A Kyriakou," University of Athens, Athens, Greece.
91. Department of Immunology and Allergology, Faculty of Medicine and Faculty Hospital in Pilsen, Charles University in Prague, Pilsen, Czech Republic.
92. Allergy and Respiratory Diseases, Ospedale Policlinico San Martino -University of Genoa, Genoa, Italy
93. Division of Allergy and Clinical Immunology, Department of Medicine, Agency of Health ASL Salerno, "Santa Maria della Speranza" Hospital, Battipaglia, Salerno, Italy.
94. Department of Internal Medicine and Paediatrics, Section of Geriatrics, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium.
95. Department of Otorhinolaryngology, Head and Neck Surgery, Section of Rhinology and Allergy, University Hospital Marburg, Philipps-Universität Marburg, Marburg, Germany.
96. Ecole polytechnique Palaiseau, IRBA (Institut de Recherche bio-Médicale des Armées), Bretigny, France.



97. Children's Hospital Srebrnjak, Zagreb, School of Medicine, University J.J. Strossmayer, Osijek, Croatia.
98. University Hospital 'Sv Ivan Rilski"', Sofia, Bulgaria.
99. Asian Hospital And Medical Center, Manilla, Philippines.
100. Allergy and Clinical Immunology Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra and Institute of Immunology, Faculty of Medicine, University of Coimbra, and ICBR - Coimbra Institute for Clinical and Biomedical Research, CIBB, Faculty of Medicine, University of Coimbra, Coimbra, Portugal.
101. Medical University of Graz, Austria.
102. Gérontopôle de Toulouse, INSERM 1027; Toulouse, France.
103. aOasi Research Institute-IRCCS, Troina, Italy; bFondazione Mediterranea GB Morgagni, Catania, Italy.
104. Allergy Unit, Hospital Regional Universitario de Malaga, Malaga, & Allergy Research Group, Instituto de Investigación Biomedica de Malaga-IBIMA and ARADyAL, Malaga, Spain.
105. Division of Allergy Asthma and Clinical Immunology, Emek Medical Center, Afula, and Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.
106. Department of Otolaryngology-Head and Neck Surgery, Eye and Ear University Hospital, Beirut, Lebanon.
107. Société Française de Gériatrie et Gérontologie, Paris, France.
108. Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Poland.
109. Department of Women and Children's Health (Paediatric Allergy), School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London and Peter Gorer Department of Immunobiology, School of Immunology and Microbial Sciences, Faculty of Life Sciences and Medicine, King's College London, and Children's Allergy Service, Evelina London Children's Hospital Guy's and St Thomas' Hospital, London, Asthma UK Centre for Allergic Mechanisms in Asthma, London, UK.
110. Asthma Reference Center - School of Medicine of Santa Casa de Misericórdia of Vitória, Espírito Santo, Brazil.
111. Fundacion Jimenez Diaz, CIBERES, Faculty of Medicine, Autonoma University of Madrid, Spain.
112. Department of Health Services Research and Department of Family Medicine Caphri - Care and Public Health Research Institute, Maastricht University, Maastrich, NL.
113. PROMISE Department, University of Palermo, Palermo, Italy.
114. Department of Immunology, Second Faculty of Medicine, Charles University and Motol University Hospital, Prague, Czech Republic.
115. Immunomodulation and Tolerance Group, Imperial College London, and Allergy and Clinical Immunology, Imperial College London, London, UK.
116. Usher Institute, The University of Edinburgh, Edinburgh, UK.
117. Royal Brompton and Harefield NHS Foundation Trust, London, UK.
118. Department of Clinical Immunology, Wroclaw Medical University, Wroclaw, & "ALL-MED" Medical Research Institute, Wroclaw, Poland.
119. Christine Kühne - Center for Allergy Research and Education (CK-CARE, Davos, Switzerland).
120. Department of Respiratory Medicine, University Hospital Olomouc, Czech Republic.

121. Pulmonary Division, Heart Institute (InCor), Hospital da Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil.
122. Department of Dermatology and Venerology, Medical University of Graz, Graz, Austria Outpatient Allergy Clinic Reumannplatz, Vienna, Austria.
123. Department of Respiratory Medicine, Copenhagen University Hospital-Hvidovre, and Institute of Clinical Medicine, University of Copenhagen, Denmark.
124. Imunoalergologia, Centro Hospitalar Universitário de Coimbra and Faculty of Medicine, University of Coimbra, Portugal.
125. Health Planning Unit, Department of Social Medicine, Faculty of Medicine, University of Crete, Greece and International Primary Care Respiratory Group IPCRG, Aberdeen, Scotland.
126. Allergy Unit, Málaga Regional University Hospital-IBIMA, Málaga, Spain.
127. Institute of Pathophysiology and Allergy Research, Center of Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria.
128. Universidade Federal dos Pampas, Uruguaiiana, Brazil
129. Vilnius University Faculty of Medicine, Institute of Clinical Medicine & Institute of Health Sciences, Vilnius, Lithuania; European Academy of Paediatrics (EAP/UEMS-SP), Brussels, Belgium.
130. Aix-Marseille University, IRD, APHM, MEPHI, Marseille& IHU Méditerranée Infection, Marseille and IDESP, INSERM, University of Montpellier, Montpellier, France.
131. Nova Southeastern University, Fort Lauderdale, Florida, USA.
132. Department of Occupational Diseases and Environmental Health, Nofer Institute of Occupational Medicine, Lodz, Poland.
133. Department of Otolaryngology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore.
134. Department of Pulmonary Diseases, Celal Bayar University, Faculty of Medicine, Manisa, Turkey
135. The Allergy and Asthma Institute, Islamabad, Pakistan.
136. Universidad Católica de Córdoba, Universidad Nacional de Villa María, Villa María, Argentina.
137. University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia.
138. School of Medicine, University CEU San Pablo, Madrid, Spain.
139. Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland.
140. Department of Otolaryngology, Head and Neck Surgery, Universitätsmedizin Mainz, Mainz, and Center for Rhinology and Allergology, Wiesbaden, Germany.
141. MEDCIDS – Department of Community Medicine, Information and Health Decision Sciences; Faculty of Medicine, University of Porto, Portugal

**Short title: COVID-19 vaccine anaphylaxis in older people**

**Address for correspondence**

Professor Jean Bousquet

273 avenue d'Occitanie, 34090 Montpellier, France Tel +33 611 42 88 47, Fax +33 467 41 67 01

jean.bousquet@orange.fr

## Abstract

Older adults, especially men and/or those with diabetes, hypertension and/or obesity, are prone to severe COVID-19. In some countries, older adults, particularly those residing in nursing homes, have been prioritised to receive COVID-19 vaccines due to high risk of death. In very rare instances, the COVID-19 vaccines can induce anaphylaxis, and the management of anaphylaxis in older people should be considered carefully. An ARIA-EAACI-EuGMS (Allergic Rhinitis and its Impact on Asthma, European Academy of Allergy and Clinical Immunology, and European Geriatric Medicine Society) Working Group has proposed some recommendations for older adults receiving the COVID-19 vaccines. Anaphylaxis to COVID-19 vaccines is extremely rare (from 1 per 100,000 to 5 per million injections). Symptoms are similar in younger and older adults but they tend to be more severe in the older patients. Adrenaline is the mainstay treatment and should be readily available. A flowchart is proposed to manage anaphylaxis in the older patients.

