

# Physician Perspectives on Vaccination in Patients With Autoimmune Inflammatory Rheumatic Diseases: An International Survey

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**ABSTRACT.** *Objective.* To evaluate the perspective of physicians who care for patients with autoimmune inflammatory rheumatic disease (AIIRD) toward vaccination.

*Methods.* Physicians who care for patients with AIIRD were invited to participate in an online survey regarding their vaccination perspectives in adult patients with AIIRD.

*Results.* Survey responses of 370 physicians from Asia (41.1%), North America (41.6%), Europe (13.8%), and other countries (3.5%) were analyzed. Participants stated that rheumatologists (58.2%) should be primarily responsible for vaccination coverage, followed by general internists (19.3%) and family medicine practitioners (12.8%). Additionally, 96.7% of participants considered vaccination very important ( $\geq 4/5$  rating) for patients with AIIRD. Despite these sentiments, only one-third (37%) reported vaccinating the majority ( $\geq 60\%$ ) of their patients.

*Conclusion.* Physicians who care for patients with AIIRD agree that vaccines are effective and safe in patients with AIIRD. Unfortunately, they often do not ensure that their patients are adequately vaccinated. Further studies are needed to investigate how to improve vaccination coverage for this high-risk patient population.

*Key Indexing Terms:* autoimmune disease, guideline, immunosuppressant, survey, vaccination

Vaccinations against preventable diseases are strongly recommended for patients with autoimmune inflammatory rheumatic disease (AIIRD) who are at increased risk of infections due to underlying immune dysfunction and treatment-induced

immunosuppression.<sup>1-6</sup> Several rheumatology societies, including the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR), have formulated vaccination guidelines for patients with AIIRD, including rheumatoid arthritis (RA).<sup>4,6-8</sup> Despite this, vaccination coverage for patients with AIIRD is low.<sup>9-11</sup>

Uncertainty regarding the impact of autoimmune disease and treatment-associated immunosuppression on vaccine safety and efficacy might contribute to hesitancy to administer vaccines. Live-attenuated vaccines, such as yellow fever, raise specific concerns, due to their theoretical potential to induce infection or disease flare in patients with AIIRD.<sup>11-13</sup> This uncertainty became even more evident in the midst of the coronavirus disease 2019 (COVID-19) pandemic. Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been associated with usual adverse events such as vaccination-induced thrombocytopenic thrombosis and myocarditis, further contributing to vaccine hesitancy among patients and healthcare providers (HCPs) alike.<sup>14-16</sup> Therefore, it is more important than ever that rheumatologists be prepared to take a leading role in managing vaccinations for patients with AIIRD and to guide patients and other healthcare providers in this time of uncertainty.<sup>17,18</sup>

To understand the obstacles to providing broad vaccination coverage of patients with AIIRD, we conducted an international survey to evaluate the perspective of the HCPs who care for patients with AIIRD regarding vaccination.

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## METHODS

**Survey.** Physicians who care for patients with AIIRD were invited to participate in an anonymous online survey approximately 15 minutes long, regarding their general vaccination practices. Participants were asked to rate their level of agreement, confidence, or familiarity using a 5-point Likert scale with the following anchors: 1 = strongly disagree or not at all, and 5 = strongly agree or very well.

**Survey distribution and data collection.** An email was sent to 8535 HCPs using email lists provided by rheumatology societies. The Japan College of Rheumatology and Korean College of Rheumatology actively disseminated the survey to their members. In addition, a link to the survey was posted in a monthly EULAR newsletter (May 2020).

The Google Forms survey platform was used for data collection. The survey was conducted between April 2020 and June 2020. This study was conducted in compliance with the Declaration of Helsinki and was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 2004-023-1115).

**Statistical analysis.** Continuous variables and categorical data were compared using *t* test or ANOVA with Bonferroni correction, and chi-square or

Fisher exact test, as appropriate. Statistical analyses were performed using SPSS version 22.0 (IBM Corp). *P* values < 0.05 were considered statistically significant.