**Key words:** COVID-19 vaccines, anaphylaxis, older (adults/people), adrenaline,

## Introduction

Older adults (over 65 years of age),<sup>1,2</sup> especially men and/or those with diabetes,<sup>3</sup> hypertension<sup>4</sup> and/or obesity<sup>5</sup>, are prone to severe COVID-19. Older men have more severe COVID-19 infections than women of the same age.<sup>6-9</sup> Frailty is a risk factor for mortality from COVID-19<sup>10,11</sup>. The population residing in nursing homes generally includes subjects who are both old and suffering from multimorbidity. Residential context increases social contacts in the same setting. A large number of COVID-19-related deaths have been reported in nursing homes<sup>12-16</sup>, and recommendations to control COVID-19 in these settings have been issued.<sup>16-18</sup> Discharge from hospitals to nursing homes also puts residents at risk.

In some countries, older adults, particularly those residing in nursing homes, have been prioritised to receive COVID-19 vaccines due to high risk of death.

There are several peculiarities of the immune response to COVID-19 vaccines in older people. For example, vaccine-induced local and systemic reactogenicity - such as pain, fatigue, headache or fever - was generally lower in older recipients of mRNA-based COVID-19 than in younger ones during the clinical trial phases.

However, in very rare instances, COVID-19 vaccines can induce anaphylaxis<sup>19-21</sup>. Anaphylaxis in older people is not uncommon and is often more severe than in younger adults<sup>22</sup>. Vaccinations are known to cause anaphylaxis, although very rarely.<sup>23,24</sup> The benefit of the vaccination clearly outweighs the risk of severe anaphylaxis reaction to the COVID-19 vaccines, even in older people suffering from severe allergic diseases.

The staff responsible for vaccinating in nursing homes may come from different educational backgrounds and include primary care staff or geriatricians who may not have had much experience in the management of anaphylaxis. Potential rapid evaluation and differential diagnosis of symptoms are therefore important. Moreover, in many countries, the equipment is insufficient in nursing homes (e.g., lack of emergency medication, no possibility to provide IV therapy or infusion).

An ARIA-EAACI-EuGMS (Allergic Rhinitis and its Impact on Asthma, European Academy of Allergy and Clinical Immunology, European Geriatric Medicine Society) Working Group has proposed some recommendations for older adults receiving the COVID-19 vaccines.

### **1- Anaphylaxis to COVID-19 vaccines**

Several adverse reactions are reported for the COVID-19 vaccines. They are classified into very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), very rare ( $< 1/10,000$ ), and not known (cannot be estimated from the available data). Currently, due to lack of sufficient confirmed data, anaphylaxis/hypersensitivity are included under the “not known” category.

Following the approval of the COVID-19 vaccine BNT162b2 (Pfizer-BioNTech), several severe anaphylaxis cases occurred within the first few days of public vaccination.<sup>19,21</sup> A first analysis of the data reported in the Vaccine Adverse Events Reporting System (VAERS, <https://vaers.hhs.gov>) of the United States showed an incidence of 11.1 cases of anaphylaxis per million doses of the COVID-19 vaccine BNT162b2. The VAERS report of January 18, 2021 reports a rate of 5 anaphylaxis per million doses administered for the BNT162b2 and 2.8 per million for the Moderna vaccine.<sup>25</sup> Polyethylene glycol (PEG) contained in PEGylated excipients has been proposed to be an allergenic component of the vaccines.<sup>26</sup> The median age of patients with anaphylaxis was 40 years (range = 27–60 years), and 90% of the reported cases occurred in women<sup>27</sup>. Allergic reactions often, but not always, occurred in people with a previous history of severe allergic reactions, many of them carrying an adrenaline (epinephrine) auto-injector. Moreover, during the clinical trial phases, vaccine-induced local and systemic reactogenicity, such as pain, fatigue, headache or fever, were generally lower in older recipients of the mRNA-based COVID-19 vaccine than in younger ones. Similar reactions occurred with the Moderna vaccine albeit at a lower frequency (around 2.5 per million), but possibly more severe<sup>28</sup>.

The COVID-19 vaccines will be administered to billions of individuals worldwide and there are raised concerns that severe adverse reactions - requiring continuous alertness and careful management - might sometimes occur. With the current information, the European Academy of Allergy and Clinical Immunology (EAACI) stated its position for preliminary recommendations that are to be revised as soon as more data emerge.<sup>21, 27, 29</sup>

## **2- Symptoms of anaphylaxis in older people**

The European Anaphylaxis Registry includes data from 1,123 patients over 65 years of age with anaphylactic reactions. These data are provided by tertiary referral centres specialised in allergology and/or dermatology in Austria, Bulgaria, France, Germany, Italy, Poland, Spain and Switzerland.<sup>30</sup> In the registry, anaphylactic symptoms were similar in younger adults and older people, but their frequency differed: cardiovascular symptoms occurred more frequently in older people (80% compared to 75% in adults). This confirmed previous observations that in patients presenting with anaphylaxis at the Emergency Department, an age of 65 or older was associated with an increased likelihood of cardiovascular symptoms.<sup>31</sup> A major cardiovascular symptom was loss of consciousness (33%), while dizziness and

tachycardia were more prevalent in younger adults. Cardiac arrest occurred in 3% of older persons and in 2% of younger adults. The skin was the most frequently involved organ system. Urticaria and angioedema are two clinical manifestations of anaphylaxis and usually appear before other symptoms. The severity of anaphylactic reactions in older patients without skin symptoms was increased in comparison to younger adults. Gastrointestinal symptoms occurred in a similar proportion in both groups. The respiratory system, especially dyspnoea, was less frequently affected in older persons (63% compared to 70% in younger adults). However, cyanosis, syncope and dizziness are highly predictive of shock development in older people. Severe anaphylactic reactions, including grade III (47%) and grade IV (4%) of the anaphylaxis Ring and Messmer classification,<sup>32</sup> were more prevalent in people aged 65+.

This registry indicates that symptoms are similar in younger/middle-aged adults and older people but that they are more severe in the older age group (Figure 1). Adrenaline was administered in 30% of older patients. Hospitalisation was required in 60%, and 19% of older patients were treated in an intensive care unit (ICU). Significantly more older people as compared to younger and middle-aged adults with grade II and III anaphylaxis needed hospitalisation and ICU care <sup>32</sup> (Figure 1 and Table 1). Considering different triggers of anaphylaxis, higher age has been consistently associated with increased rates of fatal drug anaphylaxis. This may be related to an increased prevalence of drug allergy following an increased drug exposure, and/or to an increased underlying cardiovascular vulnerability.<sup>33</sup>

Anaphylaxis is usually graded according to Ring and Messmer<sup>32</sup> (Table 1), although there are proposals for new grading systems <sup>34,35</sup>. However, WHO and regulatory authorities recommend the use of the Brighton Collaboration Anaphylaxis Working Group for pharmacovigilance registers.<sup>23</sup>

Classification according to the most severe symptom is mandatory.

### **3- Risk factors for severity of anaphylaxis in older people**

#### **a- Comorbidity**

In the European Anaphylaxis Registry, older age (excluding the confounding factor of concomitant cardiovascular or other diseases) and concomitant mastocytosis<sup>38</sup> were the most important predictors for an increased risk of severe anaphylaxis. <sup>30,37,39,40</sup> Hereditary alpha-tryptasemia is another risk factor. Anaphylaxis is more severe and has an increased risk of death in patients with coronary artery disease because both the number of mast cells and the production of their vasoactive mediators are increased in ischaemic cardiomyopathy. In addition, atherosclerotic lesions make coronary arteries more susceptible to

the effects of mast cell- and basophil-derived mediators,<sup>41</sup> and individuals with an underlying vascular illness less tolerant to hypoxia and hypotension during anaphylaxis.

In older people from the registry, cardiovascular diseases, thyroid diseases and cancer were more common than in younger adults.<sup>37</sup>

#### **b- Polypharmacy and medications used in older people**

In the European Anaphylaxis Registry, medications associated with an increased risk of severe anaphylaxis risk cofactors - such as ACE-inhibitors (angiotensin converting enzyme inhibitor), AT-2-antagonists (Angiotensin II receptor type 2),  $\beta$ -blockers, acetylcholine, and proton pump inhibitors - were significantly more frequently prescribed in older people (57%) than in younger adults (18%).<sup>39</sup>

Independent of the age of the patient,  $\beta$ -blockers and ACE inhibitors administered close to allergen immunotherapy increased the risk of developing severe anaphylaxis, while aspirin and AT-2 did not.<sup>39</sup> However, a systematic review with low quality evidence showed that  $\beta$ -blockers and ACE inhibitors increased the severity of anaphylaxis, due to differences in confounders, in particular cardiovascular diseases<sup>42</sup>.

It is important to highlight the significant number of older patients who are being treated with anxiolytics, antidepressants, hypnotics and other drugs that can act on the central nervous system and alter the individual person's recognition and perception of the symptoms and signs of anaphylaxis.

### **4- Management of anaphylaxis in older people**

#### **a. The ABCDE approach**

The Airway, Breathing, Circulation, Disability, Exposure (ABCDE) algorithm is applicable in all clinical emergencies for immediate assessment and treatment<sup>43</sup> (Figure 2). If anaphylaxis is suspected, every patient should receive rapid evaluation of vital functions via ABCDE, and problems should be addressed in a targeted manner.

The aims of the ABCDE approach are<sup>43</sup>:

- to provide life-saving treatment
- to break down complex clinical situations into more manageable parts
- to serve as an assessment and treatment algorithm



- to establish common situational awareness among all treatment providers
- to buy time to establish a final diagnosis and treatment.

### **b. Adrenaline in older people**

Guidelines from EAACI<sup>44</sup> and the World Allergy Organization<sup>45</sup> recommend prompt intramuscular injection of adrenaline as first-line therapy for anaphylaxis. Adrenaline can counteract most severe symptoms of anaphylaxis in older people<sup>22</sup>. Intramuscular administration of adrenaline, if possible using a ready-to-use preparation or auto-injector, is recommended. The initial dose is 0.3-0.5 ml of a 1:1000 dilution (1 mg/ml). The patient should then be monitored, and, if ineffective, the administration can be repeated after at least a 5-minute interval<sup>22</sup>. The subcutaneous route should not be used because the vasoconstrictor effect of adrenaline injected into the subcutaneous tissue potentially delays adrenaline absorption<sup>46</sup>. The intra-vascular route should be avoided since most cardiovascular adverse events of adrenaline appear to occur via this route<sup>47</sup>. Intravenous continuous infusion should only be given to patients not responding to intramuscular injection under careful ECG monitoring<sup>44</sup>.

During an anaphylactic reaction occurring in patients with cardiovascular disease, the benefits versus the harms of adrenaline injection should be weighed carefully. The presence of cardiovascular disease does not exclude the use of adrenaline in anaphylaxis since no other medications have life-saving effects in this medical emergency.<sup>41</sup> There are no absolute contraindications to the prescription of self-injectable adrenaline in older patients or in those with a cardiovascular disease who are at risk of anaphylaxis. Serious adverse effects, such as ventricular arrhythmias, hypertension or myocardial ischemia, have not been reported following the use of adrenaline autoinjectors.<sup>48</sup> However, older patients with anaphylaxis seem to be more likely to experience a cardiac adverse event after adrenaline injection, with those older than 80 years having the highest risk.<sup>49</sup>

### **c. Other treatments**

Regular intake of multiple medications is frequent in older patients (polypharmacy). Co-medication may modify the evolution of anaphylaxis, and also its management. The therapeutic effect of adrenaline may be blunted by  $\beta$ -blockers. In this situation, if epinephrine is not effective, glucagon can be administered intravenously, as it has a mechanism of action independent of the  $\beta$ -receptors.<sup>50,51</sup> Older patients may be using sedating or psychotropic drugs, and these could affect the recognition and perception of anaphylactic symptoms.<sup>52</sup>

### **d. Equipment needed to perform vaccination safely in older people**

- Vaccination should always be performed in a healthcare setting, which may be a mobile unit
- All necessary aids and rescue drugs must be available in the vaccination setting
- All medical personnel assigned should receive training and be able to immediately recognise and manage an emergency situation, including anaphylaxis.