## RESULTS

**Participants.** Survey responses from 370 physicians were included in this analysis. The majority of responses came from Asia (*n* = 152, 41.1%) and North America (*n* = 154, 41.6%), followed by Europe (*n* = 51, 13.8%). Up to 80% of the participants had graduated from medical school over 10 years prior to completion of the survey. With regard to practice setting, 65.9% worked in a university-based or university-affiliated medical center, whereas 21.4% worked primarily in an outpatient clinic and 12.7% worked in a community hospital-based practice (Table). The proportion of respondents who were rheumatologists was 88.9%, followed by general internists (3.5%), and orthopedic surgeons (2.2%).

**General perspective on vaccination.** Most participants (96.7%)

Table. Baseline characteristics of participants by region.

	Asia, n = 152	North America, n = 154	Europe, n = 51	Others, n = 13	Total, N = 370
<b>Age group, yrs</b>					
20-30	1 (0.7)	5 (3.2)	7 (13.7)	0 (0)	13 (3.5)
31-40	30 (19.7)	40 (26)	22 (43.1)	2 (15.4)	94 (25.4)
41-50	69 (45.4)	33 (21.4)	11 (21.6)	2 (15.4)	115 (31.1)
51-60	39 (25.7)	31 (20.1)	6 (11.8)	2 (15.4)	78 (21.1)
61-70	10 (6.6)	33 (21.4)	5 (9.8)	6 (46.2)	54 (14.6)
> 70	3 (2)	12 (7.8)	0 (0)	1 (7.7)	16 (4.3)
<b>Sex</b>					
Female	48 (31.6)	76 (49.4)	16 (31.4)	6 (46.2)	146 (39.5)
Male	104 (68.4)	78 (50.6)	35 (68.6)	7 (53.8)	224 (60.5)
<b>Work experience, yrs</b>					
1-5	6 (3.9)	16 (10.4)	5 (9.8)	1 (7.7)	28 (7.6)
6-10	6 (3.9)	16 (10.4)	5 (9.8)	1 (7.7)	48 (13)
11-15	21 (13.8)	17 (11)	13 (25.5)	2 (15.4)	53 (14.3)
16-20	37 (24.3)	21 (13.6)	6 (11.8)	0 (0)	64 (17.3)
21-25	30 (19.7)	16 (10.4)	4 (7.8)	0 (0)	50 (13.5)
26-30	17 (11.2)	20 (13)	2 (3.9)	1 (7.7)	40 (10.8)
> 30	29 (19.1)	42 (27.3)	8 (15.7)	8 (61.5)	87 (23.5)
<b>Medical specialty</b>					
Rheumatology	129 (84.9)	149 (96.8)	39 (76.5)	12 (92.3)	329 (88.9)
Internal medicine	6 (3.9)	0 (0)	6 (11.8)	1 (7.7)	13 (3.5)
Orthopedic surgery	7 (4.6)	0 (0)	1 (2)	0 (0)	8 (2.2)
Family medicine	3 (2)	1 (0.6)	0 (0)	0 (0)	4 (1.1)
Infectious disease	0 (0)	1 (0.6)	0 (0)	0 (0)	1 (0.3)
Others	7 (4.6)	3 (1.9)	5 (9.8)	0 (0)	15 (4.1)
<b>Practice setting<sup>a</sup></b>					
Primary care	24 (15.8)	49 (31.8)	3 (5.9)	3 (23.1)	79 (21.4)
Secondary care	25 (16.4)	12 (7.8)	9 (17.6)	1 (7.7)	47 (12.7)
Tertiary care	103 (67.8)	93 (60.4)	39 (76.5)	9 (69.2)	244 (65.9)
<b>Clinic volume<sup>b</sup>, no. of patients</b>					
< 10	11 (7.2)	101 (65.6)	25 (49)	3 (23.1)	140 (37.8)
11-20	48 (31.6)	48 (31.2)	23 (45.1)	8 (61.5)	127 (34.3)
21-30	42 (27.6)	3 (1.9)	3 (5.9)	2 (15.4)	50 (13.5)
31-40	27 (17.8)	1 (0.6)	0 (0)	0 (0)	28 (7.6)
41-50	12 (7.9)	0 (0)	0 (0)	0 (0)	12 (3.2)
> 50	12 (7.9)	1 (0.6)	0 (0)	0 (0)	13 (3.5)

<sup>a</sup>Primary care setting includes private practice; secondary care setting includes general hospital (not university-affiliated); tertiary care/academic medical center (university-based or university-affiliated). <sup>b</sup>No. of patients per half-day (3-5 h) clinic.