## **5- Practical prevention and management of an anaphylactic reaction**

As proposed in three ARIA-EAACI Position Papers on anaphylaxis to COVID-19 vaccines, recommendations have been adapted for older patients.<sup>21,28,29</sup>

- Patients with a history of allergic diseases should not be excluded from the vaccines as the exclusion of all these patients from vaccination may have a significant impact on reaching the goal of herd immunity. However, without an allergist advice, a previously known allergy to the substances contained in the vaccines presents a contraindication, as well as a reaction to the first dose of the COVID-19 vaccine, which presents a contraindication for administering the second dose. A previous severe anaphylactic reaction to other vaccines or drugs does not represent a contraindication. However, consultation with an allergist may be helpful to assess the individual situation.
- Healthcare practitioners vaccinating against COVID-19 are required to be sufficiently prepared to recognise and treat anaphylaxis properly, particularly since older patients tend to have more severe anaphylactic symptoms. If a severe reaction occurs, hospitalisation may be considered more readily than for younger adults after first-aid action.
- After vaccine administration, a mandatory observation period of at least 15 minutes is necessary for all individuals. This should include the possibility to administer adrenaline intra-muscularly (IM) in a sufficient dose. The observation period should be extended to 30 minutes for patients deemed at putative risk for anaphylactic reaction.
- The person injecting the vaccine should be capable of managing an anaphylaxis reaction at first instance and should have all the relevant medication for management readily available.
- In the case of COVID-19 vaccines, there will be new procedures outside of the medical setting. Thus, it is imperative that the relevant emergency medication (adrenaline and saline) is readily available at the setting - particularly in nursing homes or vaccine caravans - and that training of the personnel has been accomplished.
- The EAACI recently published the practical management of anaphylaxis (Figure 3)<sup>29</sup>

Accepted Article

**Table 1: Symptoms and anaphylaxis grades** (from Ring and Messmer<sup>32,36</sup>)

Grades	Skin	Abdomen	Airways	Cardiovascular system
I	Itch			
II	Flush Urticaria Angioedema	Nausea Cramps	Rhinorrhea Hoarseness Dyspnea	Tachycardia (>120/min) Hypotension (< 90 mm Hg syst) Arrhythmia
III		Vomiting Defecation	Laryngeal oedema Bronchospasm Cyanosis	Shock
IV			Respiratory arrest	Cardiac arrest

**Figure 1: Hospitalisations and intensive care units in older people** (from <sup>30</sup>)

Grades of anaphylaxis according to Ring and Messner

Old age people: N=1,123, adults: N=5,768

\*\*\*: p<0.001

In this study, hospitalization and ICU were differentiated between adults and old age people

**Figure 2: The ABCDE approach in emergencies** (from <sup>43</sup>)

**Figure 3: Diagnosis and management of severe allergic reactions after COVID-19 vaccination in the vaccination center** (from<sup>29</sup>)

## Abbreviations

ACE-inhibitors (angiotensin converting enzyme inhibitor)

Airway, Breathing, Circulation, Disability, Exposure (ABCDE)

ARIA: Allergic Rhinitis and its Impact on Asthma

AT-2-antagonists (Angiotensin II receptor type 2)

EAACI: European Academy of Allergy and Clinical Immunology

EuGMS: European Geriatric Medicine Society

ICU: intensive care unit

IM: intramuscular

IV: Intravenous

### Conflict of interest :

IA reports is Associate Editor Allergy and CTA.

JB reports personal fees from Chiesi, Cipla, Hikma, Menarini, Mundipharma, Mylan, Novartis, Sanofi-Aventis, Takeda, Teva, Uriach, other from KYomed-Innov, personal fees from Purina,

VC reports personal fees from ALK, Allergy Therapeutics, LETI, Thermofisher, Merck, Astrazeneca, GSK,

AC reports personal fees from BMS, MSD,

ME reports personal fees from DBV Technologies, Mylan,

MFR reports grants from ISCII (Spanish Government), Aimmune, Diater, personal fees from Aimmune, DBV, Novartis, SPRIM, ALK, Allergy Therapeutics, Diater, GSK, Thermofisher

BG reports grants from Astrazeneca, Novartis, MSD, Deva, Abdi Ibrahim, GSK

TH reports personal fees from GSK, Mundipharma, OrionPharma, Sanofi,

LK reports grants and personal fees from Allergopharma, LETI Pharma, MEDA/Mylan, Sanofi, personal fees from HAL Allergie, Allergy Therapeut., Cassella med, grants from ALK Abelló, Stallergenes, Quintiles ASIT biotech, Lofarma, AstraZeneca, GSK, Inmunotk, and Membership: AeDA, DGHNO, Deutsche Akademie fürAllergologie und klinischeImmunologie, HNO-BV, GPA, EAACI.

PK reports personal fees from Adamed, AstraZeneca, Berlin Chemie, Boehringer Ingelheim, Hal Allergy, Lekam, Mylan, GSK, Novartis, Polpharma, Sanofi, from Teva

VK reports non-financial support from AstraZeneca, DIMUNA, BerlinChemieMenarini Baltic

RL reports grants from Astra Zeneca, Chiesi, GSK, other from Astra Zeneca, Novartis, GSK, Sanofi,

JM reports personal fees and other from SANOFI-GENZYME & REGENERON, NOVARTIS, ALLAKOS, grants and personal fees from MYLAN Pharma, URIACH Group, personal fees from Mitsubishi-Tanabe, Menarini, UCB, AstraZeneca, GSK, MSD,

MO reports grants from Astra Zeneca, Chiesi, GSK, DBV Technologies, Aimmune, Novartis, Pfizer, Regeneron, Sanofi, BoehringerIngelheim; and volunteer President of the European Federation of Allergy and Airways Diseases Patients' Associations EFA who receives unrestricted grants from pharmaceutical companies. Second Vice President of the Swedish Asthma and Allergy Association, who receives no income from companies. Takes part in Novartis Asthma Patient Advisory Committee, GSK Global Respiratory Patient Advisory Group and have participated/presented in AstraZeneca events. Whenever there was a honorarium, this went to EFA.

OP reports research grants from Inmunotek S.L., Novartis and MINECO. fees for giving scientific lectures or participation in Advisory Boards from Allergy Therapeutics, Amgen, AstraZeneca, Diater, GlaxoSmithKline, S.A, Inmunotek S.L, Novartis, Sanofi-Genzyme and Stallergenes.

NP reports personal fees from Novartis, Nutricia, HAL, MENARINI/FAES FARMA, SANOFI, MYLAN/MEDA, BIOMAY, AstraZeneca, GSK, MSD, ASIT BIOTECH, Boehringer Ingelheim, grants from Gerolyatos International SA, Capricare,

OP reports grants and personal fees from ALK-Abelló, Allergopharma, Stallergenes Greer, HAL Allergy Holding B.V./HAL Allergie GmbH, BencardAllergie GmbH/Allergy Therapeutics, Lofarma, ASIT Biotech Tools S.A., rom Laboratorios LETI/LETI Pharma, Anergis S.A., Glaxo Smith Kline, personal fees from Astellas Pharma Global, MEDA Pharma/MYLAN, EUFOREA, ROXALL Medizin, Novartis, Sanofi-Aventis and Sanofi-Genzyme, Med Update Europe GmbH, streamdup! GmbH, John Wiley and Sons, AS, Paul-Martini-Stiftung (PMS), Mobile Chamber Experts (a GA2LEN Partner), Indoor Biotechnologies grants from Pohl-Boskamp, Inmunotek S.L., Biomay, Circassia,

DP reports grants and personal fees from GlaxoSmithKline, personal fees and non-financial support from Boehringer Ingelheim, personal fees from Belupo, AbbVie, MSD, Chiesi, Menarini, Pliva, Revenio, non-financial support from Philips,

YR reports grants from BIOPHYTIS, NOVARTIS

BS reports personal fees from Allergopharma, Viatrix, TEVA, ADAMED, patient ombudsman, Polish Allergology Society grants from AstraZeneca, National Health Programm, grant and personal fees from Polpharma, AstraZeneca,

AS reports grants and personal fees from Medical Research Council, Thermofisher, Buhlmann, Infomed, Nutricia and Nestle, Allergy Therapeutics, Novartis and Stallergenes, grants from Food Allergy Research and Education, Asthma UK, NIAID / Immune Tolerance Network, non-financial support from National Institute for Health Research, Thermofisher and Buhlmann,

Dr. Serpa reports personal fees from Takeda, personal fees and other from Novartis, personal fees from Sanofi, personal fees from GSK, other from Astra Zeneca

JS reports grants and personal fees from SANOFI, personal fees from GSK, NOVARTIS, ASTRA ZENECA, MUNDIPHARMA, FAES FARMA

AS reports grants from HDRUK,

MS reports grants from Swiss National Science Foundation (SNF), GlaxoSmithKline (GSK),

RS reports grants from São Paulo Research Foundation, MSD, grants and personal fees from Novartis, grants, personal fees and non-financial support from AstraZeneca, grants, personal fees and non-financial support from Chiesi, personal fees and non-financial support from Boehringer Ingelheim

GS reports grants and personal fees from ALK Abello, personal fees from Novartis, Bencard, Stallergens, HAL, Allergopharma, Mylan

AMTB reports grants and personal fees from Teva, AstraZeneca, GSK (GlaxoSmithKline), Sanofi, Mundipharma, personal fees from Bial, grants from Leti, Novartis,

STS reports personal fees from AstraZeneca, ERT, Novartis, Sanofi Pharma, Roche Products, grants from GSK,

MT reports grants from European Commission, SEAIC, ISCIII, personal fees from Diater laboratory, Leti laboratory, Aimmune Therapeutics,

IT reports personal fees from Honoraria for educational activities, speaking engagements, advisory boards from Boehringer Ingelheim, Astra Zeneca, GSK, Novartis and grants from GSK Hellas and Elpen.

CSU reports personal fees from Astra Zeneca, personal fees from Chiesi, grants and personal fees from Novartis, Boehringer-Ingelheim, personal fees from ALK-Abello, TEVA, Orion Pharma, grants Sanofi Genzyme, personal fees and non-financial support from GSK,

IV reports personal fees from Novartis, Sanofi, personal fees and non-financial support from Thermo Fisher, non-financial support from Beckman Coulter,

DW reports other from Kaleo, Mylan, and on the AAAAI/ACAAI Joint Task Force on Practice Parameters updating the Anaphylaxis practice parameter.

SW reports other from Pfizer, Kaleo, Bausch Lomb

MW reports other from Regeneron Pharmaceuticals, DBV Technologies S.A, Stallergenes GmbH, HAL Allergie GmbH, BencardAllergie GmbH, Allergopharma GmbH & Co. KG, ALK-AbellóArzneimittel GmbH, Mylan Germany GmbH, Leo Pharma GmbH, Sanofi-Aventis Deutschland GmbH, Aimmune Therapeutics UK Limited, Actelion Pharmaceuticals Deutschland GmbH, Novartis AG, Biotest AG, AbbVie Deutschland GmbH & Co. KG, Lilly Deutschland GmbH,

TZ reports and Organizational affiliations: Committee member: WHO-Initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA), Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI), Board Chairman: European Centre for Allergy Research Foundation (ECARF)

President: Global Allergy and Asthma European Network (GA<sup>2</sup>LEN), Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO).

## References

1. Esteve A, Permanyer I, Boertien D, Vaupel JW. National age and coresidence patterns shape COVID-19 vulnerability. *Proc Natl Acad Sci U S A*. 2020;117(28):16118-16120.
2. Giangreco G. Case fatality rate analysis of Italian COVID-19 outbreak. *J Med Virol*. 2020;92(7):919-923.
3. Mantovani A, Dalbeni A, Beatrice G. Coronavirus disease 2019 (COVID-19): we don't leave women alone. *Int J Public Health*. 2020;65(3):235-236.