agreed or strongly agreed ( $\geq 4/5$  rating) that vaccination was important for patients with AIIRD (Figure 1A). Whereas 75.3% of the participants felt confident or very confident ( $\geq 4/5$  rating) managing vaccination coverage for their patients, only 37% of the participants managed vaccination for  $\geq 60\%$  of their patients (Figures 1B,C). Interestingly, vaccination coverage was not associated with patient volume or practice setting (data not shown). Participants stated that rheumatologists (58.2%) should be primarily responsible for vaccination coverage of patients with AIIRD, followed by general internists (19.3%) and family medicine practitioners (12.8%; Figure 1D).

*Familiarity with and adherence to vaccination guideline.* Participants were less familiar with the ACR 2012 and the 2011 EULAR vaccination guidelines, but they were more familiar with the vaccination recommendations included in the 2015 ACR guideline for the treatment of RA and the 2019 update of the EULAR vaccination guideline (Figure 2).

Participants indicated that they believed that vaccines are safe and effective and that they trust the vaccination guidelines. They noted that lack of time and insufficient experience with vaccination were reasons for not complying with the vaccination guidelines (Figure 3).

*Difference by regions of practice.* Responses from participants from North America ( $n = 154$ ), East Asia ( $n = 132$ ) and Europe ( $n = 51$ ) were examined. In Europe and North America, the majority of participants treated up to 20 patients per half-day (eg, 3-5 hours) outpatient clinic session, whereas  $> 60\%$  of participants from Asia reported seeing  $> 20$  patients per session (Table).

Participants from Europe noted that they were very familiar with the 2019 EULAR guidelines and felt confident managing

vaccinations (Figure 4). The majority of participants from all 3 regions reported that vaccination guidelines were important and helpful and felt confident in their understanding of vaccination guidelines. Notably, 45.1% and 43.1% of the participants from Europe and North America, respectively, responded that rheumatologists should be primarily responsible for vaccination coverage for patients with AIIRD. In contrast, 77% of participants from Asia responded that rheumatologists should be primarily responsible for vaccination coverage. Last, 74.5% of the participants from Europe, 39.7% from North America and 28.9% from Asia managed vaccination for  $\geq 60\%$  of their patients.

*Perspectives of rheumatologists on vaccination.* As the vast majority of responders were rheumatologists and the ACR and EULAR guidelines were directed toward them, we analyzed the data from the rheumatologist subgroup only. The response was similar to that of the total participants (Supplementary Figures, available with the online version of this article.)

## DISCUSSION

This international survey is the first to evaluate physicians' perspective on vaccination of patients with AIIRD. In general, physicians agreed that vaccinations for patients with AIIRD were safe, effective, and important; they also felt confident managing vaccination for their patients. However, a substantial number of participants did not actively provide adequate vaccination coverage for the majority of their patients, due, in part, to lack of time and inexperience with vaccination.

The complex effects of autoimmune disease and immunosuppressive treatment on vaccine safety and efficacy in patients with AIIRD could make HCPs uncomfortable with making