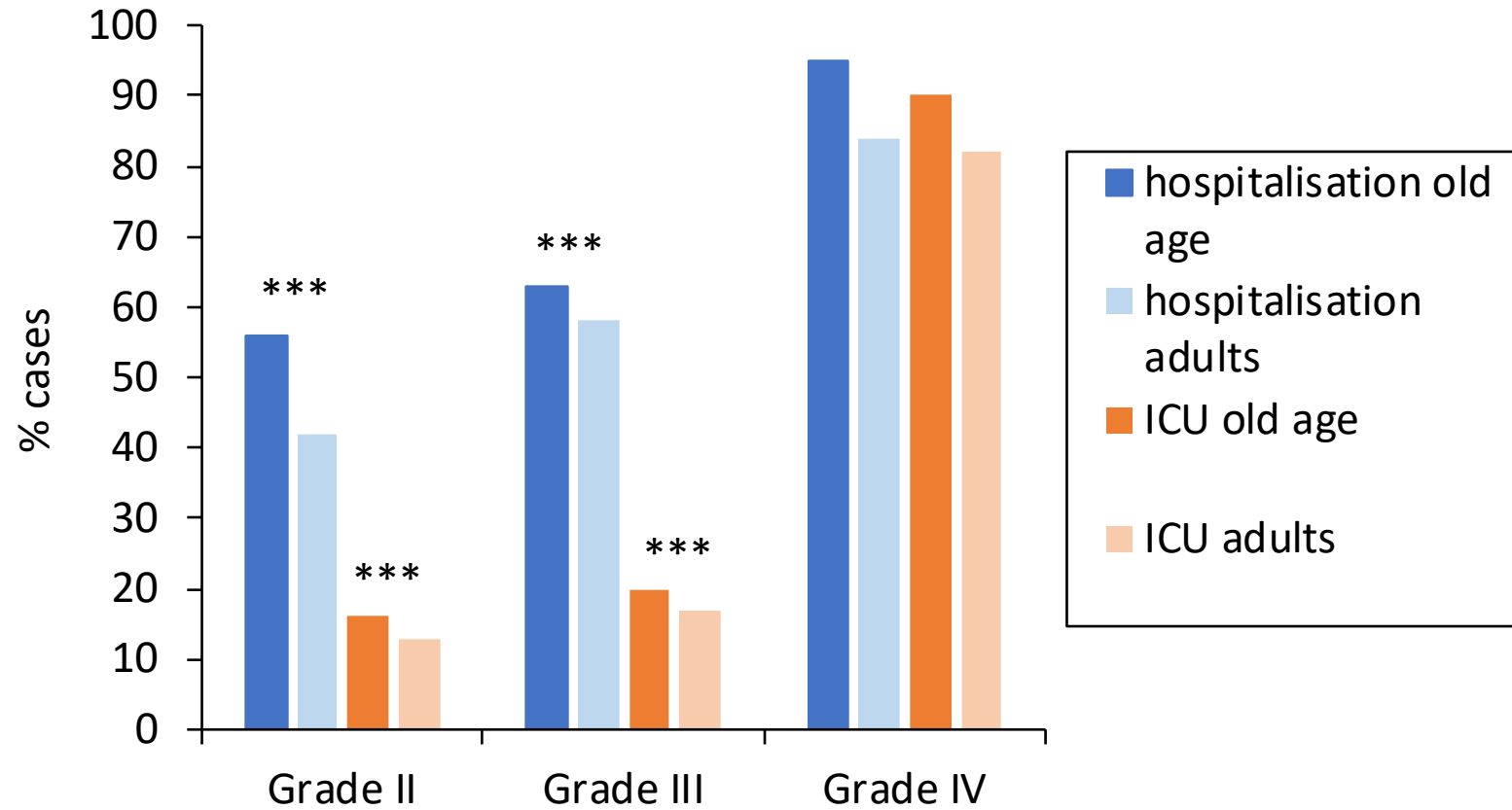
4. Iaccarino G, Grassi G, Borghi C, et al. Age and Multimorbidity Predict Death Among COVID-19 Patients: Results of the SARS-RAS Study of the Italian Society of Hypertension. *Hypertension*. 2020;76(2):366-372.
5. Finucane FM, Davenport C. Coronavirus and Obesity: Could Insulin Resistance Mediate the Severity of Covid-19 Infection? *Front Public Health*. 2020;8:184.
6. Klein SL, Dhakal S, Ursin RL, Deshpande S, Sandberg K, Mauvais-Jarvis F. Biological sex impacts COVID-19 outcomes. *PLoS Pathog*. 2020;16(6):e1008570.
7. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. *Biol Sex Differ*. 2020;11(1):29.
8. Barek MA, Aziz MA, Islam MS. Impact of age, sex, comorbidities and clinical symptoms on the severity of COVID-19 cases: A meta-analysis with 55 studies and 10014 cases. *Heliyon*. 2020;6(12):e05684.
9. Scortichini M, Schneider Dos Santos R, De' Donato F, et al. Excess mortality during the COVID-19 outbreak in Italy: a two-stage interrupted time-series analysis. *Int J Epidemiol*. 2020.
10. Pranata R, Henrina J, Lim MA, et al. Clinical frailty scale and mortality in COVID-19: A systematic review and dose-response meta-analysis. *Arch Gerontol Geriatr*. 2020;93:104324.
11. Hewitt J, Carter B, Vilches-Moraga A, et al. The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. *Lancet Public Health*. 2020;5(8):e444-e451.
12. McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a Long-Term Care Facility in King County, Washington. *N Engl J Med*. 2020.
13. Blain H, Rolland Y, Tuaille E, et al. Efficacy of a Test-Retest Strategy in Residents and Health Care Personnel of a Nursing Home Facing a COVID-19 Outbreak. *J Am Med Dir Assoc*. 2020;21(7):933-936.
14. Telford CT, Onwubiko U, Holland D, et al. Mass Screening for SARS-CoV-2 Infection among Residents and Staff in Twenty-eight Long-term Care Facilities in Fulton County, Georgia. *medRxiv*. 2020.
15. He M, Li Y, Fang F. Is There a Link between Nursing Home Reported Quality and COVID-19 Cases? Evidence from California Skilled Nursing Facilities. *J Am Med Dir Assoc*. 2020;21(7):905-908.
16. Grabowski DC, Mor V. Nursing Home Care in Crisis in the Wake of COVID-19. *JAMA*. 2020.
17. Gordon AL, Goodman C, Achterberg W, et al. Commentary: COVID in Care Homes-Challenges and Dilemmas in Healthcare Delivery. *Age Ageing*. 2020.
18. Blain H, Rolland Y, Schols J, et al. August 2020 Interim EuGMS guidance to prepare European Long-Term Care Facilities for COVID-19. *Eur Geriatr Med*. 2020;11(6):899-913.

19. Banerji A, Wickner PG, Saff R, et al. mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Approach. *J Allergy Clin Immunol Pract*. 2020.
20. Garvey LH, Nasser S. Anaphylaxis to the first COVID-19 vaccine: is polyethylene glycol (PEG) the culprit? *Br J Anaesth*. 2020.
21. Klimek L, Jutel M, Akdis CA, et al. ARIA-EAACI statement on severe allergic reactions to COVID-19 vaccines - an EAACI-ARIA position paper. *Allergy*. 2020.
22. Ventura MT, Boni E, Cecere R, et al. Importance of hypersensitivity in adverse reactions to drugs in the elderly. *Clin Mol Allergy*. 2018;16:7.
23. Rugeberg JU, Gold MS, Bayas JM, et al. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*. 2007;25(31):5675-5684.
24. Su JR, Moro PL, Ng CS, Lewis PW, Said MA, Cano MV. Anaphylaxis after vaccination reported to the Vaccine Adverse Event Reporting System, 1990-2016. *J Allergy Clin Immunol*. 2019;143(4):1465-1473.
25. Shimabukuro T. COVID-19 vaccine safety update. Advisory Committee on Immunization Practices (ACIP) January 27, 2021. *National Center for Immunization and respiratory diseases CDC* <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf>. 2021.
26. Cabanillas B, Akdis C, Novak N. Allergic reactions to the first COVID-19 vaccine: a potential role of Polyethylene glycol? *Allergy*. 2020.
27. Shimabukuro T, Nair N. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine. *JAMA*. 2021.
28. Klimek L, Cabanillas B, Jutel M, Bousquet J, Akdis C. Potential allergenic components of the mRNA-1273 vaccine for COVID-19: possible roles for polyethylene glycol and IgG-mediated complement activation. *Allergy*. 2021:in press.
29. Sokolowska M, Eiwegger T, Ollert M, et al. EAACI statement on the diagnosis, management and prevention of severe allergic reactions to COVID-19 vaccines. *Allergy*. 2021.
30. Aurich S, Dolle-Bierke S, Francuzik W, et al. Anaphylaxis in Elderly Patients-Data From the European Anaphylaxis Registry. *Front Immunol*. 2019;10:750.
31. Campbell RL, Hagan JB, Li JT, et al. Anaphylaxis in emergency department patients 50 or 65 years or older. *Ann Allergy Asthma Immunol*. 2011;106(5):401-406.
32. Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet*. 1977;1(8009):466-469.
33. Jerschow E, Lin RY, Scaperotti MM, McGinn AP. Fatal anaphylaxis in the United States, 1999-2010: temporal patterns and demographic associations. *J Allergy Clin Immunol*. 2014;134(6):1318-1328 e1317.