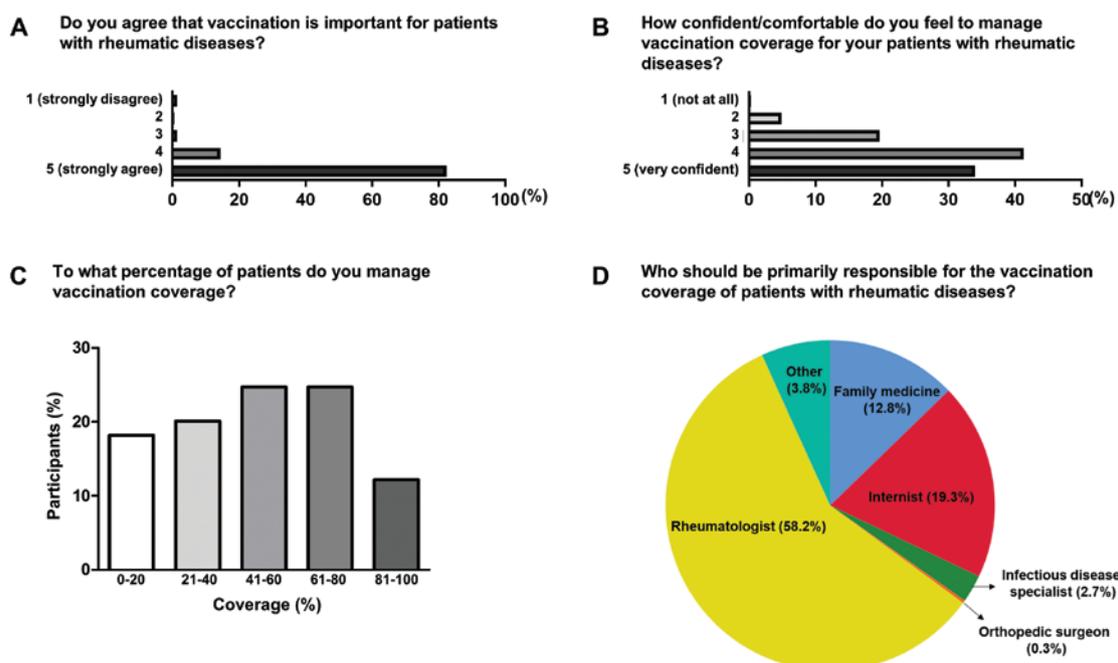


Figure 1. General perspectives on vaccination for patients with autoimmune inflammatory rheumatic disease. (A) Importance of vaccination. (B) Confidence to provide vaccination coverage were rated on 1-5 scale (1 = not at all, 5 = very important or very confident). (C) Vaccination coverage in practice. (D) Physician who should be responsible for vaccination coverage.

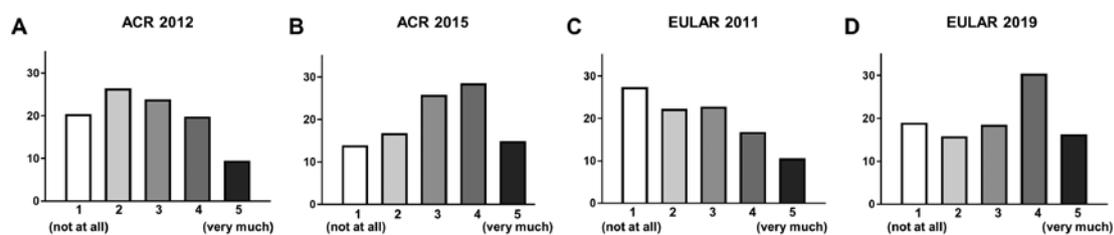


Figure 2. Familiarity with vaccination guidelines. Awareness of vaccination guidelines included in the (A) 2012 and (B) 2015 ACR guidelines for rheumatoid arthritis treatment and the (C) 2011 and (D) 2019 EULAR vaccination guidelines were rated on scale of 1 to 5 (1 = not at all, 5 = very much). Numbers are in % of participants. ACR: American College of Rheumatology, EULAR: European Alliance of Associations for Rheumatology.