34. Niggemann B, Beyer K. Time for a new grading system for allergic reactions? *Allergy*. 2016;71(2):135-136.
35. Muraro A, Fernandez-Rivas M, Beyer K, et al. The urgent need for a harmonized severity scoring system for acute allergic reactions. *Allergy*. 2018;73(9):1792-1800.
36. Ring J, Beyer K, Biedermann T, et al. Guideline for acute therapy and management of anaphylaxis: S2 Guideline of the German Society for Allergology and Clinical Immunology (DGAKI), the Association of German Allergologists (AeDA), the Society of Pediatric Allergy and Environmental Medicine (GPA), the German Academy of Allergology and Environmental Medicine (DAAU), the German Professional Association of Pediatricians (BVKJ), the Austrian Society for Allergology and Immunology (OGAI), the Swiss Society for Allergy and Immunology (SGAI), the German Society of Anaesthesiology and Intensive Care Medicine (DGAI), the German Society of Pharmacology (DGP), the German Society for Psychosomatic Medicine (DGPM), the German Working Group of Anaphylaxis Training and Education (AGATE) and the patient organization German Allergy and Asthma Association (DAAB). *Allergo J Int*. 2014;23(3):96-112.
37. Dolle-Bierke S, Siebenhaar F, Burmeister T, Worm M. Detection of KIT D816V mutation in patients with severe anaphylaxis and normal basal tryptase—first data from the Anaphylaxis Registry (NORA). *J Allergy Clin Immunol*. 2019;144(5):1448-1450 e1441.
38. Brockow K, Jofer C, Behrendt H, Ring J. Anaphylaxis in patients with mastocytosis: a study on history, clinical features and risk factors in 120 patients. *Allergy*. 2008;63(2):226-232.
39. Worm M, Francuzik W, Renaudin JM, et al. Factors increasing the risk for a severe reaction in anaphylaxis: An analysis of data from The European Anaphylaxis Registry. *Allergy*. 2018;73(6):1322-1330.
40. Bilo MB, Martini M, Tontini C, Corsi A, Antonicelli L. Anaphylaxis. *Eur Ann Allergy Clin Immunol*. 2020.
41. Lieberman P, Simons FE. Anaphylaxis and cardiovascular disease: therapeutic dilemmas. *Clin Exp Allergy*. 2015;45(8):1288-1295.
42. Tejedor-Alonso MA, Farias-Aquino E, Perez-Fernandez E, Grifol-Clar E, Moro-Moro M, Rosado-Ingelmo A. Relationship Between Anaphylaxis and Use of Beta-Blockers and Angiotensin-Converting Enzyme Inhibitors: A Systematic Review and Meta-Analysis of Observational Studies. *J Allergy Clin Immunol Pract*. 2019;7(3):879-897 e875.
43. Thim T, Krarup NH, Grove EL, Rohde CV, Lofgren B. Initial assessment and treatment with the Airway, Breathing, Circulation, Disability, Exposure (ABCDE) approach. *Int J Gen Med*. 2012;5:117-121.
44. Muraro A, Roberts G, Worm M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy*. 2014;69(8):1026-1045.

- Accepted Article
45. Simons FE, Ebisawa M, Sanchez-Borges M, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organ J.* 2015;8(1):32.
  46. Simons KJ, Simons FE. Epinephrine and its use in anaphylaxis: current issues. *Curr Opin Allergy Clin Immunol.* 2010;10(4):354-361.
  47. Campbell RL, Bellolio MF, Knutson BD, et al. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. *J Allergy Clin Immunol Pract.* 2015;3(1):76-80.
  48. Bilo MB, Cichocka-Jarosz E, Pumphrey R, et al. Self-medication of anaphylactic reactions due to Hymenoptera stings-an EAACI Task Force Consensus Statement. *Allergy.* 2016;71(7):931-943.
  49. O'Brien ME, Koehl JL, Raja AS, Erickson TB, Hayes BD. Age-related cardiovascular outcomes in older adults receiving epinephrine for anaphylaxis in the emergency department. *J Allergy Clin Immunol Pract.* 2019;7(8):2888-2890.
  50. Rukma P. Glucagon for Refractory Anaphylaxis. *Am J Ther.* 2019;26(6):e755-e756.
  51. McLure M, Eastwood K, Parr M, Bray J. A Rapid review of advanced life support guidelines for cardiac arrest associated with anaphylaxis. *Resuscitation.* 2020.
  52. Lieberman PL. Recognition and first-line treatment of anaphylaxis. *Am J Med.* 2014;127(1 Suppl):S6-11.



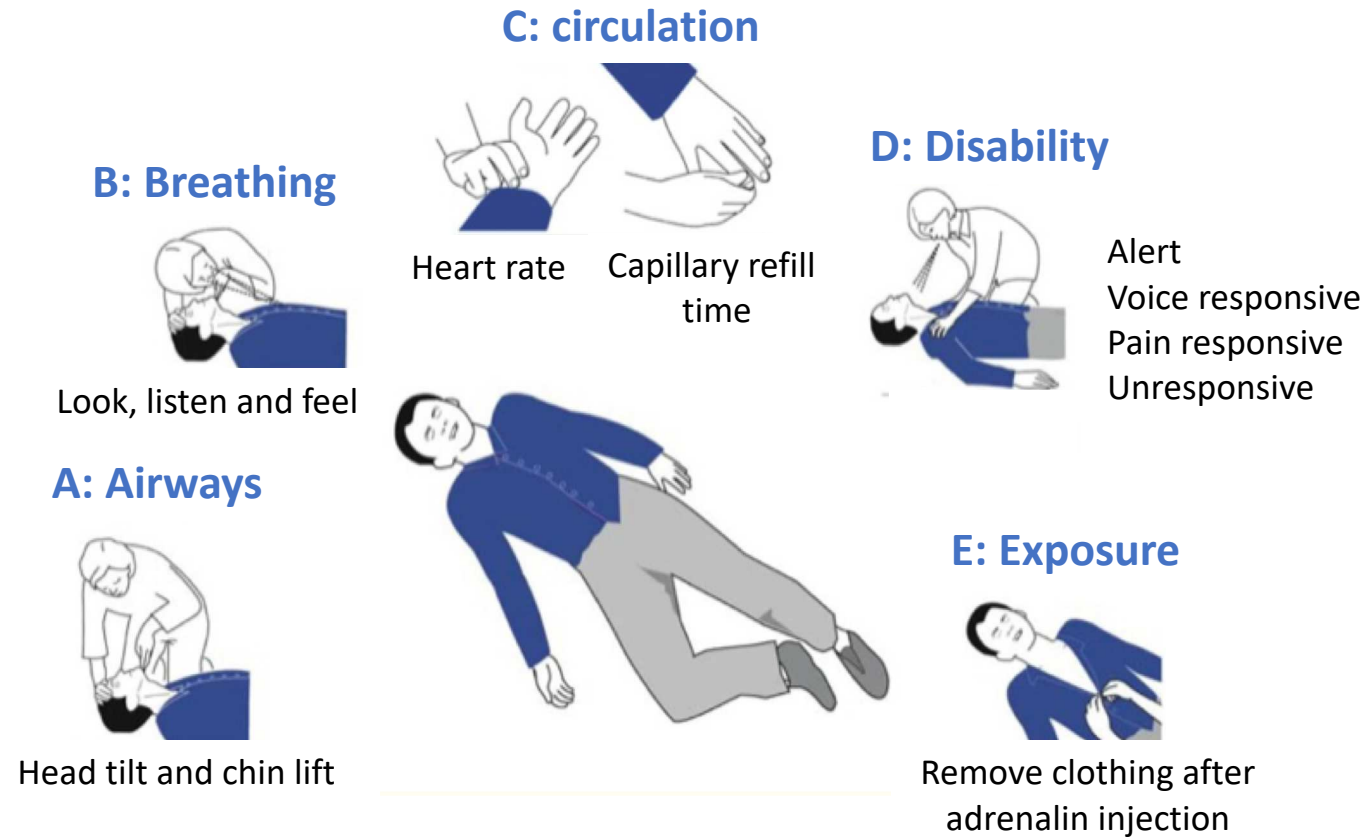


Fig. 1. Diagnosis and management of severe allergic reactions after COVID-19 vaccination in the vaccination center

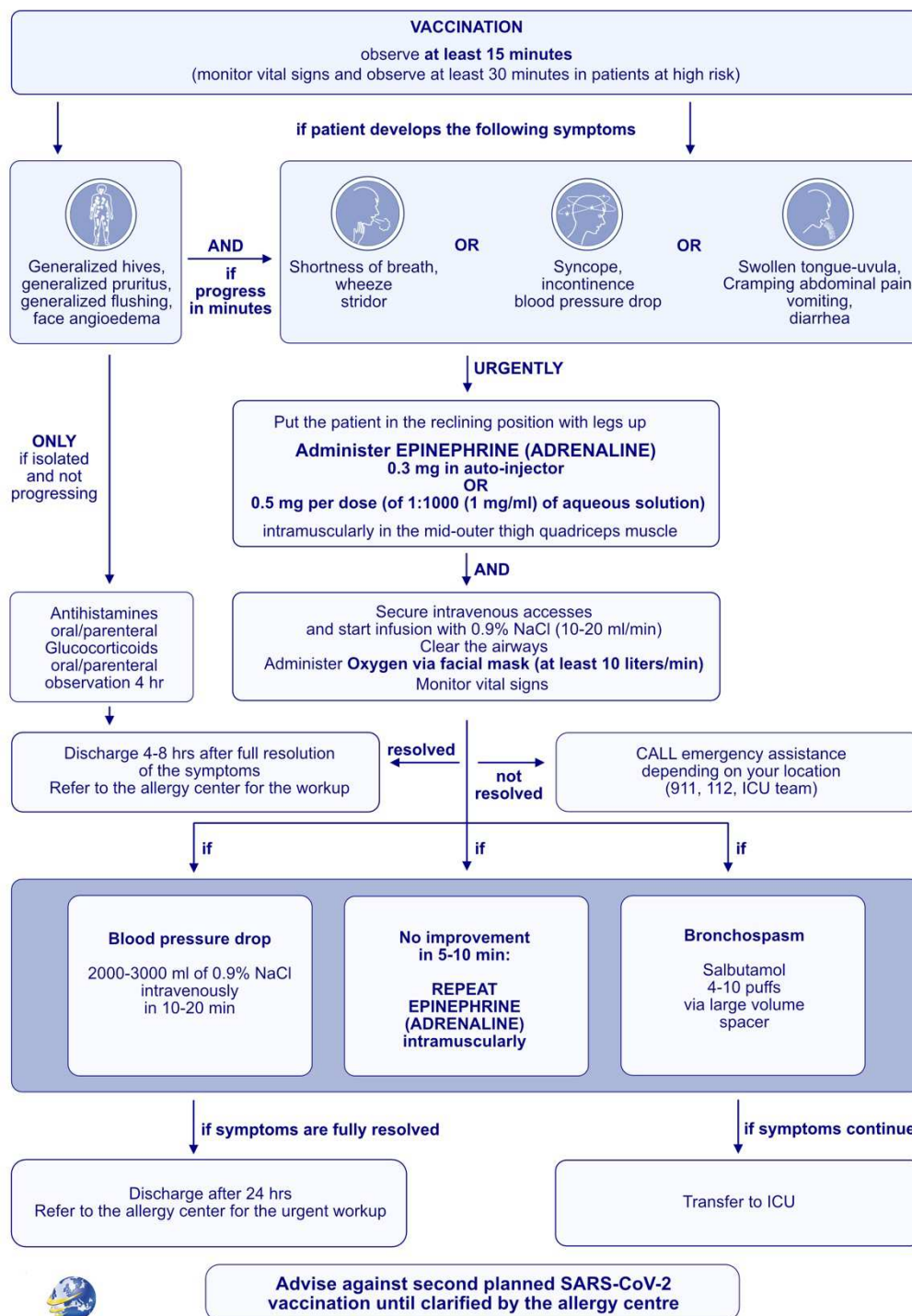


Figure 1\_Sokolowska et al.