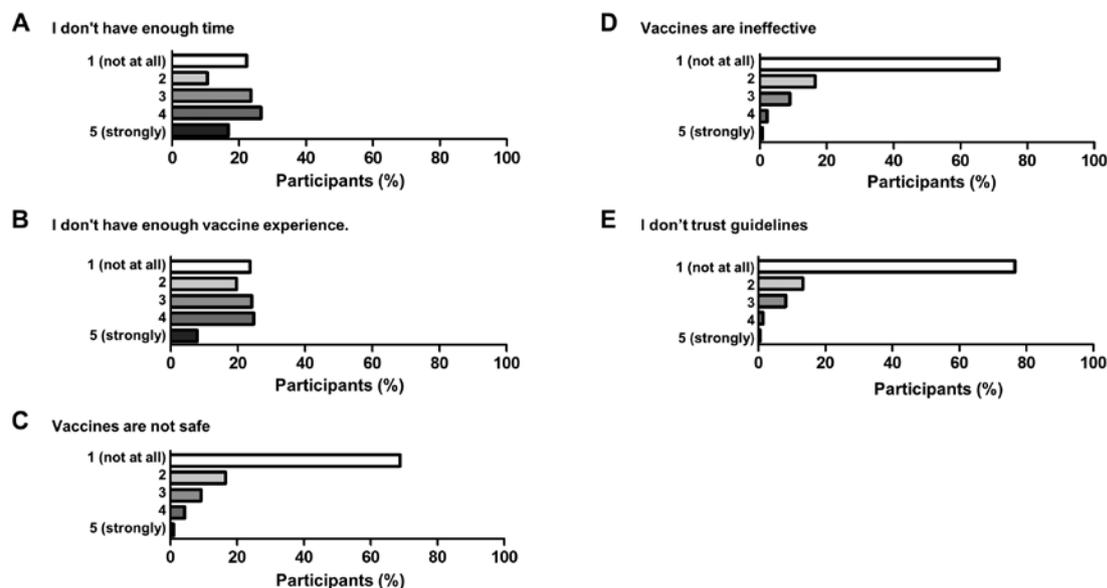


Figure 3. Reasons for nonadherence to the vaccination guidelines. Available time for vaccination, level of vaccine experience, agreement with vaccine safety and efficacy, as well as trust in guidelines were rated on scale of 1 to 5 (1 = not at all, 5 = strongly).

clinical decisions about vaccination. Management of immunosuppressants and the possibility of disease flare during or after vaccination contribute to the reluctance of HCPs to engage in these issues. Only 37% of the participants provide vaccination coverage for  $\geq 60\%$  of their patients, indicating relatively low vaccination coverage for patients with AIIRD.<sup>9-11</sup>

Only 58.2% of participants felt that rheumatologists should be primarily responsible for vaccination coverage of patients with AIIRD, although the ACR, EULAR, and other rheumatology societies recommend that rheumatologists take a lead role in vaccinating patients with AIIRD.<sup>6,7,19</sup> This suboptimal coverage can be explained by the fact that a substantial number of HCPs were not familiar with the vaccination guidelines (Figure 2). Lack of time and inexperience with vaccination may also contribute to suboptimal vaccination coverage, since rheumatologists, as specialists, may focus on treating autoimmune diseases, leaving vaccination to other providers.

Attitudes toward vaccination differed regionally. Participants in Europe were familiar with the new EULAR guidelines, felt confident in their ability to follow the guidelines, and reported high rates of vaccination coverage for their patients. In contrast,

providers from Asia were more likely to respond that rheumatologists should be responsible for vaccination coverage but were less likely to actually provide such coverage for their patients (Figure 4). This suggests that adherence to the vaccination guidelines might be hampered by the local practice setting and competing demands on the individual practitioner's time. Interestingly, the patient volume per clinic session and medical care setting were not associated with rates of vaccination coverage (data not shown).

Understanding the hurdles faced by physicians when it comes to vaccinations may help improve vaccination coverage. Initiatives designed to train HCPs about the available guidelines and their implementation may be especially effective.

The unprecedented medical and socioeconomic challenges created by the COVID-19 pandemic highlight the important role of rheumatologists in promoting vaccination coverage for patients with AIIRD, especially now that vaccine hesitancy is emerging as a global phenomenon.<sup>20</sup> HCPs need to help restore public trust in vaccinations and guide both patients and policy makers in a time of widespread disinformation.

This study has several limitations. First, the response rate was

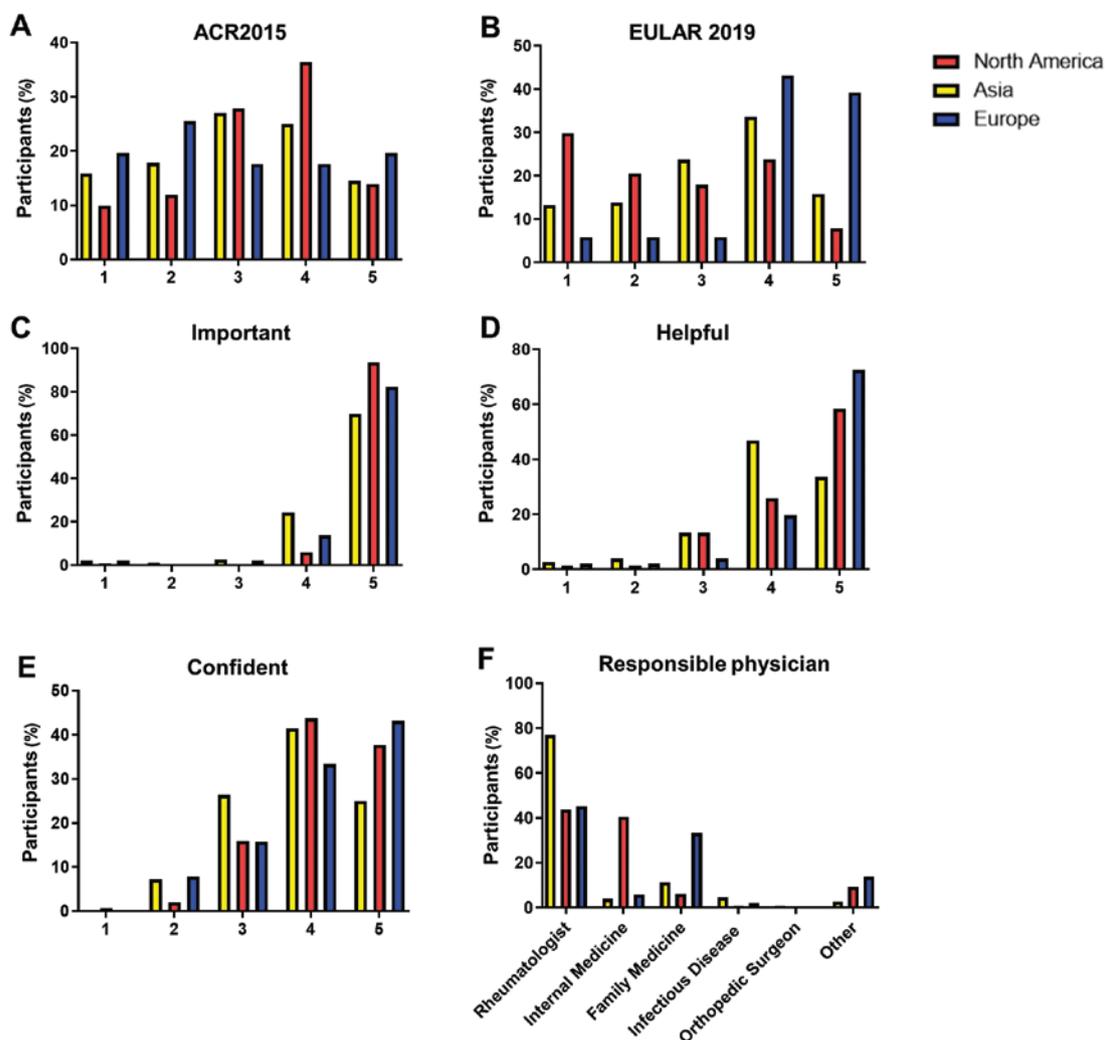


Figure 4. Perspective on vaccination by regions. Familiarity with the (A) ACR 2015 and the (B) EULAR 2019 guidelines, agreement on the (C) importance and (D) usefulness of the vaccination guidelines as well as the (E) level of confidence with vaccination coverage were rated on scale of 1 to 5 (1 = not at all, 5 = very much). (F) Physicians who should be responsible for vaccination coverage. ACR: American College of Rheumatology, EULAR: European Alliance of Associations for Rheumatology.

low (ie, 381 responses out of > 8535 official invitations). This may have created a selection bias that favored participants with a specific interest in vaccination, which may have led us to overestimate the rates of vaccination coverage by providers who care for patients with AIIRD. Second, recall bias may have led providers to overestimate their vaccination coverage rates. A prospective study would be able to better assess actual physician behaviors. Third, the total clinic volume and proportion of different rheumatic and nonrheumatic diseases were not considered in the analysis.

Finally, this survey was conducted prior to the controversies associated with the COVID-19 vaccines. Experience with these issues may have led providers to change their own perspective and practices regarding vaccination.

In conclusion, physicians who care for patients with AIIRD agree that vaccines are effective and safe, but the adequate vaccination coverage of those patients is suboptimal. Further studies

are needed to examine how to overcome region-specific obstacles to implementing adequate vaccination coverage for this high-risk patient population.

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#### DATA AVAILABILITY

Data are available from the corresponding author on reasonable request.

#### ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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